

Hrvatski institut za istraživanje mozga
Medicinskog fakulteta Sveučilišta u Zagrebu
25 godina^{1990 - 2015}

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POGLAVLJE 1

*Osnutak, izgradnja i otvorenje
Hrvatskog instituta za istraživanje
mozga*

CHAPTER 1

*Founding, construction and Grand
opening of the Croatian Institute for
Brain Research*



OSNUTAK, IZGRADNJA I SVEČANO OTVORENJE HRVATSKOG INSTITUTA ZA ISTRAŽIVANJE MOZGA

Svjesne činjenice da je razvoj neuroznanosti transnacionalan i multidisciplinarni pothvat od iznimnog značenja za unapređenje zdravlja i ekonomskog blagostanja svih naroda, vlade razvijenih zemalja Europe,

FOUNDING, CONSTRUCTION AND GRAND OPENING OF THE CROATIAN INSTITUTE FOR BRAIN RESEARCH

Keeping in mind that development of neuroscience is transnational and multidisciplinary endeavour with extraordinary influence on the advancement of health and economic wellbeing of all nations, the





Sjeverne Amerike i Japana proglasile su posljednje desetljeće 20. stoljeća „Desetljećem mozga“. Početak Desetljeća mozga (1990.) poklopio se s početkom demokratske obnove i osamostaljenja Republike Hrvatske, što je Medicinskom fakultetu omogućilo da izravno, učinkovito i u punoj mjeri iskaže svoju ulogu čelne biomedicinske ustanove i poticatelja i predvodnika svih ključnih pothvata na unapređenju biomedicinske znanosti u Hrvatskoj. I prije 1990., Medicinski fakultet je bio sjedište svih glavnih skupina istraživača u području temeljne i kliničke neuroznanosti te

governments of the Europe, North America and Japan declared the last decade of the 20th century as a “Decade of the Brain”. Beginning of the “Decade of the Brain” coincided with the beginning of the democratic changes and liberation of the Croatia. These processes enabled the University of Zagreb School of Medicine to directly, efficiently and fully demonstrate its role as a leading biomedical institution and driving force and a leader of all key ventures on the advancement of biomedical sciences in Croatia. Even before 1990 School of Medicine was the centre of all leading re-





REPUBLIKA HRVATSKA
PREDSJEDNIK

Prof. dr. sc. MATO GRANIĆ, dekan
Medicinskog fakulteta Sveučilišta
u Zagrebu,

Prof. dr. sc. IVICA KOSTOVIĆ, prodekan
za znanost i glavni koordinator Hrvatskog
instituta za istraživanje mozga Medicin-
skog fakulteta Sveučilišta u Zagrebu

Štovani profesori Graniću i Kostoviću,

Prije svega želim se zahvaliti na vašem pismu od 11. prosinca 1990, u kojem mi predlažete prihvaćanje pokroviteljstva nad utemeljenjem Hrvatskog instituta za istraživanje mozga i zgrade temeljnih medicinskih znanosti pri vašem i našem Medicinskom fakultetu Sveučilišta u Zagrebu.

Vaš prijedlog prihvaćam sa zadovoljstvom. Posebno se nadam da će utemeljenje Instituta pridonijeti razvoju temeljnih biomedicinskih znanosti u Zagrebu i Hrvatskoj, ali i ostvarenju važnog cilja koji spominjete u vašem pismu: "... povratku naših znanstveno nadarenih istraživača iz cijelog svijeta, gdje se sada nalaze na usavršavanju na vodećim sveučilištima svijeta (npr. Yale, McGill)".

Pošto sam osobno zainteresiran za brz i uspješan razvoj Instituta kojem sam od ovog trenutka pokrovitelj, to vas molim da me povremeno obavijestite o napretku u ostvarivanju tog projekta.

Uz izraze štovanja,

Dr. Franjo Tuđman

Zagreb, 12. prosinca 1990.

Slika 1 (prethodna stranica)

Pismo predsjednika Republike Hrvatske, dr. Franje Tuđmana, kojim prihvaća osobno pokroviteljstvo nad projektom izgradnje Hrvatskog instituta za istraživanje mozga.

Figure 1 (previous page)

The letter from the President of Croatia, dr. Franjo Tuđman, in which he personally accepts a sponsorship over the founding of the Croatian Institute for Brain Research.

imao kontinuiranu i vrlo razvijenu međunarodnu suradnju u tom području. To se posebice odnosi na osnivača i utemeljitelja Hrvatskog instituta za istraživanje mozga, akademika Ivicu Kostovića. Stoga je Fakultetu, na temelju poticaja i jasno obrazloženog prijedloga Ivica Kostovića, bilo lako prepoznati sljedeće ključne činjenice:

1. Da se istraživanja mozga diljem svijeta ubrzano razvijaju kao odgovor na kritične medicinske, socijalne i ekonomske probleme, jer mentalne i neurološke bolesti te bolesti ovisnosti predstavljaju golemo humanitarno i financijsko opterećenje za svaku populaciju, što je sve izraženije s produljenjem životnog vijeka i poboljšanjem općeg životnog standarda;
2. Da ulaganja u istraživanja na području

Slika 2 (dolje)

Početak gradnje instituta (ljetno 1992.) i polaganje temelja zgrade. Vidi se da zgrada nastaje kao produženo krilo stare zgrade Zavoda za patologiju.

Figure 2 (bottom)

Beginning of the construction of the Institute (summer 1992) and laying of the buildings foundation. Note that the building is constructed as a new wing of the old building of the Department of Pathology.

search groups in fields of basic and clinical neuroscience and had continuous and well established international collaboration in the field of neuroscience. This is particularly true for the founder and originator of the Croatian Institute for Brain Research – academic Ivica Kostović. Therefore, it was easy for the School of Medicine, based on the incentives and well justified proposal by Ivica Kostović, to acknowledge the following key facts:

1. Brain research throughout the world is rapidly developing as a response to the key social and economic challenges; such as mental and neurological disorders as well as various addictions. They represent enormous humanitarian and financial burden for every population; which is even more





neuroznanosti predstavljaju s jedne strane tek djelić ukupne društvene cijene mentalnih i neuroloških bolesti i poremećaja, a s druge strane jedinu nadu za uspješno rješavanje tog problema;

3. Da je, u okolnostima u kojima se nalazi Hrvatska, tijesno povezivanje temeljnih i kliničkih istraživanja s jedne strane, a čvrsta integracija znanstvenih istraživanja s nastavnim procesom s druge strane, pristup koji jedini jamči bitno unapređenje hrvatske neuroznanosti i njezino uključivanje u svjetske tokove znanja;

4. Da je u vremenu, u kojem su financijske mogućnosti objektivno ograničene, sredstva prijeko potrebno ulagati na način koji omogućuje optimalno iskorištenje uloženi sredstava;

5. Da, s obzirom na veličinu populacije Hrvatske te broj postojećih istraživača i projekata u području temeljne i kliničke neuroznanosti, okupljanje vodećih stručnjaka i materijalnih resursa u okviru jedne mod-

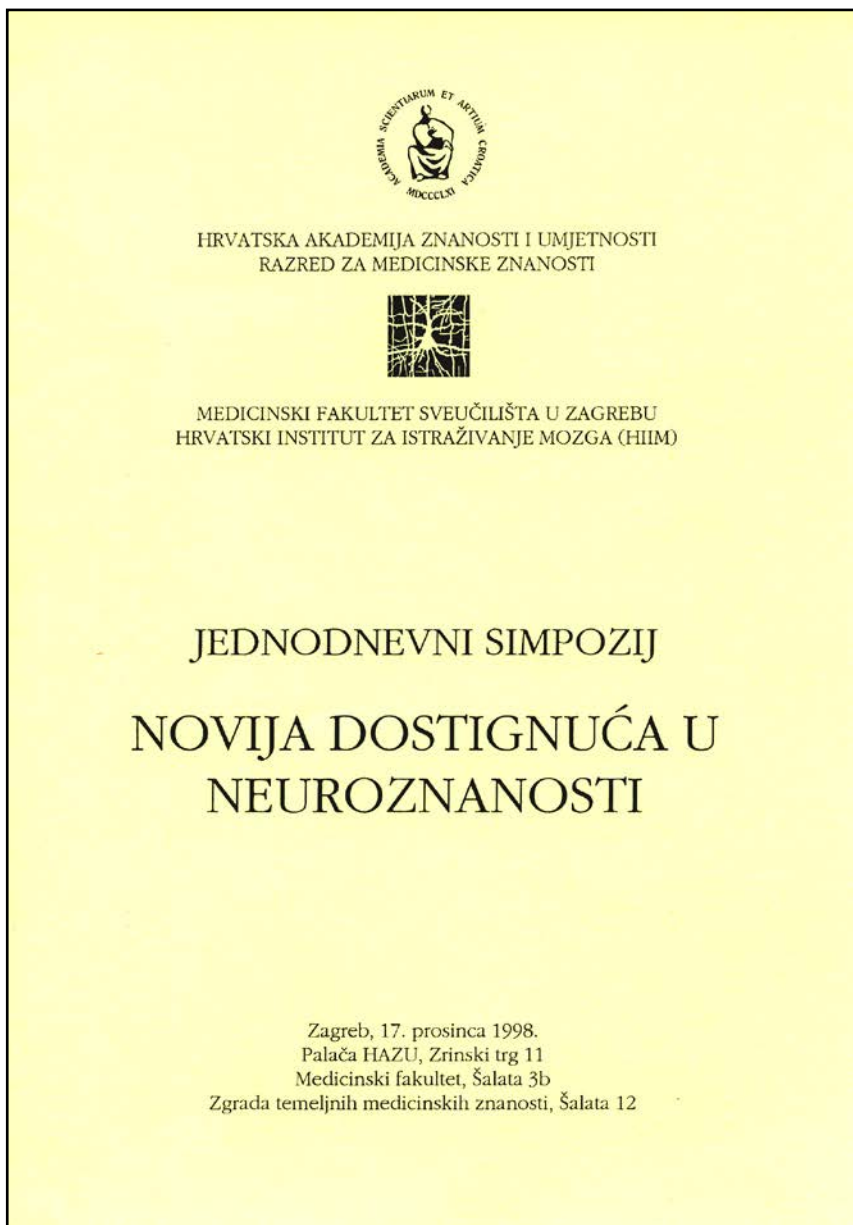
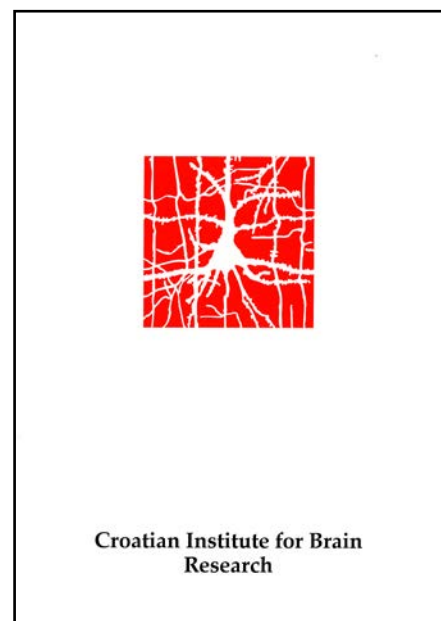
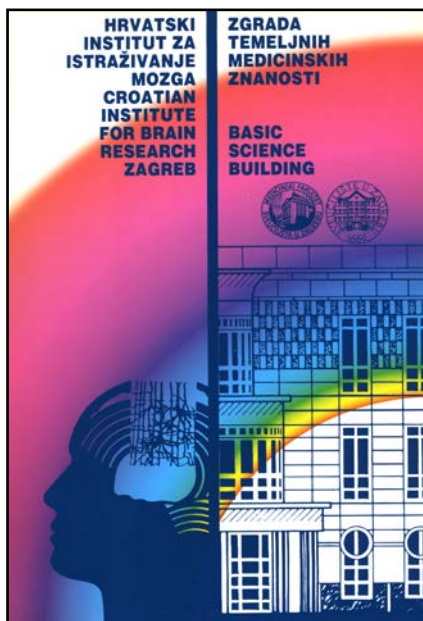
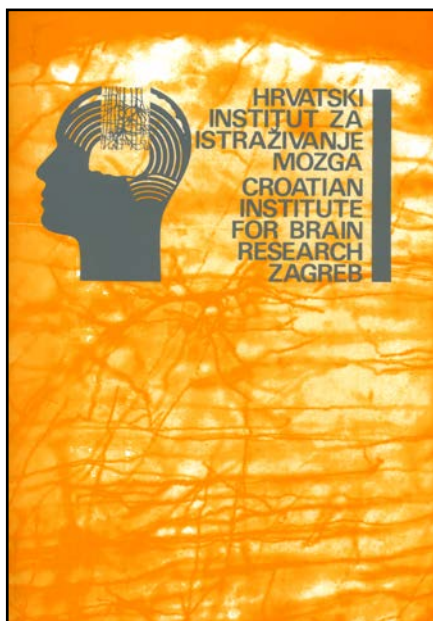
highlighted by the prolongation of lifespan and general living standards.

2. Investments in the field of brain research represent just a small fraction of total burden of mental and neurological disorders, and provide only hope for the successful treatment of these problems.

3. That, considering the circumstances in Croatia, intimate connection between basic and clinical research on the one side, and firm integration of scientific research into teaching process on the other side, is the only approach that guarantees significant advancement of Croatian neuroscience and its involvement into global flows of knowledge.

4. It is of utmost importance that in the times of limited financial possibilities, investments are used optimally to allocated funds.

5. That, considering the size of Croatia and number of existing researchers and research projects in the fields of basic and clinical



Slika 3 (prethodna stranica)

Krajem 1993. godine, zgrada je već bila pod krovom (dovršena Rohbau konstrukcija).

Figure 3 (previous page)

At the end of 1993 the building was completed and put under the roof (finished Rohbau construction).

Slika 4 (gore)

Tijekom izgradnje instituta, aktivno su razvijani i znanstveni programi instituta (naslovnice 3 uzastopne publikacije o ciljevima i programima instituta iz 1991., 1994. i 1998. godine).

Figure 4 (top)

During the construction of the Institute the scientific programs of the Institute continued to develop (Front pages of the three successive publications about programs and goals of the Institute form 1991, 1994 and 1997)

Slika 5 (lijevo)

Svečano otvaranje Hrvatskog instituta za istraživanje mozga na Dan Medicinskog fakulteta 17. prosinca 1998. bilo je praćeno znanstvenim skupom „Novija dostignuća u neuroznanosti“.

Figure 5 (left)

Grand opening of the Croatian Institute for Brain Research was held on the 17th December 1998 (at the 80th anniversary of the School of Medicine) and accompanied by a scientific symposia “New achievements in the neuroscience”.

Slika 6

Predsjednik Hrvatske akademije znanosti i umjetnosti, akademik Ivo Padovan, svečano otvara skup "Novija dostignuća u neuroznanosti" u Palači HAZU.

Figure 6

The President of the Croatian Academy of Sciences and Arts, academic Ivo Padovan, officially opened the symposia "New achievements in the neuroscience" at the Palace of the Croatian Academy of Sciences and Arts.



erno opremljene zgrade (Zgrada temeljnih medicinskih znanosti) i zajedničkog interdisciplinarnog istraživačkog programa, omogućuje najbolje iskorištenje postojećih kadrova i opreme, racionalno i plansko postupanje pri nabavi nove opreme, kao i najučinkovitiji mehanizam odgoja i obrazovanja mladih istraživača, njihovog dodatnog usavršavanja u vodećim svjetskim centrima, te njihovog povratka iz inozemstva u Hrvatsku (uz moguće privlačenje i drugih inozemnih znanstvenika).

neuroscience; the most efficient and prudent way is to gather all leading researchers and material resources under the roof of a single, modern building (The Building of Basic Medical Sciences) and joint interdisciplinary research program. This would enable the most efficient use of existing human potential and equipment; rational and planned purchase of new equipment, as well as the most efficient mechanism of training and educating of new young researchers, their additional training at leading centres in the World, and their return from abroad to Croatia (with the possibility to attract additional foreign researchers).

Slika 7

Osnivač instituta, Ivica Kostović, umjesto na svečanom otvorenju instituta, morao je biti po službenoj dužnosti u posjetu ruskom predsjedniku Borisu Jeljcinu.

Figure 7

Founder of the Institute, Ivica Kostović, on an official visit to Moscow with the President of the Russian Federation Boris Yeltsin, instead at a Grand opening of the Institute.



Na temelju iznesenog, Medicinski fakultet Sveučilišta u Zagrebu pokrenuo je inicijativu za osnivanje Hrvatskog instituta za istraživanje mozga i Zgrade temeljnih medicinskih znanosti. Ta je inicijativa ubrzo pretvorena u konkretan projekt, ne samo zbog iznimnog zalaganja djelatnika Fakulteta, nego i zbog činjenice da je predsjednik Republike Hrvatske, dr. Franjo Tuđman, prihvatio osobno pokroviteljstvo nad tim projektom (Slika 1). Početna i najznačajnija sredstva dobivena su, nakon obrazloženog zahtjeva, od još uvijek aktivnog SIZ-a (Samoupravne interesne zajednice) za znanost. I Vlada Republike Hrvatske jasno je prepoznala značenje neuroznanosti na međunarodnoj sceni te je istraživanja mozga uvrstila u prioritetna istraživanja, a projekt izgradnje Hrvatskog instituta za istraživanje mozga proglasila prioritetnim projektom hrvatske znanosti i već u prosincu 1990. godine dostavila Medicinskom fakultetu početna sredstva za realizaciju tog projekta.

Nakon što je Medicinski fakultet dobio suglasnost i čvrstu potporu Vlade Republike Hrvatske i Ministarstva znanosti i tehnologije, odluka o osnivanju Hrvatskog instituta za istraživanje mozga i Zgrade temeljnih medicinskih znanosti donesena je 14. veljače 1991. godine na sjednici Savjeta Medicinskog fakulteta Sveučilišta u Zagrebu.

Izgradnja se odvijala postupno, tijekom sljedećih osam godina (Slike 2 i 3), sukladno mogućnostima državnog proračuna u resoru znanosti i visokog školstva. Međutim, kroz cijelo to vrijeme, naši neuroznanstvenici su nastavili svoja znanstvena istraživanja u starim laboratorijima i uspješno objavljivali radove u međunarodnim časopisima – iako su mnogi istodobno bili i liječnici dragovoljci Domovinskog rata i sudjelovali u obrani i izgradnji Domovine. Nadalje, od 1991. do 1997. je također kroz niz koordinacijskih sastanaka sustavno razvijan i budući program znanstvene djelatnosti Hrvatskog instituta za istraživanje mozga (Slika 4),

Based on the aforementioned facts, University of Zagreb School of Medicine has initiated a proposal for the establishment of the Croatian Institute for Brain Research and the Building of Basic Medical Sciences. That initiative has soon become a real project; not only because of the exceptional commitment of the School of Medicine staff, but also because president of the Croatia dr. Franjo Tuđman had accepted personal sponsorship over this project (Fig. 1). Croatian government had also recognized the importance of neuroscience on the international scene, and included brain research into priority research areas, and the project of building the Croatian Institute for Brain Research was declared as a priority project of Croatian science. Thus, Croatian government allocated initial funds needed to realize this project in the December of 1990.

On the 14th February 1991, the School of Medicine Council, upon approval and strong support by the Croatian government and the Ministry of Science and Technology, made the decision to establish the Croatian Institute for Brain Research and the Building of Basic Medical Sciences.

The construction of the CIBR took place gradually, over the next eight years (Figs 2. & 3), according to the ability to allocate funds from the national budget for science and higher education. However, our neuroscientist continued their scientific research, throughout this entire period, in the old labs and successfully published the results in international journals – although many of them were also doctors volunteers in the War in Croatia, and participated in the defence and establishment of Croatia. Furthermore, between 1991 and 1997 there was a series of coordination meetings where future scientific program of the Croatian Institute for Brain Research has been developed (Fig. 4). As a result, we welcomed the opening of the CIBR ready with clear scientific and organizational goals.

The Building of Basic Medical Sciences was finally completed in the 1998., and a Grand

tako da smo useljenje u novu zgradu dočekali spremni i s jasno postavljenim znanstvenim i organizacijskim ciljevima i zadaćama.

Zgrada temeljnih medicinskih znanosti je napokon dovršena krajem 1998. godine, a svečano otvaranje Hrvatskog instituta za istraživanje mozga bilo je na Dan Medicinskog fakulteta 17. prosinca 1998. godine. Tom prigodom organiziran je jednodnevni simpozij pod naslovom „Novija dostignuća u neuroznanosti“ (Slika 5). Uvodno predavanje održano je u Palači Hrvatske akademije znanosti i umjetnosti (Slika 6), a potom je ostatak skupa održan na Medicinskom fakultetu Sveučilišta u Zagrebu, nakon čega je uslijedio i obilazak nove zgrade za brojne goste i uzvanike. No, idejni začetnik i osnivač instituta, Ivica Kostović, nije mogao biti nazočan na samom otvaranju svog životnog djela! Naime, u isto vrijeme morao je po službenoj dužnosti zajedno s predsjednikom Republike Hrvatske dr. Franjom Tuđmanom biti u Moskvi, na pregovorima s ruskim predsjednikom Borisom Jeljcinom (Slika 7).

Preseljenje u novu zgradu te postupno osposobljavanje svih njezinih kapaciteta (laboratoriji, računalna mreža, učionice, knjižnica, Odsjek za laboratorijske životinje, organiziranje tehničke i administrativne službe, itd.) trajalo je cijelu 1999. godinu, pa i dio 2000. godine. No, o svemu što se zbivalo u tih 25 godina neprekidne borbe, danonoćnog rada i napora te ustrajne želje i volje za stalnim razvojem i napretkom, planiramo objaviti detaljnu i opsežnu monografiju u najskorije vrijeme. Za sada je dovoljno kratko prikazati rezultat svih tih napora – što je Hrvatski institut za istraživanje mozga danas (2015.), čime se bave njegovi znanstvenici i nastavnici te koji su naši dosadašnji uspjesi na međunarodnoj i domaćoj sceni.

opening of the Croatian Institute for Brain Research was on the 17th December 1998 (80th anniversary of the School of Medicine). For that occasion a one day symposia entitled “New achievements in the neuroscience” was organized (Fig. 5). Introductory lecture was in the Palace of the Croatian Academy of Sciences and Arts (Fig. 6.). The rest was held at the School of Medicine, followed by the tour of the new building for many guests and dignitaries. Unfortunately, the creator and founder of the institute, Ivica Kostović, could not attend the Grand opening of his life achievement. At the same time, he was on an official visit to Moscow (as an official representative of Croatian Government) with the President of Croatia dr. Franjo Tuđman, conducting negotiations with the President of the Russian Federation Boris Yeltsin (Fig. 7).

Moving into a new building and gradual set up of all capacities (laboratories, computer network, classrooms, library, Animal housing facility, organization of technical and administrative services, etc.) were ongoing throughout entire 1999 as well as a part of 2000. However, a detailed account of everything that transpired over 25 years of continuous struggle, day-and-night hard work, and continuous wish and will for further growth and advancement of the CIBR is planned to be published in an encompassing monograph promptly. Until then, here is a short overview of results of these endeavours – what is the Croatian Institute for Brain Research today (2015), what its scientists and teachers do and what are our current achievements on domestic and international stage.

POGLAVLJE 2

*Hrvatski institut za istraživanje
mozga danas*

CHAPTER 2

*Croatian institute for brain research
today*



HRVATSKI INSTITUT ZA ISTRAŽIVANJE MOZGA DANAS

*Kratki pregled: zgrada, oprema, ustroj,
istraživači i projekti*

Hrvatski institut za istraživanje mozga dio je Medicinskog fakulteta Sveučilišta u Zagrebu, a svi djelatnici Instituta su zaposlenici Fakulteta. Institut je znanstveno-nastavna podružnica Medicinskog fakulteta, osnovana 1990. godine (vidi prethodno poglavlje), a svečano otvorena na

CROATIAN INSTITUTE FOR BRAIN RESEARCH TODAY

*Short overview: building, equipment,
organization, researchers and projects*

The Croatian Institute for Brain Research (CIBR) is a part of the University of Zagreb, School of Medicine and all employees of the CIBR are also employees of the School of Medicine. The CIBR is scientific and teaching subsidiary of the School of Medicine, founded in 1990 (see previous



Dan Medicinskog fakulteta 17. prosinca 1998. godine.

HIIM je rješenjem Trgovačkog suda u Zagrebu od 16. rujna 1998. godine u sudski registar ustanova upisan u registarski uložak s matičnim brojem subjekta upisa (MBS) 080159956, kao „podružnica broj 001, Sveučilište u Zagrebu, Medicinski fakultet, Hrvatski institut za istraživanje mozga – skraćeni naziv: HIIM“. Stoga u daljnjem tekstu, zbog jednostavnosti, koristim skraćenicu „HIIM“ ili jednostavno „Institut“.

chapter), and officially opened on the 17th December 1998 on the 80th anniversary of the School of Medicine.

The CIBR is by the decree of the Commercial Court in Zagreb, dated 16th September 1998, registered at the Registry of the Institutions under unique number (MBS) 080159956, as a “subsidiary number 001” of the School of Medicine, Croatian Institute for Brain Research – short name: CIBR”. Therefore, in the following text, due to simplicity we will use short name “CIBR” or simply “The Institute”.



Pionirska uloga u povezivanju temeljne, kliničke i translacijske neuroznanosti

Smisao osnivanja i izgradnje HIIM-a bio je da se u susjedne laboratorije smjeste multidisciplinarni timovi istraživača iz područja temeljne i kliničke neuroznanosti, koji imaju dugogodišnje iskustvo i dovoljnu međunarodnu prepoznatost u području

Slike na prethodnoj stranici (u smjeru kazaljke na satu)

- Istraživačke skupine Ivica Kostovića, Miloša Judaša i Zdravka Petanjka u zajedničkom laboratoriju (2013.). Ivana Pogledić, Lana Vasung, Nataša Jovanoy Milošević, Miloš Judaš, Maja Horvat, Marko Čuljat, Zdravko Petanjek, Danica Budinščak, Mario Vukšić, Božica Popović. Ivica Kostović u prvom planu, a u pozadini desno je Milan Radoš.
- Mario Vukšić u Laboratoriju za konfokalnu mikroskopiju (prizemlje).
- Darko Orešković (Institut Ruđer Bošković) i Marijan Klarica (snimljeni u uredu Marijana Klarice 2015. godine).
- Istraživačka skupina Miloša Judaša (projekt HRZZ) snimljena na stubištu HIIM-a 2012. godine: Zdravko Petanjek, Goran Sedmak, Božo Krušlin, Nataša Jovanov-Milošević, Miloš Judaš, Maja Capanec i Željka Krsnik.

A pioneering role in combining basic, clinical and translational neuroscience

The purpose of establishing and construction of the CIBR was to bring together in the neighbouring laboratories multidisciplinary research teams from the various fields of basic and clinical neuroscience, with the years of experience and signif-

Figures on the previous page (clockwise from top)

- Research groups of Ivica Kostović, Miloš Judaš and Zdravko Petanjek in the joint laboratory (2013) Ivana Pogledić, Lana Vasung, Nataša Jovanov-Milošević, Miloš Judaš, Maja Horvat, Marko Čuljat, Zdravko Petanjek, Danica Budinščak, Mario Vukšić, Božica Popović, Ivica Kostović in front, and Milan Radoš at the back.
- Mario Vukšić in the Confocal microscopy laboratory (ground floor).
- Darko Orešković (Institute Ruđer Bošković) and Marijan Klarica (photographed at the office of Marijan Klarica in 2015).
- Research group of Miloš Judaš (CSF research grant) photographed at the main staircase at the CIBR in 2012: Zdravko Petanjek Goran Sedmak, Božo Krušlin, Nataša Jovanov-Milošević, Miloš Judaš, Maja Capanec, Željka Krsnik.



Slika 1

Ulazna (zapadna) strana zgrade koja je izgrađena na mjestu planiranog (ali nikad izvedenog) krila zgrade Zavoda za patologiju.

Vidljiv je i položaj zgrade u odnosu na zgradu Zavoda za anatomiju, Zavoda za farmakologiju i Zavoda za sudsku medicinu.

istraživanja normalne građe i razvoja ljudskog mozga, psihijatrijskih i neuroloških bolesti i poremećaja mozga, te razvojnih poremećaja mozga. Na taj način nastojimo istražiti neurobiološku podlogu normalnog i poremećenog psihološkog i socijalnog razvoja čovjeka na molekularnoj, staničnoj, sistemskoj i individualno-osobnoj razini. Ovakvo interdisciplinarno i interaktivno okružje nam osigurava da na brojne i različite znanstvene probleme primijenimo široki spektar temeljnih i kliničkih istraživačkih metoda (molekularna i stanična neurobiologija; neurogenetika, citogenetika i genomika; neuroanatomija, neurohistologija i razvojna neurobiologija; stanična i sistemska neurofiziologija;

Figure 1

Entrance (west) side of the building constructed at the site of planned (but never completed) wing of the Department of pathology building.

icant international visibility in fields of normal development and anatomy of the human brain, psychiatric and neurological disorders and diseases and developmental brain disorders. We are thus trying to explore neurobiological foundations of normal and abnormal psychological and social human development on the molecular, cellular, systems and individual level. Interdisciplinary and interactive environment is providing us with the opportunity to apply wide range of basic and clinical research methods (molecular and cellular neurobiology, neurogenetics, cytogenetics and genomics, neuroanatomy, neurohistology and developmental neurobiology, cellular and systems neurophysiology, animal

rad s pokusnim životinjama, uključujući i tkivne i stanične kulture te matične stanice; analiza ljudskog ponašanja na razini psihologije, neurolingvistike, neurologije, pedijatrijske neurologije, psihijatrije te suvremenih metoda za *in vivo* prikaz građe i funkcije ljudskog mozga – tzv. „neuroimaging“). Stoga je HIIM specifična i poticajna akademska sredina, u kojoj se tijesno povezuju znanstveno istraživanje i nastava na svim akademskim razinama, ali se isto tako koriste rezultati temeljnih istraživanja za poboljšanje dijagnostičkih i terapijskih pristupa osobama s bolestima i poremećajima živčanog sustava.

Dugogodišnjim zajedničkim radom ostvarili smo uspješnu kombinaciju temeljne, kliničke i translacijske neuroznanosti. Znanstvenici i nastavnici HIIM-a su zaposleni u sljedećim ustrojbenim jedinicama Medicinskog fakulteta: Zavodu za neuroznanost (HIIM), Zavodu za anatomiju, Zavodu za histologiju i embriologiju, Zavodu za biologiju, Zavodu za kemiju i biokemiju, Zavodu

Slika 2

Položaj zgrade u odnosu na Zavod za patologiju. U podrumu Zavoda za patologiju (prozori uz tlo) smještena je Jedinica za magnetsku rezonanciju.

models, cellular and tissue cultures, stem cells, psychological analysis of the human behaviour, neurolinguistics, neurology, paediatric neurology, psychiatry and modern *in vivo* methods for the visualisation of structure and function of the human brain – “neuroimaging methods”) on numerous different scientific questions. Therefore, the CIBR is unique and stimulating academic environment, in which scientific research is closely linked with education at all academic levels (from undergraduate to post-doctoral). Furthermore, the results of basic research are used to enhance and improve diagnostic and therapeutic procedures in patients with disorders of the central nervous system.

Over many years we have accomplished successful combination of basic, clinical and translational neuroscience. Researchers and teachers at the CIBR are employed at the following departments of the School of Medicine: Department of Neuroscience (CIBR), Department of Anatomy, Department of Histology and Embryology,

Figure 2

Position of the building in a relation to the Department of the pathology. Unit for magnetic resonance is located in the basement of the Department of Pathology (windows adjacent to the ground).





za fiziologiju, Zavodu za farmakologiju, Zavodu za patologiju, kao i na Klinikama za neurologiju, neurokirurgiju, psihijatriju, pedijatriju i ginekologiju Kliničkog bolničkog centra Zagreb (naše najveće i vodeće sveučilišne bolnice i nastavne baze Medicinskog fakulteta) te drugih kliničkih nastavnih baza Medicinskog fakulteta.

Slika 3

Predvorje zgrade, iz kojeg se ulazi u HIIM (ravno) i u Jedinicu za magnetsku rezonanciju (lijevo) u podrumu Zavoda za patologiju.

Figure 3

The lobby of the building with the main entrance to the CIBR (straight ahead) and entrance to the Unit for magnetic resonance (left) in the basement of the Department of Pathology.

Department of Biology, Department of Chemistry and Biochemistry, Department of Physiology, Department of Pharmacology, Department of Pathology, as well as clinics of Clinical Hospital Centre Zagreb which is the largest and leading University hospital in the Croatia and teaching site of the School of Medicine (Department of



Slika 4 (desno)

Središnje stubište zgrade, koje je arhitekt Zlatko Jurić dizajnirao po uzoru na dvostruku uzvojniju molekule DNA.

Figure 4 (right)

The architect Zlatko Jurić designed the main staircase according to the double helix molecule of the DNA.

Slika 5 (dolje)

U dormitoriju je i jedan apartman za uglednije goste („senior scientists“), s lijepim pogledom na sjeverni dio Šalate.

Figure 5 (bottom)

There is also one suite in the dormitory for the use of distinguished guests (“senior scientists”) with a wonderful landscape of the north part of Šalata.



Povrh toga, naši izvanjski suradnici (voditelji tzv. „ekstramuralnih“ projekata) su zaposleni na drugim sastavnicama Sveučilišta u Zagrebu: Prirodoslovno-matematičkom fakultetu (Biološki odsjek), Edukacijsko-rehabilitacijskom fakultetu, Filozofskom fakultetu (psihologija, lingvistika), Hrvatskim studijima (studij psihologije) i Fakultetu elektrotehnike i računarstva. Neke ekstramuralne projekte vode djelatnici Instituta Ruđer Bošković, Medicinskog fakulteta Sveučilišta u Osijeku i Zdravstvenog veleučilišta u Zagrebu.

Neurology, Department of Neurosurgery, Department of Psychiatry, Department of Paediatrics, Department of Gynaecology and Obstetrics) and other clinics and departments of the School of Medicine. Furthermore, our external associates (heads of the so-called “extramural” projects) are employed at other faculties within University of Zagreb: Faculty of Science (Biology division), Faculty of Education and Rehabilitation Sciences, Faculty of Humanities and Social Sciences (Division of Psychology and Division of Linguistics), Centre for Croatian Studies (Division of Psychology) and Faculty of Electrical Engineering



ti zaključiti da HIIM još od 1999. godine djeluje kao nacionalni i regionalni centar izvrsnosti u području temeljne, kliničke i translacijske neuroznanosti, što se temelji na sljedećim bitnim pokazateljima:

1. Znanstvena izvrsnost uz kontinuirano objavljivanje radova u vodećim međunarodnim časopisima te izvrsne pokazatelje u bazi Web of Science (vidi Prilog);
2. Dugogodišnja i široka mreža znanstvene suradnje na domaćoj i međunarodnoj znanstvenoj sceni;
3. Diseminacija znanja na svim razinama akademskog obrazovanja, organizacija brojnih međunarodnih ljetnih škola, tečajeva, radionica i znanstvenih skupova;
4. Javna diseminacija i promičba istraživanja mozga;
5. Sudjelovanje u stručnim i upravnim tijelima vodećih međunarodnih organizacija neuroznanosti te prosudbenim skupinama za znanstvene projekte;
6. Posjedovanje izvrsne znanstvene infrastrukture i opreme te jasno ustrojena i učinkovita organizacija i vodstvo (vidi niže);
7. Osiguranje izvrsne međunarodne izobrazbe za brojne doktorande, uspješan razvoj znanstvenih karijera naših mladih istraživača u inozemstvu te uspješan povratak dijela tih istraživača natrag u Hrvatsku;
8. Brojne nagrade i priznanja koje su naši znanstvenici dobili za individualnu znanstvenu izvrsnost;
9. Jasno definirani dugoročni istraživački ciljevi, koji su interdisciplinarni, multidisciplinarni i transdisciplinarni, a ostvaruju se kroz kompetitivno dobivene projekte;
10. Postojanje jedinstvenog istraživačkog resursa s dodatnom međunarodnom vrijednošću – Zagrebačke zbirke mozгова (vidi niže).

Navedimo samo nekoliko jasnih pokazatelja znanstvene izvrsnosti i uspješnosti:

and Computing. Some of the extramural projects are led by employees of the Institute Ruđer Bošković, University of Osijek School of Medicine and University of Applied Health Sciences.

In summary, we can with pure heart and clear conscience conclude that since 1999 the CIBR is operating as a national and regional Centre of Excellence in the field of basic, clinical and translational neuroscience, which can be corroborated with the following key indicators:

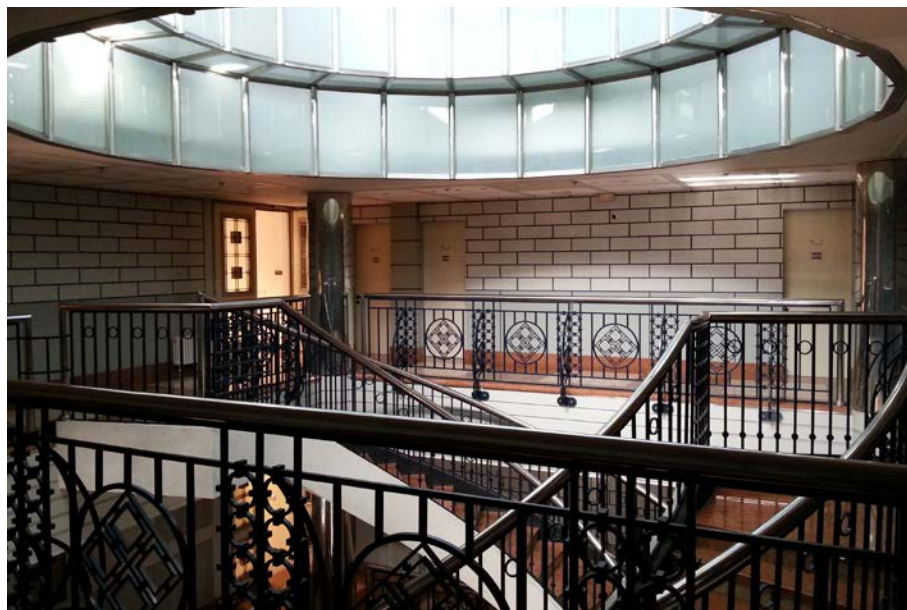
1. Scientific excellence proven by the continuous publication of research papers in the leading international journals and excellent indicators in the Web of knowledge database (see Annex 1).
2. Wide, long-term collaboration network with the leading domestic and international institutions.
3. Knowledge dissemination at all levels of academic education, organization of numerous international summer schools, courses, workshops and scientific conferences.
4. Public dissemination and promotion of brain research.
5. Participation in the professional and governing bodies of leading international neuroscience organizations, and as evaluators in review boards for international peer-reviewed grant applications.
6. Excellent scientific equipment and infrastructure, and clear and efficient organization and leadership (see below).
7. Exceptional international education of PhD students, successful career development of our young investigators abroad and successful return of some of those investigators in Croatia.
8. Numerous awards and recognitions awarded to the CIBR's scientists for individual scientific excellence.
9. Clearly defined long-term interdisciplinary, multidisciplinary and transdisciplinary research goals, accomplished through

Slika 6

Vrh stubišta u potkrovlju zgrade, gdje su smješteni dormitorij i klub.

Figure 6

The top of the main staircase at the penthouse, with dormitory and the Club.



Naši znanstvenici do danas su objavili (Web of Science – Core Collection) 589 radova, od kojih je 206 u časopisima iz prve kvartile (Q1), 125 u Q2, 167 u Q3 te 91 u Q4 (Prilog 1). Ti radovi do sada imaju ukupno 12.703 neovisna citata. Naši znanstvenici (samo oni koji su voditelji Odsjeka i Laboratorija u HIIM-u!) do sada su bili mentori za 114 obranjenih doktorskih radova (Prilog 4), 57 obranjenih magistarskih radova (Prilog 3) te 105 obranjenih diplomskih radova studenata (Prilog 2).

HIIM je živi akademski organizam koji se trajno razvija i napreduje, prilagođava suvremenim međunarodnim trendovima usvajanjem novih metoda i tehnika te nastoji privući i odgojiti istraživače koji su sposobni ostvariti bitan iskorak i doprinos u svom području istraživanja. Naš trajni cilj i zadaća jest da budemo predvodnik događanja u neuroznanosti te da postanemo i ostanemo nacionalni centar izvrsnosti u temeljnoj, kliničkoj i translacijskoj neuroznanosti. Kad pročitate ovu knjigu, vjerujem da će vam ovo zvučati kao realan i ostvariv cilj.

U preambuli Pravilnika HIIM-a, koji je donio dekan Medicinskog fakulteta 8. veljače 2000. godine, jasno su istaknuti ciljevi i namjena Instituta te njegova posebna uloga u okviru Fakulteta. Pritom je jasno istaknuto da je HIIM od samog početka zamišljen

competitively awarded research grants.

10. Existence of a unique research resource with internationally added value – The Zagreb Brain Collection (see below).

Let us mention just a few clear key indicators of scientific excellence and success:

Our researchers have to date published (according to the Web of Science – Core Collection) 589 papers, of which 206 are in the Q1 journals, 125 in the Q2, 167 in the Q3, and 91 in the Q4 (Annex 1). Aforementioned papers have been independently cited in total 12.703 times. The CIBR's researchers (only Heads of Departments and Laboratories) have been mentors for 114 successfully defended doctoral theses, 57 master's theses and 105 graduates (Annex 2).

The CIBR is vigorous and growing academic organism, constantly evolving and advancing, adapting to contemporary international trends in neuroscience research by incorporating novel methods and techniques, and by trying to attract and educate new researchers capable of making significant advancements and contributions in their respective fields of research. Our permanent goal and task is to be at the leading edge of developments in the neuroscience, and to become and continue to be the National Centre of Excellence in basic, clinical



da se razvije u središte izvrsnosti u području neuroznanosti, prepoznato i priznato na međunarodnoj razini. Dakle, to je ne samo naše htijenje i izraz naših nadanja, nego i naše poslanje i obveza utvrđena službenim aktom (Pravilnikom). U tom smislu vrijedi citirati odgovarajući odlomak spomenutog Pravilnika:

„Temeljni cilj i namjena Instituta je da služi kao središte za istraživanje neurobiološke podloge i plastičnosti normalnog kognitivnog razvoja te kognitivnih poremećaja i procesa plastičnosti i reorganizacije u odgovoru na leziju u onim neurološkim i psihijatrijskim bolestima i poremećajima razvojne i odrasle dobi koji su značajni u javno-zdravstvenom i ekonomskom pogledu za cijelo društvo. Ti se ciljevi ostvaruju kroz interdisciplinarnu primjenu širokog raspona istraživačkih metoda (od histoloških i molekularnobioloških, preko eksperimentalnih do metoda oslikavanja građe i funkcije mozga u živih osoba), tijesno povezivanje temeljne i kliničke neuroznanosti te kompetitivni odabir istraživačkih projekata na domaćoj i međunarodnoj razini. U smislu svekolikog

Slika 7

Jedna od 13 dvokrevetnih soba u dormitoriju (svaka soba ima zasebno malo predsoblje i kupaonicu, te priključak na Internet).

Figure 7

An example of one of 13 double rooms in the dormitory (each room has a small lobby and bathroom, and internet connection).

and translational neuroscience. We believe, after you finish reading this booklet, this will sound to you as a realistic and achievable goal.

The goals and purpose and special role of the CIBR are clearly pointed out in the preamble of the CIBR's Statute, approved by the Dean of the School of Medicine on the 8th February 2000. It is clearly stated that the CIBR is from its conceptions envisaged to develop into the Centre of Excellence in the field of neuroscience recognized in the international community. Therefore, it is not only our wish and expression of our hope, but also our mission and obligation established by an official act (The Statute). Thus, it is noteworthy to cite an appropriate section of the said Statute:

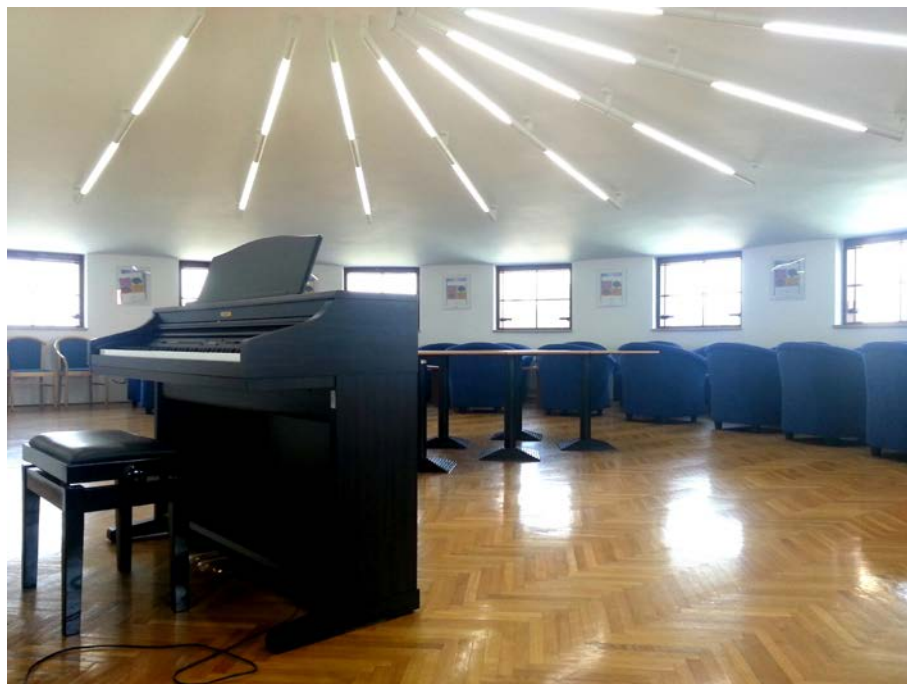
“The fundamental goal and purpose of the Institute is to serve as an Centre for the research of the neurobiological foundation and plasticity of normal cognitive development and cognitive disorders, and plasticity processes and reorganization as a response to the lesion in the neurological and psychiatric disorders and diseases of developmental and adult stage which are important for public health and economic situation of the entire society. These goals are accomplished through interdisciplinary application of wide range research methods (from histological and molecular biology, through experimental to the structural and functional imaging of the living human brain), closely linking basic and clinical neuroscience, and competitive selection of research projects at the domestic

Slika 8

U potkrovlju je i klub, kao središnje mjesto za različite proslave, domjenke, ali i prigodne radne i promotivne sastanke (npr. tijekom Tjedna mozga u Hrvatskoj ili Festivala znanosti), a u njemu vježba i studentski zbor Medicinskog fakulteta „Lege artis“.

Figure 8

The Club, located at the penthouse level, is the central place for various events and celebrations, but also for commemorative and promotional meetings (e.g. during the Brain Awareness Week or the Festival of Science in Croatia). School of Medicine student choir also rehearses in the Club.



unapređenja znanstvenog, stručnog i nastavnog rada, Institut ima posebnu i bitnu ulogu u okviru Fakulteta, koja se očituje u sljedećem:

(a) Kroz ugovoreni program trajne istraživačke djelatnosti Instituta „Neurobiologija kognitivnog razvoja i kognitivnih poremećaja“, što je ujedno prvi takav program na cijelom Sveučilištu, ostvarena je interdisciplinarna suradnja najveće skupine međunarodno prepoznatih hrvatskih neuroznanstvenika, uz tijesno povezivanje temeljne i kliničke neuroznanosti te racionalnu i učinkovitu uporabu kadrova, opreme, prostora i izravan pristup modernoj računalnoj i informacijskoj tehnologiji i drugim specijaliziranim tehnološkim resursima.

(b) Institut omogućuje, na novoj razini vrsnoće i povećane učinkovitosti, izravan uklapanje istraživačkog rada i rezultata u nastavni proces na diplomskoj i poslijediplomskoj razini te u okviru trajne edukacije liječnika i drugih stručnjaka.

(c) Institut omogućuje sustavno i učinkovito novačenje i edukaciju mladih istraživača u nekoliko ključnih područja neuroznanosti, kao i dodatno usavršavanje ostalih istraživača na naprednoj razini.

and international level. In terms of a general scientific, professional and educational advancement, the Institute has special and crucial role within the School of Medicine, which is reflected in the following:

(a) Through the agreed upon program of continuous research activity of the Institute “Neurobiology of the cognitive development and cognitive disorders”, which is also the first such program at the entire University of Zagreb, interdisciplinary collaboration between the largest group of internationally recognized Croatian neuroscientists has been accomplished by closely linking basic and clinical neuroscience, rational and efficient use of personnel, equipment, space, direct access to the modern computer and information technology and other specialized technological resources.

(b) The Institute will provide, on the new level of excellence and increased efficiency, the direct incorporation of the scientific work and its results in the educational process at undergraduate and graduate level, and as a part of continuous education of medical doctors and other health professionals.

(c) The institute provides efficient and systematic recruitment and education of new young investigators in several key areas of

(d) Zahvaljujući modernoj tehnologiji i vrhunskim infrastrukturnim resursima (koji uz laboratorije i radne kabinete obuhvaćaju i nastavne prostorije i dormitorij), Institut omogućuje pojačanu mobilnost domaćih i stranih znanstvenika kroz razmjene posjeta i organiziranje pozvanih predavanja, znanstvenih i stručnih skupova, tečajeva i škola.

(e) Izgradnjom Instituta Fakultet je napokon dobio ključni resurs za poticanje naših znanstvenika u dijaspori na povratak u Hrvatsku.

(f) Institut ima sve uvjete da djeluje kao središnja institucija za neuroznanost na području cijele Hrvatske, pa time dodatno osnaži položaj Fakulteta kao središnje državne ustanove na području biomedicine.

(g) Napokon, ali ne i najmanje važno, organizacija rada u Institutu se temelji na novom sustavu financiranja i upravljanja, što se oslanja na kompetitivni odabir istraživačkih projekata i ekspertne usluge Međunarodnog znanstvenog savjeta sastavljenog od vrhunskih svjetskih znanstvenika, kao i na izraženu ulogu načela samofinanciranja. U tom smislu, Institut služi kao model drugim ustrojbenim jedinicama Fakulteta, za pojačanje aktivnosti

neuroscience, as well as additional training of other researchers on the advanced level.

(d) Thanks to the modern technology and state of the art infrastructure resources (beside laboratories and work offices encompassing also classrooms and dormitory), the Institute allows for the increased mobility of domestic and foreign researchers through exchange visit programs, organization of invited lectures, scientific conferences, meetings, courses and summer schools.

(e) Through the construction of the Institute, the School of Medicine has finally obtained key resource for instigating the return of our scientist abroad in Croatia.

(f) The Institute has all necessary requirements to act as a central institution for neuroscience at the entire territory of Croatia, and through that strengthen the position of the School of Medicine as a central institution in the field of biomedicine.

(g) Last, but not least, the work organization at the Institute is based on the new model of financing and management, which relies on competitive selection of research projects and expert services of the International Scientific Advisory Board composed of the leading international scientists, as well as at the clear principle of



Slika 9

Seminarska dvorana u prizemlju. Slična dvorana (koja ujedno služi i kao telekonferencijska dvorana) smještena je na prvom katu.

Figure 9

The classroom located at the ground floor. Similar classroom (which also serves as a teleconference room) is located at the first floor.

Slika 10

Računalna učionica s 25 radnih mjesta (drugi kat).

Figure 10

Computer room with 25 work stations (second floor).



i uloge u pogledu vlastitog financiranja s jedne strane, te za osiguranje dotoka dodatnih sredstava Fakultetu kao cjelini, s druge strane.“

Kratki opis zgrade

Institut zauzima najveći dio Zgrade temeljnih medicinskih znanosti, koja je izgrađena na katastarskoj čestici broj 3951/2 K.o. Centar, u Zagrebu (Šalata 12), uz postojeću zgradu Zavoda za patologiju (Šalata 10) na mjestu izvorno planiranog, ali nikad dovršenog krila te zgrade (Slike 1 i 2).

Zgrada je izgrađena u skladu s najvišim europskim građevinskim, sigurnosnim, energetskim i ekološkim standardima. Ima vrlo složen sustav za klimatizaciju (s čak 5 ventilostrojarnica) koji je prijeko potreban za normalan rad u modernim molekularno-biološkim laboratorijima te nastambi za laboratorijske životinje. Nadalje, zgrada ima pet zasebnih kanalizacijskih sustava (oborinski, fekalijski, kiselinski, uljni i biološki) i jedinstvena je u nas po tome što se sve otpadne vode prvo prikupljaju u podzemnim uređajima filtraciju, a tek potom odlijevaju u gradsku kanalizaciju. Štoviše, otpadni materijal se prikuplja

self-financing. In this regard, the Institute serves as a model to other departments of the School of Medicine to increase activities and its roles in terms of self-financing on the one hand, and to ensure the flow of additional funds to the School of Medicine as a whole on the other hand.

Brief description of the building

The CIBR encompasses the majority of the Building of Basic Medical Sciences, which is built on the cadastral number 3951/2 K.o. Center in Zagreb (Šalata 12), next to the existing building of the Department of Pathology (Šalata 10) at the place of the originally planned, but never built, wing of this building (Figs. 1 and 2). The building was constructed in an accordance with the highest European construction, safety, energy and environmental standards. It has very complex ventilation system (with 5 different air conditioning systems) which is crucial for the proper work of the modern molecular biology laboratories and the animal facility. Furthermore, the building has 5 different waste management systems (for rainfall waters, faecal material, acids, oils and biological waste) and it is unique in Croatia due to the fact that it first col-



Slika 12

Jedan od manjih laboratorija – Jedinica za neradioaktivnu in situ hibridizaciju (prizemlje).

Figure 12

One of the smaller laboratories – Unit for the non-radioactive in-situ hybridization (ground floor).

i odlaže u zasebne prostorije (spremišta zapaljivih tekućina, radioaktivnog otpada, organskog otpada, otpada priručnih laboratorijskih materijala).

Zgrada ima ukupno površinu od 7.524 m² (ukupna korisna površina je 4.564 m²), a sastoji se od pet etaža: podruma, prizemlja, dva kata i potkrovlja. Pritom su na južnoj strani uglavnom smješteni radni kabineti, uredi i knjižnica, na sjevernoj strani seminarske dvorane, računalna učionica i klub, dok su laboratoriji smješteni na istočnoj strani (koja gleda na Voćarsku ulicu). Kroz predvorje zgrade ukrašeno visokim stupovima (Slika 3) ulazi se u sam Institut (Šalata 12), a lijevo je ulaz u Jedinicu za magnetsku rezonanciju, smještenu u podrumu Zavoda za patologiju (Šalata 10). Za izgled središnjih spiralnih stuba (Slika 4) arhitektu Zlatku Juriću nadahnuće je bila dvostruka uzvojnica molekule DNA. Na vrhu stubišta (Slika 6) je potkrovlje, u kojem se nalazi dormitorij s 13 dvokrevetnih soba (Slika 7), od kojih svaka ima zasebno predvorje i kupaonicu, te jedan apartman za uglednije goste – „senior scientists“ (Slika 5). U potkrovlju je i klub (Slika 8), koji

lects all waste waters in the underground filtration system, and after filtration releases them into the city sewage. Moreover, all waste material is collected and stored in the special storage rooms (storages for flammable liquids, radioactive waste, organic waste, laboratory waste).

The total surface of the building is 7.254 m² (the total usable surface is 4.564 m²), divided into 5 floors: basement, ground floor, first floor, second floor and penthouse. Work spaces, offices and library are located at the south side of the building, and classrooms, computer room and the Club are located at the north side of the building, while laboratories are located at the east side of the building (facing Voćarska street). The entrance to the Institute itself (Šalata 12) is located in the lobby decorated with high pillars (Fig. 3.); to the left in the lobby is located entrance to the Unit for Magnetic Resonance situated in the basement of the Department of Pathology (Šalata 10). The architect Zlatko Jurić found the inspiration for the main spiral staircase (Fig. 4.) in the double helix of the DNA molecule. The dormitory is located in the pent-

je središte različitih društvenih zbivanja – u njemu se održavaju domjenci i proslave, različiti neformalni sastanci i studentske aktivnosti (primjerice, u klubu vježbaju za svoje nastupe članovi studentskog zbora Medicinskog fakulteta „Lege artis“). Na sjevernoj strani su (osim kluba u potkrovlju) i dvije seminarske dvorane (Slika 9) te jedna računalna dvorana s 25 radnih mjesta (Slika 10), koja ujedno služi i kao telekonferencijska dvorana. U prizemlju je i prostrana knjižnica Instituta.

Za ugodan cjelodnevni boravak te učinkovit znanstveni, stručni i nastavni rad, osiguran je i niz pomoćnih prostorija: tri čajne kuhinje s blagovaonicama, dvije manje seminarske dvorane (za sastanke zasebnih istraživačkih skupina, održavanje manjih seminara i „Journal clubs“ itd.), dva veća kabineta za smještaj mladih istraživača te 18 radnih kabineta (svaki površine oko 11 m²) za rad na računalima, čitanje i pisanje i slične aktivnosti. Napokon, dio zgrade su i tri prostrana uredska prostora (ured direktora, ured Zavoda za neuroznanost, te

house at the top of the staircase (Fig. 6.). It is composed of 13 double rooms (Fig. 7.) of which every room has its own lobby and bathroom, and one suite for distinguished guests – “senior scientists” (Fig. 5.). The Club is also located at the penthouse level (Fig. 8.), and this is a main place for various social events at the CIBR – parties and celebrations, informal meetings, various student activities (e.g. members of the student Choir of the School of Medicine “Lege Artis” practice in the Club). Except the Club, at the north side of the building are also located two classrooms (Fig. 9.) and Computer room with 25 work spaces (Fig. 10.) which also serves as teleconference room. The spacious library of the CIBR is located at the ground floor.

To provide comfortable and efficient research, teaching and professional activities, the CIBR has a number of accessory facilities: 3 small kitchens, two small seminar rooms (for individual research group meetings, journal clubs etc.), two larger rooms for PhD students and 18 small of-

Slika 11

Središnji Laboratorij za neurohistologiju i kemijsku neuroanatomiju (prizemlje).

Figure 11

Central part of the Laboratory for the neurohistology and chemical neuroanatomy (ground floor).



ured koji zajednički koriste dvije sestrinske ustanove – Centar za kliničku primjenu neuroznanosti i Poliklinika „Neuron“).

Vrhunska znanstvena infrastruktura: laboratoriji i oprema

U zgradi HIIM-a je smješteno 14 velikih laboratorija (površina svakog oko 50 m²) i 16 manjih laboratorija (površina svakog oko 25 m²), kao što su Laboratorij za neurohistologiju i kemijsku neuroanatomiju (Slika 11), Laboratorij za razvojnu neuropatologiju, Laboratorij za neuromorfometriju, Laboratorij za imunohistokemiju i *in situ* hibridzaciju (Slika 12), Laboratorij za neurogenetiku i razvojnu genetiku i mnogi drugi (vidi niže, pri opisu sadašnjeg ustroja HIIM-a), uključujući i suvremeno opremljenu prosekturu za obavljanje postmortalne analize. Povrh toga, postoji još 14 manjih dodatnih laboratorijskih prostora za zajedničko korištenje: za pranje laboratorijskog posuđa, za precizno vaganje, za pohranu laboratorijskih kemikalija, ultracentrifugiranje, autoradiografiju, gel-elektroforezu, tkivne i stanične kulture, itd.

fices (each 11 m²) for non-laboratory activities such as reading, writing, computer analysis etc. Finally, there are three large office spaces: Director's office, Department of Neuroscience office, and office jointly used by two sister-organizations, Center for Clinical Research in Neuroscience and diagnostic unit Polyclinic Neuron.

Top of the line scientific infrastructure: laboratories and equipment

The CIBR has 14 large (50 m² each) and 16 smaller (25 m² each) laboratories, such as Laboratory for neurohistology and chemical neuroanatomy (Fig. 11.), Laboratory for developmental neuropathology, Laboratory for neuromorphometry, Laboratory for immunohistochemistry and *in situ* hybridization (Fig. 12.), Laboratory for neurogenetics and developmental genetics and others (see below the organizational structure of the CIBR). Furthermore, there are also 14 additional small laboratory spaces designated for common use: washing laboratory dishes, precise weighing, storage of laboratory chemicals and reagents, ultracentrifuge, autoradiography, gel-electro-



Slika 13

Dora Polšek, Dunja Gorup, Mirjana Babić, Marta Skelin u jednom od laboratorija Odsjeka za laboratorijske životinje (podrum).

Figure 13

Dora Polšek, Dunja Gorup, Mirjana Babić, Marta Skelin at the one of laboratories located at the Division of Animal facilities (basement).



Slika 14

Mladi istraživači tijekom pripreme eksperimenta u gnotobiološkom laboratoriju Odsjeka za laboratorijske životinje (podrum).

Figure 14

Young investigators during preparations of experiments in gnotobiological laboratory of the Division of Animal Facility (basement).



Slika 15

Mirjana Babić u Laboratoriju za razvojnu neuropatologiju (prizemlje).

Figure 15

Mirjana Babić at the Laboratory for developmental neuropathology (ground floor).





Slika 16

Dijagnostički MRI uređaj Siemens Trio (snage polja 3 Tesla), smješten u podrumu Zavoda za patologiju.

Figure 16

Diagnostic MRI device Siemens Trio (3T), located at the basement of the Department of Pathology.

Svi laboratoriji su u potpunosti opremljeni suvremenom znanstvenom opremom i instrumentima, kao što su: konfokalni mikroskop i brojni drugi istraživački mikroskopi; elektronski mikroskop; uređaj za virtualnu mikroskopiju Hamamatsu Nanozoomer (vidi niže, Slika 20); MRI uređaj snage polja 3 Tesla za rad s pacijentima (Slika 16); klinička oprema za sistemsku neurofiziologiju – EEG i evocirani potencijali; eksperimentalni MRI uređaj Bruker snage polja 7 Tesla za rad s pokusnim glodavcima (Slika 17); uređaj za praćenje bioluminiscencije u živom tkivu; oprema za staničnu

phoresis, tissue & cell cultures, cold room, dark room, etc. All laboratories are fully equipped with the modern scientific equipment and instruments such as: confocal microscope and various other research microscopes, electron microscope, Hamamatsu Nanozoomer scanner for virtual microscopy (see below, Fig. 20.); for clinical use: 3T MRI device (Fig. 16.) and equipment for system neurophysiology – EEG and evoked potentials, experimental 7T MRI device “Bruker” for imaging experimental animals (Fig. 17), bioluminescence equipment for live tissue sample analyses;



Slika 17

Eksperimentalni MRI uređaj Bruker za snimanje glodavaca, smješten u obnovljenom podrumu Zavoda za anatomiju.

Figure 17

Experimental MRI device Bruker for imaging rodents located at newly renovated basement of the Department of Anatomy.

neurofiziologiju i tzv. „whole cell patch-clamp“; različiti mikrotomi za klasičnu neurohistologiju, histokemiju i imunocitokemiju; oprema za *in situ* hibridizaciju te analizu DNA i RNA; računalni sustavi za kvantitativnu neurohistološku analizu, to jest stereologiju i neuromorfometriju; oprema za fluorescentnu *in situ* hibridizaciju (FISH) i citogenetiku itd.

Odsjek za laboratorijske životinje

Odsjek za laboratorijske životinje sastoji se od jedinice za sterilizaciju, nastambi sa životinjama, pomoćnih prostorijskih (spremište stelje i hrane, čisti hodnik, nečisti hodnik, praonica) te laboratorija za provođenje pokusa na životinjama. Ukupna površina je 297,41 m². Sve nastambe za životinje imaju mogućnost pojedinačnog dodatnog reguliranja povećanja temperature preko ugrađenih električnih grijača u ventilacijski kanal i termostata u nastambi. Svaka nastamba ima mogućnost automatskog paljenja i gašenja rasvjete preko podesivog vremenskog uređaja (timer). Ovlaživanje zraka u nastambama se obavlja lokalnim ovlaživačem u svakoj nastambi zasebno. Prostor je klimatiziran klimakomorom kapaciteta 6.400 mw/h, s mogućnošću odabira temperature ubačenog zraka. Ventilacijski sustav osigurava 15 izmjena na sat u prostoru nastambi, te 10 izmjena na sat u ostalim prostorijama.

Ministarstvo poljoprivrede Republike Hrvatske je 3. srpnja 2013. donijelo rješenje da se u prostorima Odsjeka za laboratorijske životinje HIIM-a odobrava uzgoj životinja namijenjenih korištenju u pokusima (miševi i štakori) i opskrba životinjama namijenjenim korištenju u pokusima te korištenje životinja u pokusima. Utvrđeno je da Odsjek ima kapacitet od 600 miševa i 100 štakora u uzgoju te 1.200 miševa i 100 štakora u pokusnoj nastambi, a udovoljava propisanim uvjetima za uzgoj miševa i opskrbu navedenim životinjama te provođenje pokusa. Stoga su Odsjek i Medicinski

equipment for cellular neurophysiology and “whole cell patch-clamp”, various microtomes for classical neurohistology, histochemistry and immunocytochemistry; facilities for *in situ* hybridization and DNA and RNA analysis; computer systems for quantitative neurohistology analysis i.e. stereology and neuromorphometry; equipment for fluorescent *in situ* hybridization (FISH) and cytogenetics; gel-electrophoresis, autoradiography, etc.

Division for Animal Care & Use

Animal Care and Use Facility consists of sterilization unit, rooms for animals and accessory spaces (storage, washing, clean and un-clean corridors) as well as laboratory for animal experiments. The total surface is 297,41 m². Each housing unit has the possibility of individual temperature adjustments through heaters installed into the ventilation channel and thermostats within the unit itself. There is also an option of automatic turning lights on and off through the timer located within the unit. Air humidifying is done through the air humidifiers located in the each unit. The space is air conditioned (unit capacity of 6.400 mw/h), with the possibility to regulate the temperature of the air introduced in the facility. The facility's ventilation system is capable of performing 15 air exchanges in an hour within the housing units, and 10 air exchanges in other parts of the facility.

On the 3rd July 2013 the Animal Facility obtained the official approval of the Croatian Ministry of Agriculture for breeding and using mice and rats for experimental purposes, with capacity for breeding of 600 mice and 100 rats and 1.200 mice and 100 rats for experiments. Therefore, the Animal Facility and School of Medicine are listed in the official registry of the Croatian Ministry of Agriculture. The Head of the Division for Animal Care and Use is Professor Nataša Jovanov-Milošević, who is also Responsible Officer for the animal rights

fakultet upisani u upisnik Ministarstva. Voditelj nastambe je prof. dr. sc. Nataša Jovanov-Milošević, koja je ujedno i odgovorna osoba za zaštitu životinja na cijelom Medicinskom fakultetu. U nastambi se trenutno koristi više od 1.000 miševa te pedesetak štakora (soj Wistar). Transgenične linije miševa proizvedene su i dovezene iz Max Planck Instituta u Göttingenu: Heterozygous for Stam 2Gt1Gaj; Heterozygous for Klf8Gt1Gaj; Heterozygous for NollGt1Gaj. Transgenične linije proizvedene i dovezene iz Kanada (Jasna Križ, Université Laval, Québec) su: Heterozygous for TLR2, Heterozygous for GAP43. Srođene (inbred) loze kupljene od The Jackson Laboratory su: Homozygous for Tlr2<tm1Kir; Homozygous for Tg(Thy1-YFP)16Jrs; Hemizyous for Tg(Thy1-YFP)2Jrs; C57Bl/6NCrl, te CD1. Soj miševa PTX 64 Black kupljen je od kompanije Charles River.

protection at the entire School of Medicine. At present, we use more than 1.000 mice and 50 Wistar rats. Some transgenic mouse lines were produced and purchased from Max Planck Institute in Göttingen: Heterozygous for Stam2 Gt1Gaj; Heterozygous for Klf8 Gt1Gaj; Heterozygous for Noll Gt1Gaj. Other lines are imported from Canada (Jasna Križ, Université Laval, Quebec) - Heterozygous for TLR2, Heterozygous for GAP43. Inbred lines were purchased from The Jackson Laboratory (Homozygous for Tlr2<tm1Kir; Homozygous for Tg(Thy1-YFP)16Jrs; Hemizyous for Tg(Thy1-YFP)2Jrs; C57Bl/6NCrl; and CD1). Finally, line PTX 64 Black was purchased from Charles River.

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Zagreb research collection of human brains for developmental neurobiologists and clinical neuroscientists

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ABSTRACT The aim of this paper was to offer for the first time a selective and systematic description of the «Zagreb Neuroembryological Collection» of human brains and to illustrate the major results of our research team. Throughout these 16 years of continuous and systematic research, we have applied different techniques for demonstrating the cytoarchitectonics (Nissl staining), neuronal morphology (Golgi impregnation), synaptogenesis (EM analysis), growing pathways (acetylcholinesterase histochemistry) and transmitter-related properties of developing neuronal populations (immunocytochemistry and acetylcholinesterase histochemistry) on several hundred human brains ranging in age from the 5th week post-conception to 90 years. The combination of classical and modern research techniques applied to the constantly growing developmental collection, as well as the continuous evaluation of our data in the light of experimental work in non-human primates, has led to the discovery of an early synaptogenesis within the human cortical anlage and hitherto undescribed transient subplate zone; our results also provided the first comprehensive evidence concerning the timing and pattern of development of afferent fiber systems in the human cortex. All this enabled us to offer a well-documented and coherent reconstruction of major histogenetic events in the human brain. We concluded that structural remodeling and reorganization of the brain, from the transient patterns of the fetal organization through the postnatal phase of transient overproduction of circuitry elements to the final maturation, is the crucial principle of development. Fetal neuronal elements (afferents, synapses and postsynaptic neurons) display transient patterns of laminar, vertical and modular organization and transient cellular interactions and competition in the subplate zone are crucial for the formation of cortical connections. The elucidation of the nature and timing of these histogenetic reorganizational events in the human brain represents the first step towards determining the neurobiological basis of the emergence of behavior, neural functions and cognition in human fetuses, infants and children, which takes place during perinatal and early postnatal life.

KEY WORDS: human brain, development, collection, cerebral cortex, transient

Introduction

Many substantial facts about the development of the human brain have been discovered through the study of valuable material from different neuroembryological collections. For example, the careful analysis, by different research groups, of brains from the Yakovlev Collection has resulted in a corpus of data on the development of early as well as later stages of human brain development (see Kretschmann et al., 1982).

The senior author decided to establish the Zagreb Neuroembryological Collection of human brains during his involvement in intensive research carried out in collaboration with Drs. Mark Moliver and Hendrik Van der Loos at The Johns Hopkins

University in Baltimore from 1972 to 1974. The combination of classical morphological and descriptive-topographical data on human brain development (His, 1904; Hochstetter, 1919; Economo and Koskinas, 1925) with modern Golgi (Poliakov, 1979) and electron microscope analysis (Moliver et al., 1973; Kostovic and Moliver, 1974) has led to the discovery of an early synaptogenesis within the human cortical anlage as well as to the delineation of the hitherto undescribed and essential compartment of the telencephalic wall and cortical anlage – the subplate zone (Kostovic and Moliver, 1974; Kostovic and Rakic, 1980, 1990). The development of a new experimental approach to the analysis of primate brain development (Rakic and Goldman-Rakic, 1985) resulted in new ideas and concepts about histogenetic events (especially proliferation and

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Slika 18

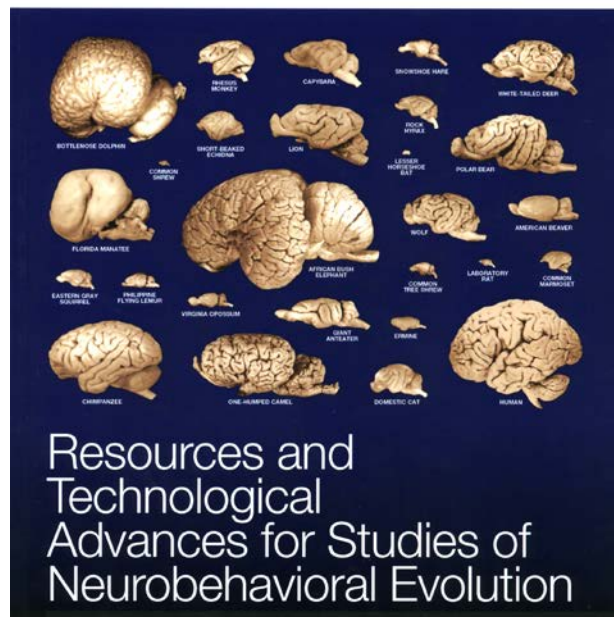
Prvi prikaz i katalog Zagrebačke zbirke mozгова iz 1991. godine.

Figure 18

First overview and catalogue of the Zagreb brain collection published in 1991.

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Resources and Technological Advances for Studies of Neurobehavioral Evolution

ISSUE EDITORS

John Irwin Johnson

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Slika 19

Novi, dopunjeni prikaz i katalog Zagrebačke zbirke mozгова iz 2011. godine.

Figure 19

New and updated overview and catalogue of the Zagreb brain collection published in 2011.

Zagrebačka zbirka mozgova – Zagrebačka neuroembriološka zbirka

Ovu zbirku fetalnih i odraslih ljudskih mozgova utemeljio je Ivica Kostović 1974. godine, a danas se sastoji od 1.331 fetalnog i odraslog ljudskog mozga (uključujući 629 fetalnih, 322 dječjih i 380 odraslih mozgova). Stoga zbirka pokriva cijeli prenatalni i postnatalni ljudski vijek, to jest od mozga zametka starog pet tjedana nakon začeća do mozga 90 godina stare osobe.

Zbirka i njezin katalog prvi puta su međunarodnoj javnosti prikazani još 1991. godine (Slika 18), a nedavno smo objavili i bitno dopunjen prikaz i katalog u posebnom broju časopisa „Annals of the New York Academy of Sciences“ u kojem su pod naslovom „Resources and Technological Advances for Studies of Neurobehavioral Evolution“ prikazane sve vodeće svjetske zbirke mozgova (Slika 19). Uzorci moždanog tkiva čuvaju se fiksirani u aldehidnim otopinama, a više od 100.000 histoloških preparata obojenih različitim klasičnim i modernim metodama čuvaju se u posebnoj prostoriji (Slika 21). Posljednjih nekoliko godina intenzivno radimo na digitalizaciji tih histoloških preparata uz pomoć skenera za virtualnu mikroskopiju Hamamatsu Nanozoomer (Slika 20), tako da dio zbirke (i cijeli njezin katalog)

Zagreb Collection of Human Brains – Zagreb Neuroembryological Collection

The Zagreb Collection of developing and adult human brains was founded in 1974 by Ivica Kostović and consists of 1.331 developing and adult human brains, including 629 fetal, 322 children, and 380 adult brains. Thus, the collection covers the entire human prenatal and postnatal lifespan, from the fifth postconceptional week human embryonic brain to the 90-year-old adult brain.

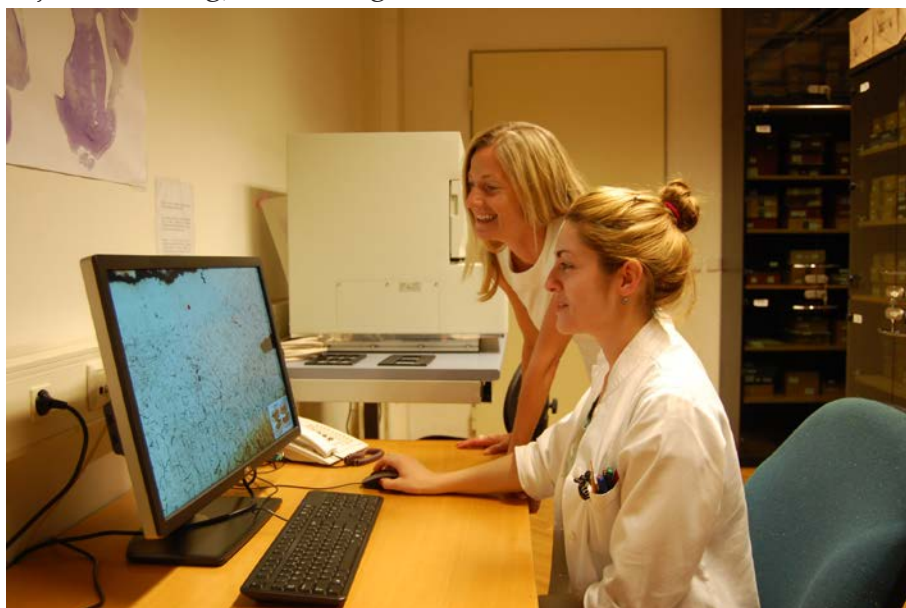
The Collection and its catalogue were first presented to the international community in 1991 (Fig. 18.), and recently significantly updated version of the Collection and its catalogue was published in the special issue of the journal “Annals of the New York Academy of Sciences” under the title “Resources and Technological Advances for Studies of Neurobehavioral Evolution”. In this special issue all leading brain collections in the World were promoted (Fig. 19.). The samples of the brain tissue are stored fixed in aldehyde solutions, and more than 100,000 histological slides stained using various classical and modern methods are kept in a separate room (Fig. 21.). In the last few years, we are actively working on the digitalization of these histological slides using Hamamatsu Nanozoomer scanner

Slika 20

Željka Krsnik i Ana Jagušć pripremaju digitalizirani online katalog histoloških preparata Zagrebačke zbirke, koristeći skener Hamamatsu za virtualnu mikroskopiju.

Figure 20

Željka Krsnik and Ana Jagušć preparing digitized online catalogue of histological sections of the Zagreb Brain Collection using Hamamatsu Nanozoomer scanner for virtual microscopy.



**Slika 21**

Zagrebačka zbirka mozgova (prizemlje – čuvanje obojenih histoloških preparata).

Figure 21

The Zagreb Brain Collection (ground floor – storage room for processed histological slides).

napokon postanu izravno dostupni svjetskoj znanstvenoj javnosti (katalog + digitalizirani preparati na mrežnim stranicama HIIM-a). Ova zbirka je jedna od najvećih zbirki fetalnih ljudskih mozgova na svijetu, a njena ključna prednost u usporedbi s najpoznatijim takvim zbirkama (Yakovlev Collection, Carnegie Collection) jest da se naša zbirka i dalje dopunjava novim uzorcima, obojenim novim metodama.

Zbirka služi kao ključni resurs s dodanom međunarodnom vrijednošću (usporediv sa zbirkom fosilnih ostataka neandertalaca u Krapini i Vindiji) za brojne specifično usmjerene znanstvene projekte, a omogućila je nekoliko ključnih doprinosa svjetskoj znanosti u području razvojne neurobiologije moždane kore sisavaca (osobito čovjeka i majmuna) – primjerice, otkriće prolazne fetalne „subplate“ zone i rane bilaminarne sinaptogeneze u embrionalnom i fetalnom ljudskom mozgu, te prvi opis rastućih aferentnih putova u fetalnom ljudskom telencefalonu. Zbirka je također središnji resurs za stalno rastuću mrežu međunarodne suradnje i predstavljala je polaznu točku za mnoge mlade istraživače koji sada

for virtual microscopy (Fig. 20.) in order to finally make the part of the Collection (and its entire catalogue) directly available to the entire international scientific community (catalogue and digitized histological slides accessed through CIBR's internet pages). This Collection is the one of the largest collections of developing human brains in the World, and its key advantage, in comparison with the most famous collections of such type (Yakovlev Collection, Carnegie Collection) is that new brain specimens and new methods are being constantly added into ours collection.

The Collection serves as a key resource, with internationally added value (comparable with the collection of Neanderthal's fossils in Krapina and Vindija), for many focused research projects and has led to several seminal contributions on mammalian cortical development (especially human and monkey), such as the discovery of the transient fetal subplate zone and of early bilaminar synaptogenesis in the embryonic and fetal human cerebral cortex, and the first description of growing afferent pathways in the human fetal telencephalon. The Zagreb Collection also serves as a core resource for ever-growing networks of international collaboration and represents the starting point for many young in-

Slika 22

Istraživačka skupina Zdravko Petanjka snimljena u Laboratoriju za neuromorfometriju 2014. godine: Ana Hladnik, Dora Mandić, Sanja Darmopil, Ivana Bičanić i Domagoj Džaja (Zdravko Petanjek u pozadini).

Figure 22

Research group of Zdravko Petanjek photographed at the Laboratory for neuromorphometry in 2014: Ana Hladnik, Dora Mandić, Sanja Darmopil, Ivana Bičanić, Domagoj Džaja (Zdravko Petanjek at the back).



nastavljaju svoje neovisne znanstvene karijere u vodećim međunarodnim institucijama.

investigators who now pursue independent research careers at leading international institutions.

Sadašnji ustroj Hrvatskog instituta za istraživanje mozga

Current organization of the Croatian institute for brain research

Sadašnji ustroj HIIM-a je uspostavljen odlukom dekana Medicinskog fakulteta (na prijedlog direktora HIIM-a – voditelji Zavoda i Odsjeka), a voditelje laboratorija (uz suglasnost pročelnika Odsjeka) imenovao je direktor HIIM-a odlukom od 20. ožujka 2013. Dugogodišnji direktor HIIM-a, akademik Ivica Kostović, umirovljen je 2013. godine, ali je potom izabran u počasno zvanje *professor emeritus* na Sveučilištu u Zagrebu pa je i dalje aktivan kao počasni direktor HIIM-a, savjetnik dekana za znanost i voditelj jednog projekta Hrvatske zaklade za znanost. Trenutno je Mario Vukšić imenovani obnašatelj dužnosti direktora HIIM-a, a izbor novog direktora biti će dovršen do kraja 2015. godine.

The current organization of the CIBR and Heads of the Department and Divisions are appointed and approved by the decree of the Dean of the School of Medicine (based on the proposal of the CIBR's director). The Heads of laboratories (with the prior approval of Division Heads) were appointed by the CIBR's director at 20th March 2013. The long-term CIBR's director, academic Ivica Kostović retired in 2013, but has been awarded the honorary title of professor emeritus at the University of Zagreb. He continues to be active at the CIBR as CIBR's honorary director, scientific advisor to the Dean and Principal Investigator of the one research grant supported by Croatian Science Foundation. The current acting director of the CIBR is Professor Mario Vukšić, and the election process for the new CIBR's director will be completed by the end of 2015.

Temeljna ustrojbeno jedinica HIIM-a je Zavod za neuroznanost, sastavljen od 11 Odsjeka s ukupno 26 laboratorija. Pored toga, u zgradi djeluje i nekoliko samostalnih („pridruženih“) laboratorija (voditelji su: Melita Šalković Petrišić, Predrag Sikirić i Danka Grčević).

The core organizational unit of the CIBR is Department of Neuroscience, composed of 11 Divisions with the total of 26 laborato-



Slika 23

Dugogodišnja voditeljica Odsjeka za elektronsku mikroskopiju Ljiljana Kostović-Knežević, sa svojim učenicima i nasljednicima (snimljeno 1998.). Srećko Gajović, laboratorijska tehničarka Sandra Grgić, Ljiljana Kostović-Knežević, Marija Čurlin i Dinko Mitrečić.

Figure 23

Long-term head of the Division for electron microscopy Ljiljana Kostović-Knežević with her students and successors (photographed in the 1994). Srećko Gajović, Laboratory technician Sandra Grgić, Ljiljana Kostović-Knežević, Marija Čurlin and Dinko Mitrečić.

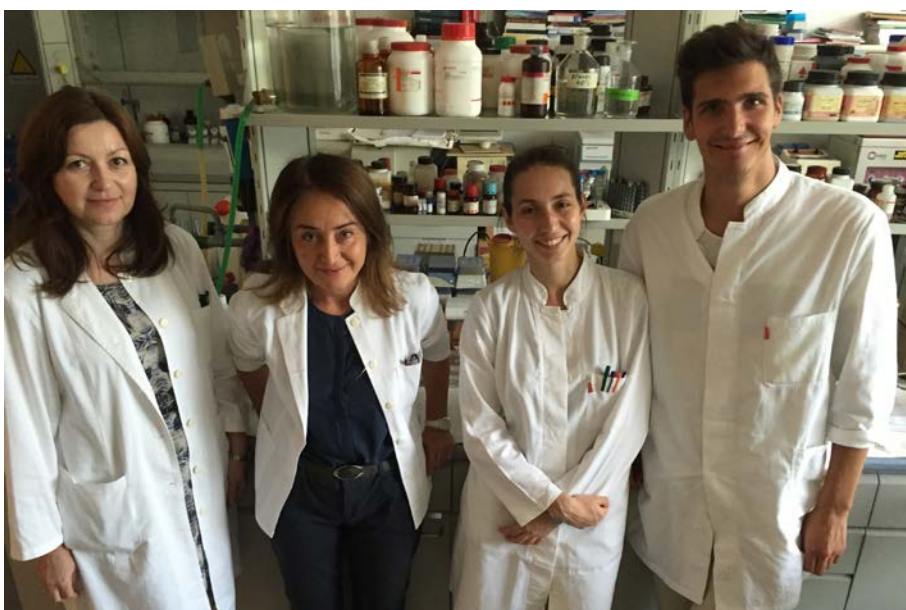


Slika 24

Srećko Gajović i Dinko Mitrečić sa suradnicima uz novopristigli eksperimentalni MRI uređaj za snimanje malih glodavaca (ljetu 2015.).

Figure 24

Srećko Gajović and Dinko Mitrečić with their associates in front of newly arrived experimental MRI device for imaging small rodents (summer 2015)



Slika 25

Dora Višnjić sa suradnicima (Laboratorij za stanične kulture i kulture tkiva): Marijana Andrijašević, Dora Višnjić, Vilma Dembitz i Hrvoje Lalić.

Figure 25

Dora Višnjić with her associates (Laboratory for cell and tissue cultures): Marijana Andrijašević, Dora Višnjić, Vilma Dembitz and Hrvoje Lalić.

Imena voditelja ustrojbenih jedinica su navedena u zagradama – u pogledu hijerarhije naziva čelnika ustrojbenih jedinica, na čelu Zavoda je predstojnik, Odsjeka pročelnik, a laboratorija voditelj. Voditelji Odsjeka, uz direktora HIIM-a i predstojnika Zavoda za neuroznanost te predstavnika Pridruženih laboratorija (Melita Šalković-Petrišić) ujedno čine i Stručno vijeće HIIM-a u užem sastavu (u širi sastav ulaze i voditelji laboratorija).

ZAVOD ZA NEUROZNANOST (Goran Šimić)

Odsjek za razvojnu neuroznanost (Miloš Judaš) – Slika na naslovnici ovog poglavlja.

Laboratorij za neurohistologiju i kemijsku anatomiju (Mario Vukšić)

Laboratorij za razvojnu neuropatologiju (Goran Šimić) – Slika 37.

Laboratorij za neuromorfometriju (Zdravko Petanjek) – Slika 22.

Laboratorij za imunohistokemiju i *in situ* hibridizaciju (Nataša Jovanov Milošević) – Slike na prvoj stranici ovog poglavlja.

Laboratorij za konfokalnu mikroskopiju (Mario Vukšić) – Slika na prvoj stranici poglavlja.

Laboratorij za razvojnu molekularnu neurobiologiju (Miloš Judaš i Nenad Šestan)

Laboratorij za neurorazvojnu analizu RNA (Željka Krsnik)

Odsjek „Zagrebačka neuroembriološka zbirka i banka tkiva“ (Zdravko Petanjek)

Laboratorij za digitalnu obradu preparata Zagrebačke neuroembriološke zbirke (Željka Krsnik)

Odsjek za slikovni prikaz mozga (Marko Radoš) – Slika 27.

Laboratorij za funkcionalno oslikavanje mozga (Milan Radoš).

Odsjek za neurogenetiku, citogenetiku i razvojnu genetiku (Srećko Gajović) – Slika 24.

Beside these laboratories, in the building are also located several independent (“associated”) laboratories (Heads: Melita Šalković Petrišić, Predrag Sikirić, Danka Grčević).

The names of all Heads of organizational units are in brackets. The CIBR’s Expert Council, in its core constitution, consists of all Heads of Divisions, the CIBR’s Director, the Head of the Department of Neuroscience and the representative of the associated laboratories (Melita Šalković Petrišić), while in its expanded form, all Heads of laboratories are also included.

DEPARTMENT OF NEUROSCIENCE (Goran Šimić)

Division of developmental neuroscience (Miloš Judaš) – Figure on the frontpage of this chapter.

Laboratory for neurohistology and chemical anatomy (Mario Vukšić)

Laboratory for developmental neuropathology (Goran Šimić) – Fig. 37.

Laboratory for neuromorphometry (Zdravko Petanjek) – Fig. 22.

Laboratory for immunohistochemistry and *in situ* hybridization (Nataša Jovanov-Milošević) – Figure on the frontpage of this chapter.

Laboratory for confocal microscopy (Mario Vukšić) – Figure on the frontpage of this chapter.

Laboratory for developmental molecular neurobiology (Miloš Judaš & Nenad Šestan)

Laboratory for developmental analysis of RNA (Željka Krsnik) - Fig. 20.

Division “The Zagreb Neuroembryological Collection and Brain Bank” (Zdravko Petanjek)

Laboratory for the digitization of the Zagreb Neuroembryological Collection’s slides (Željka Krsnik) - Fig. 20.



Slika 26 (lijevo)
Hrvoje Banfić, predstojnik Odsjeka za biokemiju i molekularnu biologiju.

Figure 26 (left)
Hrvoje Banfić, Head of the Division for biochemistry and molecular biology.

Slika 27 (lijevo)
Marko Radoš, pročelnik Odsjeka za slikovni prikaz mozga.

Figure 27 (left)
Marko Radoš, Head of the Division for neuroimaging.

Slika 28 (lijevo)
Aleksandra Sindić, voditeljica Laboratoriza za neurofiziologiju i „whole cell patch-clamp“

Figure 28 (left)
Aleksandra Sindić, Head of the Laboratory for neurophysiology and “whole cell patch-clamp”.

Slika 29 (lijevo)
Neven Henigsberg, pročelnik Odsjeka za neuropsihofarmakologiju i farmakologiju ponasanja.

Figure 29 (left)
Neven Henigsberg, Head of the Division for neuropsychopharmacology and pharmacology of the behaviour.

Slika 30 (desno)
Božo Krušlin, pročelnik Odsjeka za kliničku primjenu neuroznanosti.

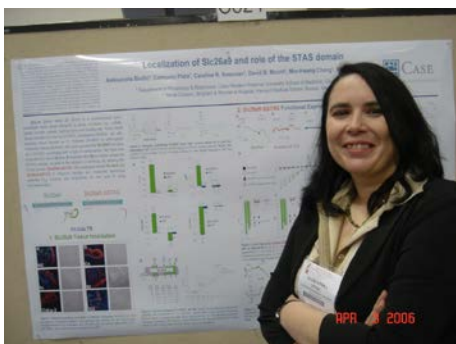
Figure 30 (right)
Božo Krušlin, Head of the Division for clinical research in neuroscience.

Slika 31 (desno)
Lukrecija Brečević, dugogodišnja voditeljica Laboratorija za molekularnu citogenetiku

Figure 31 (right)
Lukrecija Brečević long-term Head of the Laboratory for molecular cytogenetics.

Slika 32 (desno)
Vlatka Mejaški-Bošnjak, dugogodišnja voditeljica Laboratorija za razvojnu neurologiju

Figure 32 (right)
Vlatka Mejaški Bošnjak, long-term head of the Laboratory for developmental neurology.



Slika 33

Mirna Kostović-Srzentić, voditeljica Laboratorija za razvojnu kognitivnu psihologiju, na slici su i (slijeva) Milivoj Veličković, Paško Rakić i Ivica Kostović.

Figure 33

Mirna Kostović Srzentić, Head of the Laboratory for developmental cognitive psychology.



Slika 34

Članice Laboratorija za razvojnu neurolingvistiku (HIIM, 2013.): Maja Cepanec, Draženka Blaži, Blaženka Brozović, Sanja Šimleša, Jasmina Ivšac Pavliša i njihova dugogodišnja voditeljica i mentorica Marta Ljubešić.

Figure 34

Members of the Laboratory for the developmental neurolinguistics (CIBR, 2013): Maja Cepanec, Draženka Blaži, Blaženka Brozović, Sanja Šimleša, Jasmina Ivšac Plavšić and their long-term leader and mentor Marta Ljubešić.



Slika 35

Vera Folnegović Šmalc, dugogodišnja voditeljica Laboratorija za neurofarmakologiju ponašanja (snimljeno tijekom Neurobiološkog simpozija u prosincu 1995.). Vera Folnegović Šmalc, Branimir Jernej, Marin Bulat i Živan Deanović.

Figure 35

Vera Folnegović Šmalc, long-term Head of the Laboratory for neuropharmacology of behaviour (photographed during Neurobiological Symposia in the December of 1995.). Vera Folnegović Šmalc, Branimir Jernej, Marin Bulat and Živan Deanović.



Laboratorij za neurogenetiku i razvojnu genetiku (Srećko Gajović)

Laboratorij za molekularnu citogenetiku (Lukrecija Brečević) – Slika 31.

Laboratorij za medicinsku genetiku (Nina Canki Klain – u mirovini od 2015.)

Laboratorij za matične stanice (Dinko Mitrečić)

Odsjek za elektronsku mikroskopiju (Dinko Mitrečić) – Slika 24.

Odsjek za biokemiju i molekularnu biologiju (Hrvoje Banfić) – Slika 26.

Laboratorij za druge glasnike (Hrvoje Banfić)

Laboratorij za radioaktivne nuklide (Vladiana Crljen).

Laboratorij za stanične kulture i kulture tkiva (Dora Višnjić) – Slika 25.

Laboratorij za molekularnu neurobiologiju i neurokemiju (Svjetlana Kalanj Bognar).

Laboratorij za neuroonkologiju (Nives Pećina Šlaus).

Odsjek za neurofiziologiju (Marijan Klarica) – Slika na prvoj stranici ovog poglavlja.

Laboratorij za neurofiziologiju i „whole cell patch-clamp“ (Aleksandra Sindić) – Slika 28.

Laboratorij za neuropatofiziologiju likvora (Marijan Klarica)

Laboratorij za eksperimentalnu neurokirurgiju (Pavle Miklić – u mirovini od 2015.)

Odsjek za neuropsihofarmakologiju i farmakologiju ponašanja (Neven Henigsberg) – Slika 29.

Laboratorij za neurofarmakologiju ponašanja (Vera Folnegović Šmalc i Petra Kalember).

Odsjek za kliničku primjenu neuroznosti (Božo Krušlin) – Slika 30.

Odsjek za laboratorijske životinje (Nataša Jovanov Milošević)

Odsjek za razvojnu kognitivnu neurozna-

Division for Brain imaging (Marko Radoš) – Fig. 27.

Laboratory for the functional magnetic resonance imaging (Milan Radoš)

Division for neurogenetics, cytogenetics and developmental genetics (Srećko Gajović) – Fig. 24.

Laboratory for neurogenetics and developmental genetics (Srećko Gajović)

Laboratory for molecular cytogenetics (Lukrecija Brečević) – Fig. 31.

Laboratory for medical genetics (Nina Canki Klain – retired since 2015)

Laboratory for Stem Cells (Dinko Mitrečić)

Division for electron microscopy (Dinko Mitrečić) – Fig 24.

Division for biochemistry and molecular biology (Hrvoje Banfić) – Fig. 26.

Laboratory for second messengers (Hrvoje Banfić)

Laboratory for radioactive nuclides (Vladiana Crljen)

Laboratory for cell and tissue cultures (Dora Višnjić) – Fig. 25.

Laboratory for molecular neurobiology and neurochemistry (Svjetlana Kalanj Bognar)

Laboratory for neurooncology (Nives Pećina Šlaus)

Division for neurophysiology (Marijan Klarica) – Figure on the frontpage of this chapter.

Laboratory for neurophysiology and “whole cell patch-clamp” (Aleksandra Sindić) – Fig. 28.

Laboratory for neuropathophysiology of CSF (Marijan Klarica)

Laboratory for experimental neurosurgery (Pavle Miklić – retired since 2015)

Division for neuropsychopharmacology and pharmacology of behaviour (Neven Henigsberg) – Fig. 29.

nost (Neven Henigsberg)

Laboratorij za razvojnu neurolingvistiku (Maja Capanec) – Slika 34.

Laboratorij za razvojnu kognitivnu psihologiju (Mirna Kostović-Srzić) – Slika 33.

Laboratorij za razvojnu neurologiju (Vlatka Mejaški Bošnjak – u mirovini od 2015.) – Slika 32.

Laboratorij za EEG i evocirane potencijale (Goran Ivkić)

Pridruženi laboratoriji na HIIM-u (Melita Šalković-Petrišić – status voditelja Odsjeka)

Pionirska uloga u razvoju struke i javne promičbe neuroznanosti

U Institutu je sjedište Hrvatskog društva za neuroznanost, koje je osnovano u prosincu 2000. godine. Prvi predsjednik Društva bio je *professor emeritus* Marin Bulat (tri godine), a od tada do danas predsjednik je akademik Ivica Kostović. Miloš Judaš bio je tajnik Društva od 2000. do 2012. godine, a od tada do danas je potpredsjednik Društva.

Društvo je 2002. postalo članica glavne europske organizacije FENS (Federation of European Neuroscience Societies) i glavne svjetske organizacije IBRO (International Brain Research Organization). Društvo je do sada organiziralo četiri Hrvatska kongresa neuroznanosti (a peti kongres će se održati od 17. do 19. rujna 2015. godine u Splitu) i petnaest godina za redom organizira Tjedan mozga u Hrvatskoj. Zahvaljujući toj aktivnosti, Društvo je punopravni član svjetskih organizacija Dana Alliance for Brain Initiatives i European Dana Alliance & Brain Campaign.

Od 2012. godine u Institutu je i sjedište Hrvatskog vijeća za mozak (Croatian Brain Council) koje je dio europske mreže takvih organizacija (European Brain Council). Predsjednik Hrvatskog vijeća za mozak je Ivica Kostović, dopredsjednica Vida De-

Laboratory for neuropharmacology of behaviour (Vera Folnegović Šmalc and Petra Kalember).

Division for clinical application of neuroscience (Božo Krušlin) – Fig. 30.

Division for animal care and use (Nataša Jovanov-Milošević)

Division for developmental cognitive neuroscience (Neven Henigsberg)

Laboratory for developmental neurolinguistics (Maja Capanec) – Fig. 34.

Laboratory for developmental cognitive psychology (Mirna Kostović-Srzić) – Fig. 33.

Laboratory for developmental neurology (Vlatka Mejaški Bošnjak – retired since 2015.) – Fig. 32.

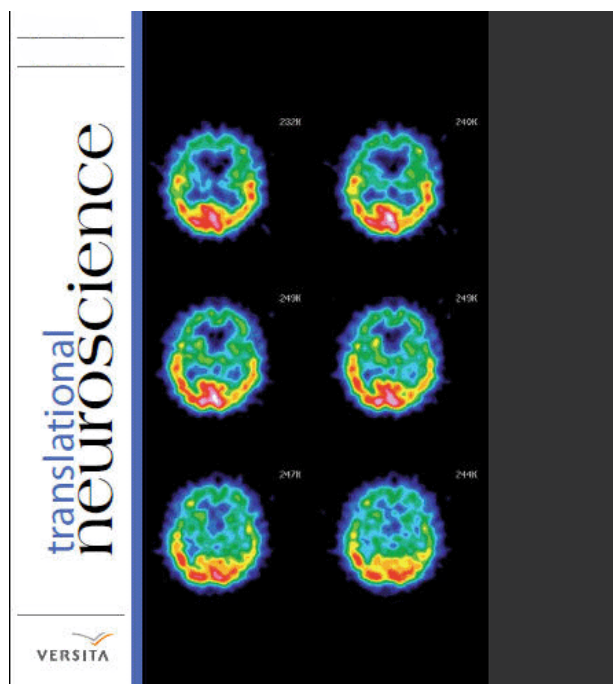
Laboratory for EEG and evoked potentials (Goran Ivkić)

Associated laboratories at the CIBR (Melita Šalković Petrišić – same status as a Head of Division)

The pioneering role in the development of the profession and public promotion of the neuroscience

The CIBR is the seat of the Croatian Society for Neuroscience (CSFN), founded in the December 2000. The first president of the CSFN was professor emeritus Marin Bulat (for three years), followed by academic Ivica Kostović (to date). The secretary of the CSFN in the period 2000 – 2012 was Miloš Judaš and since 2012 to date has been the vice-president of CSFN.

In 2002 the CSFN became member of the main European neuroscience organization the FENS (Federation of European Neuroscience Societies) and main World organization the IBRO (International Brain Research Organization). The CSFN has organized four neuroscience meetings (and fifth congress will be held in Split from 17th to 19th September 2015.). In the last



Slika 36

Naslovnica prvog broja časopisa „Translational Neuroscience“.

Figure 36

The first cover page of the journal “Translational Neuroscience”.

marin, a izvršni tajnik Dinko Mitrečić.

Međunarodni časopis „Translational Neuroscience“

U Institutu je također sjedište međunarodnog časopisa „Translational Neuroscience“. Časopis je pokrenut 1. siječnja 2010. kao međunarodni i kompetitivno recenzirani (peer-reviewed) časopis. Glavni i odgovorni urednik časopisa je prof. dr. sc. Goran Šimić (Slika 37), a stariji savjetodavni urednik je Patrick R. Hof (Mount Sinai School of

fifteen years, the CSFN annually organizes Brain Awareness Week. Hence, the CSFN is a full member of the Dana Alliance for Brain Initiatives and European Dana Alliance & Brain Campaign.

In 2012 the CIBR also became the seat of the Croatian Brain Council, which is a part of the European network of similar organisations (European Brain Council). The president of the Croatian Brain Council is academic Ivica Kostović, vice-president is Vida Demarin and executive secretary is Dinko Mitrečić.



Slika 37

Goran Šimić, predstojnik Zavoda za neuroznanost, voditelj Laboratorija za razvojnu neuropatologiju i glavni urednik međunarodnog časopisa „Translational Neuroscience“.

Figure 37

Goran Šimić, Head of the Department of Neuroscience, Head of the Laboratory for developmental neuropathology and the Editor-in-Chief of international peer-reviewed journal “Translational Neuroscience”.

Medicine, U.S.A.). U uredničkom odboru su, uz brojne ugledne međunarodne znanstvenike, sljedeći znanstvenici našeg Instituta: Ivica Kostović, Miloš Judaš, Svjetlana Kalanj-Bognar, Marijan Klarica, Neven Henigsberg i Vesna Lukinović-Škudar.

Izdavači časopisa isprava su bili Versita i Springer Verlag (Slika 36). Od 1. siječnja 2015. godine, novi vlasnik časopisa, Walter de Gruyter GmbH, odlučio je promijeniti izdavački model u model otvorenog pristupa (Open Access). Mrežna stranica časopisa je <http://www.degruyter.com/view/j/tnsci>.

Prvi čimbenik odjeka časopisa je bio 0.482 (u 2013., za 2012. godinu). Sljedeće godine se povećao na 0.716 (u 2014., za 2013. godinu), a nedavno je ponovno porastao na 1.319 (u 2015., za 2014. godinu). Broj citata radova iz tog časopisa do sada je (prema Web of Science na dan 15. srpnja 2015. godine) ukupno 424. Prema SCImago rangiranju časopisa (www.scimagojr.com), Translational Neuroscience je za područje neuroznanosti u 2014. godini bio na 84. mjestu (treća kvartila, Q3) od 135 časopisa u području neuroznanosti. Obzirom da godišnje objavljujemo 4 broja (issue) te da je do sada izašlo tek 6 svezaka (volumes) s ukupno 225 objavljenih članaka, vjerujemo da će se dosadašnji pozitivni trend porasta citiranosti i čimbenika odjeka (impact factor) nastaviti.

Časopis je danas indeksiran u sljedećim bazama podataka: Web of Science; EBSCO Discovery Service; Elsevier – EMBASE; Elsevier – SCOPUS; Google Scholar; SCImago (SJR); Thomson Reuters – Biological Abstracts, BIOSIS Previews, Journal Citation Reports/Science Edition, Science Citation Index Expanded; te još desetak drugih baza.

International journal “Translational Neuroscience”

The CIBR is also the seat of the international journal “Translational Neuroscience”. The journal was initiated at the 1st January 2010 as an international, peer-reviewed journal. The Editor-in-Chief of the journal is Professor Goran Šimić (Fig. 37.) and Senior Advisory Editor is Patrick R. Hof (Mount Sinai School of Medicine, U.S.A.). The Editorial Board is comprised of many prominent international scientist among which are the following CIBR’s scientists: Ivica Kostović, Miloš Judaš, Svjetlana Kalanj-Bognar, Marijan Klarica, Neven Henigsberg and Vesna Lukinović Škudar. The original publishers of the journal were Versita and Springer Verlag (Fig. 36.). Since 1st January 2015, the new publisher of the journal, Walter de Gruyter GmbH, has decided to change the publishing model into Open Access model. Web page of the journal is <http://www.degruyter.com/view/j/tnsci>.

The first impact factor of the journal was only 0.482 (in the 2013 for year 2012). In the following year the IF increased at 0.716 (in the 2014 for year 2013), and recently has again increased at 1.319 (in 2015. for year 2014). The number of total journal’s citations (according to the Web of Science from the 15th July 2015) is 424. According to the SCImago journal rankings (www.scimagojr.com), Translational Neuroscience was at the 84 place out of 135 journal in 2014 in the field of neuroscience (third quartile, Q3). Since only 4 issues per year are published, to date there are only 6 volumes with total of 225 papers published, we believe that current positive rising trends for the number of citations and impact factor will continue in the future.

The journal is currently indexed in the following data bases: Web of Science; EBSCO Discovery Service; Elsevier – EMBASE; Elsevier – SCOPUS; Google Scholar; SCImago (SJR); Thomson Reuters – Biological Ab-

**Sestrinske ustanove (ustanove-kćeri):
Centar za kliničku primjenu neuroznanosti i Poliklinika „Neuron“**

Na drugom katu zgrade HIIM-a smještene su dvije sestrinske ustanove, Centar za kliničku primjenu neuroznanosti (CKPN – osnovan 1998.) i Poliklinika „Neuron“ (osnovana 1999.). Obje ustanove su osnovane s ciljem da pospješe rad Instituta u području kliničke i translacijske neuroznanosti, a u njihovim statutima jasno je propisana njihova tijesna suradnja s Institutom i klinikama Medicinskog fakulteta u izvođenju znanstvene, nastavne i stručne aktivnosti.

Centar za kliničku primjenu neuroznanosti (CKPN; Zagreb, Šalata 10 i Šalata 12 – zgrada HIIM-a) je osnovan na neodređeno vrijeme 1998. godine. Osnivač Centra je Medicinski fakultet Sveučilišta u Zagrebu. Odluku o osnivanju Centra za kliničku primjenu neuroznanosti donijelo je Fakultetsko vijeće Osnivača 14. srpnja 1998. Upravno vijeće Sveučilišta u Zagrebu je 16. srpnja 1998. dalo suglasnost na odluku osnivača o osnivanju Centra. Centar je upisan u Upisnik znanstvenoistraživačkih pravnih osoba Ministarstva znanosti i tehnologije Republike Hrvatske pod rednim brojem 0220 u znanstvenom području medicinskih znanosti rješenjem Ministarstva znanosti i tehnologije Republike Hrvatske od 22. srpnja 1998. godine. Centar je stekao svojstvo pravne osobe upisom u sudski registar ustanova, kod Trgovačkog suda u Zagrebu 16. rujna 1998. Državni zavod za statistiku Republike Hrvatske razvrstao je Centar prema Nacionalnoj klasifikaciji djelatnosti 26. listopada 1998. za sljedeću djelatnost: istraživanje i eksperimentalni razvoj u prirodnim znanostima (brojčana oznaka podrazreda: 73101).

Centar za kliničku primjenu neuroznanosti i Medicinski fakultet Sveučilišta u Zagrebu sklopili su dana 20. svibnja 1999. ugovor kojim Fakultet (kao davatelj na korištenje) i Centar (kao korisnik) uređuju uzajamne odnose u svezi korištenja poslovnih pros-

tracts, BIOSIS Previews, Journal Citation Reports/Science Edition, Science Citation Index Expanded; and more than dozen other data bases.

Sister institutions: Centre for clinical research in neuroscience (CCRN) and diagnostic unit „Polyclinic Neuron“

Two CIBR's sister institutions Centre for Clinical Research in Neuroscience (CCRN – founded in 1998) and Diagnostic unit “Polyclinic Neuron” (founded 1999) are located at the CIBR's building second floor. Both institutions were founded with a goal to improve CIBR's work in the field of clinical and translational neuroscience. Theirs close cooperation with the CIBR and clinics of the School of Medicine in performing scientific, professional and educational activities is clearly defined in their respective statutes.

Centre for Clinical Research in Neuroscience (CCRN, Zagreb, Šalata 10 and Šalata 12 – CIBR's building) was founded in 1998. The founder of the CCRN is University of Zagreb School of Medicine. The founding act of the Centre for Clinical Research in Neuroscience, was approved by the Assembly of the School of Medicine (14th July 1998). The Governing Council of the University of Zagreb has also approved the founding act (on 16th July 1998.). The Centre is listed in the Registry of the Scientific Research Legal Entities of the Croatian Ministry of Science and Technology under the number 0220 in the scientific field of biomedicine (of 22nd July 1998). The Centre has acquired legal entity rights by registering in the Court's Registry of Institutions, at the Commercial Court in Zagreb (16th September 1998). Croatian Bureau of Statistics has issued the decree (of 26th October 1998), classifying the Centre according to the National Classification of Activities for the following activities: research and experimental development in natural sciences (numerical code of subclass:

torija u zgradu Fakulteta, na adresi Šalata 10 i 12, poradi obavljanja poslova iz registrirane djelatnosti korisnika. Ugovorom je potvrđeno da je Fakultet osnivač Centra i vlasnik zgrade HIIM-a, te da Centar prima na korištenje poslovni prostor ukupne površine od 822,69 m², te da Centar taj prostor (ili dio prostora) može dati na korištenje Poliklinici Neuron ili drugim korisnicima samo uz prethodnu suglasnost Fakulteta. Ugovor je sklopljen na neodređeno vrijeme uz uvjet da Fakultet svake treće godine ima pravo obavljati nadzor namjenskog korištenja i održavanja prostora koji je predmet tog ugovora.

Statutom Centra za kliničku primjenu neuroznanosti (članak 9) njegova djelatnost je definirana ovako:

„Djelatnost Centra je: obavljanje znanstvenog i visokostručnog rada iz znanstvenog područja biomedicine i neuroznanosti; provođenje programa dugoročnog istraživanja s područja neuroznanosti u neurologiji, neuroradiologiji, neurokirurgiji, psihijatriji i srodnim medicinskim granama u suradnji s Hrvatskim institutom za istraživanje mozga i klinikama Medicinskog fakulteta; koordinacija i suradnja s drugim visokim učilištima, kliničkim ustanovama te znanstvenim i nastavnim institucijama u znanstvenom i nastavnom radu; suradnja sa znanstvenim i zdravstvenim ustanovama i institutima u provođenju edukacije; ustrojavanje i izvođenje programa trajnog usavršavanja za zdravstvene i znanstvene djelatnike; davanje stručnih mišljenja i obavljanje medicinskih vještačenja; izdavačka, bibliotečna i informatička djelatnost.“

Nadalje, Statutom (članak 10) je definirano da:

„Centar će ustrojavanje i izvođenje programa trajnog usavršavanja s područja temeljne i kliničke neuroznanosti za zdravstvene i znanstvene djelatnike obavljati u tijesnoj suradnji sa Zavodom za neuroznanost Hrvatskog instituta za istraživanje mozga Medicinskog fakulteta Sveučilišta u Za-

73101). The Centre for Clinical Research in Neuroscience and University of Zagreb School of Medicine have made agreement (of 20th May 1999) that regulates relationship between the School of Medicine (as the provider) and the Centre (as the user) pertaining to the use of business offices in buildings of the School of Medicine located at Šalata 10 and 12, in order to perform registered activities. The agreement has confirmed that the School of Medicine is the founder of the Centre and the owner of the CIBR building, and that the Centre is given to use business office space total surface of 822,69 m², and that the Centre can sublease entire space (or just part of the space) to the Polyclinic “Neuron” or other users with prior approval from the School of Medicine. The agreement was concluded for the indefinite time period, under the condition that the School of Medicine every three years has the right to perform the oversight of how the office spaces in question are used and if they are properly maintained.

The Statute of the Centre for Clinical Research in Neuroscience (article 9) is defining its activity as follows:

“The activity of the Centre is: to perform scientific and professional work in the field of biomedicine and neuroscience; to conduct the long-term research program in the field of neuroscience in the neurology, neuroradiology, neurosurgery, psychiatry and related fields of medicine in cooperation with the Croatian Institute for Brain Research and clinics of the School of Medicine; coordination and cooperation with other institutions of higher education, clinical institutions and scientific and educational institution in scientific and educational activities; cooperation with scientific and health care institutions in education, development and performance of programs of continuous education for health and science professionals, providing expert opinions and conducting medical assessments, publishing, librarian and IT activity.”

Furthermore, the Statute (article 10) has de-

grebu“.

Isto tako, člankom 11. stavak 1., propisano je da:

„Centar se obvezuje da će svoju izdavačku i informatičku djelatnost poglavito, no ne i isključivo, usmjeriti na sljedeća područja aktivnosti: a) izdavanja djela značajnih za odvijanje i unapređenje svih oblika diplomatske i poslijediplomske fakultetske, međufakultetske i sveučilišne nastave u području neuroznanosti, a posebice djela autora s Hrvatskog instituta za istraživanje mozga i drugih ustrojbenih jedinica Osnivača; b) izdavanje djela značajnih za promicanje i tumačenje značaja dostignuća moderne neuroznanosti u domaćoj javnosti; c) izdavanje djela značajnih za promicanje rada i rezultata hrvatskih neuroznanstvenika u međunarodnoj javnosti.“

Napokon, Statutom (članak 28, stavak 2) je također definirano da:

„Upravno vijeće CKPN-a ima predsjednika i četiri člana koje imenuje Osnivač na vrijeme od 4 godine. Tri člana imenuju se iz Hrvatskog instituta za istraživanje mozga, a dva člana iz redova Dekanskog kolegija, od kojih je jedan po položaju prodekan za znanost.“

U proteklom razdoblju (1999. do danas), Centar za kliničku primjenu neuroznanosti uspješno je surađivao s Hrvatskim institutom za istraživanje mozga u izvedbi niza znanstvenih projekata, stručnih aktivnosti te aktivnosti na javnoj promičbi neuroznanosti (primjerice, organizacija Tjedna mozga u Hrvatskoj).

Poliklinika za neurologiju, psihijatriju, radiologiju i neurokirurgiju, patologiju, citogenetiku i laboratorijsku dijagnostiku „Neuron“ (Zagreb, Šalata 12 – zgrada HIIM-a; skraćeni naziv: Poliklinika „Neuron“) upisana je u registru Trgovačkog suda u Zagrebu. Poliklinika je osnovana na neodređeno vrijeme, a osnivač i vlasnik Poliklinike je Centar za kliničku primjenu neuroznanosti, Šalata 12. Statutom Po-

finied that:

“The Centre will carry on the development and execution of continuous education programs in the fields of basic and clinical neuroscience, for health and science professionals in close cooperation with the Department of Neuroscience of the Croatian Institute for Brain Research, University of Zagreb School of Medicine.”

Article 11, paragraph 1 states that:

“The Centre is obligated to focus publishing and IT activity will, particularly but not exclusively, on the following areas: a) publishing of works important for the normal conduct and advancement of all forms of undergraduate and graduate education at the School of Medicine, other faculties and University of Zagreb in the field of neuroscience, with particular emphasis on the works of authors from the Croatian Institute for Brain Research and other departments of the School of Medicine; b) publishing of works important for the promotion and understanding the importance of the modern neuroscience achievements among domestic public; c) publishing of works important for the promotion of work and results of Croatian neuroscientists in the international community.”

Finally, the Statute (article 28, paragraph 2) has also defined that:

“The Governing Council of the CCRN is composed of the president and four members who are appointed by the School of Medicine on the term of four years. Three members are appointed from the Croatian Institute for Brain Research, and two members are appointed from the members of the Dean’s College, and one of those two has to be Vice-dean for science as a part of official duties.”

In the previous period (1999 to date), the Centre for Clinical Research in Neuroscience has successfully collaborated with the Croatian Institute for Brain Research on numerous scientific projects, professional activities, and public promotion of neuro-

liklinike (članak 10) utvrđeno je da:

„Poliklinika svoju djelatnost obavlja u suradnji s Centrom za kliničku primjenu neuroznanosti i Hrvatskim institutom za istraživanje mozga Medicinskog fakulteta Sveučilišta u Zagrebu.“ Istim Statutom (članak 9.) je utvrđeno da je djelatnost Poliklinike:

„Specijalističko-konzilijarna zdravstvena zaštita, dijagnostika i medicinska rehabilitacija, osim bolničkog liječenja, iz specijalističkih područja: neurologije, psihijatrije, radiologije, neurokirurgije, patologije, citogenetike, laboratorijske dijagnostike.“

Poliklinika je također jedna od nastavnih baza Medicinskog fakulteta, jer je Ministarstvo zdravstva i socijalne skrbi Republike Hrvatske dana 25. ožujka 2011. izdalo suglasnost Poliklinici „Neuron“ za izvođenje nastave, posebno dijelova praktičnog rada za studente diplomske i poslijediplomske nastave Medicinskog fakulteta Sveučilišta u Zagrebu.

Nadalje, Poliklinika „Neuron“ i HIIM (kao dio Medicinskog fakulteta) sklopili su 5. ožujka 2013. Ugovor o znanstvenonastavnoj-stručnoj suradnji koji je nastavak prethodnog ugovora sklopljenog 14. lipnja 2010. godine, na neodređeno vrijeme. Tim ugovorom su uredili odnose uzajamne suradnje iz područja provođenja diplomske i poslijediplomske nastave u znanstvenom području biomedicine i zdravstva, u provođenju interdisciplinarnih sveučilišnih studija u znanstvenim granama radiologije i psihijatrije, tečajeva stalnog usavršavanja zdravstvenih djelatnika, te zajedničke suradnje na programima znanstvenih istraživanja u znanstvenom području biomedicine i zdravstva, a posebice neuroznanosti. Ugovorne strane se obvezuju zajednički planirati i izvoditi programe znanstvenih istraživanja, kao i nastavne programe i tečajeve, a specifični oblici suradnje određeni su godišnjim programima rada i znanstvenih istraživanja HIIM-a.

science (for example in the organization of Brain Awareness Weeks in Croatia).

Polyclinics for neurology, psychiatry, radiology, neurosurgery, pathology, cytogenetics and laboratory diagnostics “Neuron” (Zagreb, Šalata 12 – CIBR’s building; short name: Polyclinic “Neuron”) is listed in the Registry of the Commercial Court in Zagreb. The founder and owner of the Polyclinic is the Centre for Clinical Research in Neuroscience, Šalata 12. The Statute of the Polyclinic (article 10) has established that:

“All of the activities of the polyclinic are performed in cooperation with the Centre for Clinical Research in Neuroscience and the Croatian Institute for Brain Research School of Medicine, University of Zagreb.”

The same Statute (article 9) has established that the activity of the Polyclinic is;

“Specialist health care, diagnostics, and medical rehabilitation, except hospital treatments, in the clinical fields of: neurology, psychiatry, radiology, neurosurgery, pathology, cytogenetics and laboratory diagnostics.”

The Croatian Ministry of Health and Social Care has issued the approval (25th March 2011) to the Polyclinic “Neuron” to conduct education, particularly practical work for undergraduate and graduate students of the School of Medicine University of Zagreb, making the Polyclinic one of the teaching sites of the School of Medicine. Furthermore, the Polyclinic “Neuron” and the CIBR (as a part of the School of Medicine) have signed agreement (5th March 2013) about scientific-educational-professional cooperation; which is the continuation of the previous agreement signed for indefinite time period on 14th June 2010. This contract has arranged relationships between two parties as mutual cooperation to conduct undergraduate and graduate education in the field of biomedicine and health, to conduct interdisciplinary university studies in the scientific fields of radiology and psychiatry, courses of continuous education for health professionals, and

Prethodnim ugovorom Medicinskog fakulteta i Poliklinike „Neuron“ (od 14. lipnja 2010.) već je bilo utvrđeno da Poliklinika surađuje s drugim nastavnim bazama Fakulteta, a posebno u djelatnosti radiologije s nastavnim bazama KBC Zagreb, a u djelatnosti psihijatrije s nastavnim bazama KBC Zagreb i nastavnom bazom u Psihijatrijskoj bolnici Vrapče. Nadalje, zaposlenicima u znanstveno-nastavnim zvanjima koji će provoditi nastavu iz ovoga ugovora u Poliklinici, a koji su u vrijeme potpisivanja toga ugovora zaposleni na Fakultetu u kumulativnom radnom odnosu s radnim mjestom u KBC Zagreb ili Psihijatrijskoj bolnici Vrapče, Fakultet je osigurao da umjesto u zdravstvenoj ustanovi sadašnjeg zaposlenja, najmanje 30% punog radnog vremena obavljaju u Poliklinici.

Napokon, Poliklinika također ima dugogodišnji ugovor o zajedničkoj suradnji u radu Jedinice za magnetsku rezonanciju i korištenju uređaja za magnetsku rezonanciju, potpisan s KBC Zagreb i Medicinskim fakultetom Sveučilišta u Zagrebu – ugovor od 31. svibnja 1999. godine, aneks Ugovoru od 16. travnja 2003. godine, te Aneks ugovoru od 23. srpnja 2003. godine (koji se periodički godišnje obnavlja do danas). Stoga je jasno da Poliklinika „Neuron“ od svog osnutka 1999. godine njeguje čvrstu i trajnu povezanost s HIIM-om i Medicinskim fakultetom (kao i svojim osnivačem, Centrom za kliničku primjenu neuroznanosti) na stručnom, znanstvenom i edukacijskom planu.

mutual cooperation on the programs of scientific research in the field of biomedicine and health, especially in the field of neuroscience. Contracting parties undertake joint planning and carrying out of scientific research programs, as well as educational programs and courses, and specific forms of collaboration are determined by the CIBR's yearly work and scientific programs.

The previous contract between School of Medicine and Polyclinic “Neuron” (dated 14th June 2010) has already established that the Polyclinic is cooperating with other teaching sites of the School of Medicine, especially in the field of radiology with the clinics of the Clinical Hospital Centre Zagreb, and in the field of psychiatry with the Vrapče Psychiatric Hospital. Furthermore, all academic employees which will perform teaching assignments, stemming from this agreement, in the Polyclinic, and are at the time of signing of this contract part-time employed at the School of Medicine with the primary employer being Clinical Hospital Centre Zagreb or Vrapče Psychiatry hospital, the School of Medicine will allow that 30% of their FTE can be perform in the Polyclinic instead of their primary employment institution.

Finally, the Polyclinic also has long-term agreement of mutual cooperation with the Unit for Magnetic Resonance, and for the use of the magnetic resonance device, signed with Clinical Hospital Centre Zagreb and the University of Zagreb School of Medicine (contract of 31st May 1999; annex to the previous contracts of 16th April and 23rd July 2003) which are to date periodically renewed. Therefore, it is clear that the Polyclinic “Neuron”, since its inception in 1999, fosters strong and lasting bond with the CIBR and the School of Medicine (as well as with its founder The Centre for Clinical Research in Neuroscience), at the professional, scientific and educational level.

Pionirska uloga u razvoju nastave neuroznanosti na svim akademskim razinama u Hrvatskoj

Ivica Kostović i Miloš Judaš su 1997. osnovali i uveli prvi integrirani predmet Temelji neuroznanosti za studente 2. godine studija medicine te napisali prvi hrvatski udžbenik neuroznanosti. Također su uveli prvi (i još uvijek jedini) poslijediplomski doktorski studij Neuroznanost (Medicinski fakultet Sveučilišta u Zagrebu – 2002. do 2005. kao zasebni smjer u okviru dokorskog studija Biomedicina i zdravstvo, a od 2005. do danas zasebni doktorski studij Neuroznanost). Taj doktorski studij je dio europske mreže škola neuroznanosti (NENS), a na njemu nastavu održavaju i 24 ugledna znanstvenika iz inozemstva. Naši istraživači također drže nastavu za niz izbornih predmeta u studiju medicine, kolegije i predavanja u brojnim stručnim poslijediplomskim studijima pri Medicinskom fakultetu, te različite kolegije na drugim sastavnicama Sveučilišta (primjerice, na Edukacijsko-rehabilitacijskom fakultetu, Hrvatskim studijima).

Međunarodni znanstveni savjet HIIM-a

Hrvatski institut za istraživanje mozga u svoja pionirska ostvarenja u Hrvatskoj može ubrojiti i činjenicu da je od samog osnutka (1990.) do danas u njegov rad aktivno uključen Međunarodni znanstveni savjet. Pravilnikom HIIM-a (članci 59. do 62.) propisano je sljedeće:

„Članak 59.: Međunarodni znanstveni savjet Instituta čine vrsni znanstvenici iz svijeta, iz područja temeljne i kliničke neuroznanosti, a imenuje ga Fakultetsko vijeće na prijedlog direktora Instituta i uz suglasnost Dekana.

Članak 60.: Međunarodni znanstveni savjet sudjeluje u utvrđivanju strategije razvoja Instituta u svjetlu suvremenih kretanja i trendova na području neuroznanosti i bio-

Pioneering role in the development of neuroscience curriculum at all academic levels in the Croatia

Ivica Kostović and Miloš Judaš proposed and established the first integrated neuroscience curriculum (and the first neuroscience curriculum in general) for undergraduate students at the second year of School of Medicine. They also wrote the first Croatian neuroscience textbook. Furthermore, they introduced the first (and still only) postgraduate doctoral program “Neuroscience” (between 2002 and 2005 this was a separate program within the postgraduate doctoral program “Biomedicine and Health”, and since 2005 to date it is a standalone postgraduate doctoral program “Neuroscience”). This PhD program is a part of the Network of European Neuroscience Schools (NENS), and 24 prominent foreign scientist are teaching courses as a part of this PhD program. Our researcher are also teaching many elective courses at the School of Medicine, giving lectures at numerous postgraduate courses at the School of Medicine, and various courses at other faculties at the University of Zagreb (e.g. Faculty of Education and Rehabilitation Sciences, Centre for the Croatian Studies).

CIBR’s international scientific advisory board

Among the pioneering accomplishments in Croatia, we can also include the fact that from its beginning (1990) to date, in CIBR’s work is actively involved the International Scientific Advisory Board. The CIBR’s Statute (articles 59 – 62) has defined the following:

“Article 59: The CIBR’s International Scientific Advisory Board is composed of the excellent international scientist from fields of basic and clinical neuroscience, and is appointed by the School of Medicine Assem-

medicine, te sudjeluje u postupku prosudbe znanstvenih projekata i programa trajne istraživačke djelatnosti Instituta.

Članak 61.: Međunarodni znanstveni savjet ocjenjuje rad Instituta svake četiri godine, o čemu pisano izvješće dostavlja direktoru Instituta i Dekanu. Na temelju toga izvješća, Dekan i Fakultetsko vijeće ocjenjuju rad direktora Instituta, a direktor Instituta ocjenjuje rad pročelnika Odsjeka i direktora znanstvenih programa Instituta.

Članak 62.: Način rada i djelovanja Međunarodnog znanstvenog savjeta određuje se Poslovníkom o radu Međunarodnog znanstvenog savjeta, kojeg donosi direktor Instituta na temelju prijedloga članova Međunarodnog znanstvenog savjeta.“

Od 2003. do danas, Međunarodni znanstveni savjet bio je sastavljen od sljedećih uglednih svjetskih znanstvenika: Pasko Rakic i Nenad Šestan (Yale University School of Medicine), Ronald L. Schnaar (The Johns Hopkins University), Giorgio M. Innocenti i Bengt Winblad (Karolinska Institute, Stockholm), Dick F. Swaab i Harry B. M. Uylings (Free University of Amsterdam), Yehezkel Ben-Ari (INSERM, Marseille), Philippe Evrard (Paris), Roland Pochet (Bruxelles) i Tamas F. Freund (Budimpešta).

bly based on the proposal of the CIBR's director and with prior approval of the Dean.

Article 60: The International Scientific Advisory Board is participating in the formation of the developing strategy of the CIBR in the light of the contemporary trends in the field of neuroscience and biomedicine, and participates in the peer-review of scientific projects and programs of continuous research activities of the CIBR.

Article 61: Every four years, the International Scientific Advisory Board evaluates the CIBR's work, and submits written evaluation report to the CIBR's director and the Dean of the School of Medicine. Based on that evaluation report the Dean and the School of Medicine Assembly evaluate the work of the CIBR's director, and the Director is evaluating the work of Heads of Divisions and Directors of CIBR's research programs.

Article 62: Mode of action of the International Scientific Advisory Board is determined by the Rules and Procedures of Conduct of the International Scientific Advisory Board, which is approved by the CIBR's director based on the proposition made by the members of the International Scientific Advisory Board.“

Since 2003 to date, the International Scientific Advisory Board was composed of the following eminent international scientists: Pasko Rakic and Nenad Šestan (Yale University School of Medicine), Ronald L. Schnaar (The Johns Hopkins University), Giorgio M. Innocenti and Bengt Winblad (Karolinska Institute, Stockholm), Dick F. Swaab and Harry B.M. Uylings (Free University of Amsterdam), Yehezkel Ben-Ari (INSERM, Marseille), Phillippe Evrard (Paris), Roland Pochet (Bruxells) and Tamas F. Freund (Budapest).

Široka međunarodna mreža istraživačke suradnje

Od 1999., istraživačke skupine HIIM-a uspješno surađuju s nizom vodećih međunarodnih centara: Yale University School of Medicine (Pasko Rakic, Nenad Šestan); McGill University & Montreal Neurological Institute (Alan Evans); Goethe Universität, Frankfurt am Main (Thomas Deller); University of Geneva (Petra Hüppi, Jessica Dubois); University of Vienna (Daniela Prayer, Gregor Kasprian); The Johns Hopkins University (Susumu Mori); University of Texas at Dallas (Hao Huang); INSERM, Marseille (Monique Esclapez); King's College London (Peter McGuffin); Mount Sinai School of Medicine, New York (Patrick Hof); Max Planck Institute (Svante Pääbo); University of Bruxelles (Charles Nicaise, Roland Pochet).

Međunarodni utjecaj dosadašnjih istraživanja

Istraživačke skupine HIIM-a imaju jasnu međunarodnu prepoznatljivost u nekoliko područja neuroznanosti: razvojna neuroanatomija i neurobiologija čovjeka (skupine Ivica Kostovića, Miloša Judaša, Zdravka Petanjeka, Maria Vukšića, Nataše Jovanov-Milošević i Željke Krsnik) te pionirska istraživanja u području MRI-histološke korelacije ljudskog fetalnog mozga (Skupine Ivica Kostovića, Miloša Judaša i Marka Radoša); novi bitni nalazi o cjeloživotnoj reorganizaciji neuralnih krugova ljudske moždane kore (skupina Zdravka Petanjeka); novi markeri strukturnih promjena u mozgu koji stari i u Alzheimerovoj bolesti (skupina Gorana Šimića); fiziologija i patofiziologija cerebrospinalnog likvora i intrakranijskog tlaka (skupine Marijana Klarice i Darka Oreškovića); signalne molekule u membrani stanične jezgre (skupine Hrvoja Banfića i Dore Višnjić); genomski pristup

Wide international network of collaborations

Since 1999. the research groups at CIBR are successfully collaborating with many leading international centers: Yale School of Medicine (Pasko Rakic, Nenad Šestan); McGill University & Montreal Neurological Institute (Alan Evans); Goethe Universität, Frankfurt am Main (Thomas Deller); University of Geneva (Petra Hüppi, Jessica Dubois); University of Vienna (Daniela Prayer, Gregor Kasprian); The Johns Hopkins University (Susumu Mori); University of Texas at Dallas (Hao Huang); INSERM, Marseille (Monique Esclapez); King's College London (Peter McGuffin); Mount Sinai School of Medicine, New York (Patrick Hof); Max Planck Institute (Svante Pääbo); University of Bruxelles (Charles Nicaise, Roland Pochet).

International impact of previous research

The CIBR research groups have well-established international visibility in several fields of neuroscience: human developmental neuroanatomy & neurobiology (groups of Ivica Kostović, Miloš Judaš, Zdravko Petanjek, Mario Vukšić, Nataša Jovanov-Milošević and Željka Krsnik) and pioneering work in MRI-histological correlation of the human fetal brain (groups of Ivica Kostović, Miloš Judaš and Marko Radoš); novel findings in life-span cortical circuitry reorganization (Zdravko Petanjek group); new markers of structural changes in the ageing and Alzheimer's brain (Goran Šimić group); CSF and intracranial pressure physiology and pathophysiology (groups of Marijan Klarica & Darko Orešković); signalling molecules in nuclear membranes (groups of Hrvoje Banfić & Dora Višnjić); genomic approaches to individualized neuropharmacological treatment (Neven Henigsberg group); new models and approaches to stem cell applications with po-

individualiziranoj neurofarmakoterapiji i inovativni markeri terapijskog odgovora kod mentalnih poremećaja (skupina Nevena Henigsberga); novi modeli i pristupi primjeni matičnih stanica s potencijalnom terapijskom primjenom (skupine Srećka Gajovića i Dinka Mitrečića); istraživanje signalnih mehanizama između membranskih glikolipida i proteina (skupine Svjetlane Kalanj-Bognar i Marije Heffer); učinci natriuretskih peptida u fiziološkim i patološkim stanjima mozga (skupina Aleksandre Sinđić); regulacija izraženosti mezenhimalnih biljega tumora mozga (skupina Nives Pećina-Šlaus).

Edukacija i prijenos znanja na međunarodnoj razini

HIIM je organizirao nekoliko FENS/IBRO ljetnih škola (3 kao glavni organizator, 2 kao lokalni organizator), dvije PENS ljetne škole, 5 EMBO Practical Courses, te niz drugih radionica i skupova. Više od 100 uglednih svjetskih znanstvenika održalo je pozvana predavanja na HIIM-u od 1999. do danas.

Edukacija mladih istraživača koji danas imaju uspješne samostalne međunarodne karijere

Niz naših ranijih doktoranada danas razvija uspješnu i neovisnu znanstvenu karijeru u zapadnim zemljama. Nenad Šestan je profesor na Yale University; Mladen-Roko Rašin je docent na Rutgers University; Ivana Delalle je profesor na Boston University; Nenad Bogdanović je bio docent na Karolinska Institute (Stockholm), a sada je profesor na University of Oslo; Ladislav Mrzljak je više godina radio na Yale University, a potom postao istraživač u kompaniji AstraZeneca (U.S.A.); Krešimir Letinić je proveo 6 godina na Yale University, a potom postao managing director za Easton Capital Investment Group (U.S.A.); Mihovil

tential relevance for treatment (groups of Srećko Gajović & Dinko Mitrečić); research of signaling mechanisms between membrane glycolipids and proteins (groups of Svjetlana Kalanj-Bognar and Marija Heffer); effects of the natriuretic peptides in physiological and pathological brain conditions (Aleksandra Sinđić group); regulation of expression of mesenchymal markers of brain tumors (Nives Pećina-Šlaus group).

Education and knowledge transfer at the international level

The CIBR organized several IBRO/FENS Summer Schools (3 as primary organizer, and 2 as local organizer), 2 PENS Summer Schools, 5 EMBO Practical Courses, as well as number of other workshops and meetings. More than 100 distinguished foreign scientists delivered invited lectures at the CIBR since its opening in 1999.

The education of young investigators with successful independent international careers

A number of our former PhD students currently pursue successful and independent research careers in Western countries. Nenad Šestan is full professor at Yale University; Mladen-Roko Rašin is assistant professor at Rutgers University; Ivana Delalle is associate professor at Boston University; Nenad Bogdanović was associate professor at Karolinska Institute and currently is professor at University of Oslo; Ladislav Mrzljak spent 10 years at Yale and moved to become senior principal scientist at AstraZeneca, USA; Krešimir Letinić spent 6 years at Yale and moved to position of managing director of the Easton Capital Investment Group, USA; Mihovil Pletikos is currently research associate at Yale University; Ivana Pogledić is researcher at the University of Vienna; Lana Vasung is re-

Pletikos trenutno je doktorand na Yale University; Ivana Pogledić je istraživač na Sveučilištu u Beču; Lana Vasung je istraživač na Sveučilištu u Ženevi.

No, HIIM je također uspio ostvariti i tzv. „brain gain“ – 7 postdoktoranada vratilo se natrag u Zagreb (na HIIM) nakon uspješno razvijene karijere u inozemnim ustanovama.

Neki bitni pokazatelji znanstvene izvrsnosti i uspješnosti

Naši znanstvenici do danas su objavili (Web of Science – Core Collection) 589 radova, od kojih je 206 u časopisima iz prve kvartile (Q1), 125 u Q2, 167 u Q3 te 91 u Q4 (Prilog 1). Ti radovi do sada imaju ukupno 12.703 neovisna citata. Naši znanstvenici (samo oni koji su voditelji Odsjeka i Laboratorija u HIIM-u!) do sada su bili mentori za 114 obranjenih doktorskih radova (Prilog 4), 57 obranjenih magistarskih radova (Prilog 3) te 105 obranjenih diplomskih radova studenata (Prilog 2). Naši doktorandi dobivali su nagrade Medicinskog fakulteta za najuspješnijeg doktoranda (Prilog 4), a naši studenti dobili su brojne Rektorove i Dekanove nagrade za svoje studentske istraživačke radove (Prilog 2).

Brojni istraživači HIIM-a su dobitnici prestižnih domaćih i međunarodnih nagrada za individualnu znanstvenu izvrsnost. Primjerice, dobili smo 8 godišnjih državnih nagrada za znanost (Goran Šimić 1999 i 2010; Hrvoje Banfić 2005, Ivica Kostović 2009, Marijan Klarica 2010, Nives Pećina-Šlaus 2010, Miloš Judaš 2011, Darko Orešković 2014). Ivica Kostović je 1990. dobio najvišu državnu nagradu za znanost „Ruđer Bošković“, a 2007. je dobio i uglednu „Castang Award of the European Academy for Child Rehabilitation“. Nataša Jovanov-Milošević i Željka Krsnik su 2001. godine dobile „Cajal Club Award“, a Goran Šimić je 2008. dobio uglednu međunarodnu „Kurt Jellinger Prize“. Godišnju

searcher at the University of Geneva. However, the CIBR also managed to achieve the „brain gain“, i.e. to secure the return of 7 postdocs from foreign institutions back to Croatia.

Some of the key indicators of the scientific excellence and successfulness.

Our researchers have published to date (according to the Web of Science – Core Collection) 589 papers, of which 206 are in the Q1 journals, 125 in the Q2, 167 in the Q3, and 91 in the Q4 (Annex 1). Aforementioned paper have in total 12.703 independent citations. CIBR’s researchers (only Heads of Departments and Laboratories) have been mentors for 114 successfully defended doctoral thesis, 57 master’s thesis and 105 thesis (Annex 2). Our PhD students were awarded the Recognition of the School of Medicine for the most successful PhD student, and our undergraduate students received numerous Rector’s and Dean’s awards for their scientific work.

Numerous CIBR’s researchers were recipients of prestigious domestic and international awards for individual scientific excellence. As an example, we received 8 Annual Croatian State Awards for Scientific Excellence (Goran Šimić 1999 and 2010, Hrvoje Banfić 2005, Ivica Kostović 2009, Marijan Klarica 2010, Nives Pećina-Šlaus 2010, Miloš Judaš 2011, Darko Orešković 2014). In the 1990, Ivica Kostović was awarded the highest Croatian Scientific Award “Ruđer Bošković”, and in 2007, he received prestigious “Castang Award of the European Academy for Child Rehabilitation”, Nataša Jovanov-Milošević and Željka Krsnik received in 2001. “Cajal Club Award”, and Goran Šimić received in 2008 prestigious international “Kurt Jellinger Prize”. Annual Award of the Croatian Academy of Sciences and Arts was awarded to: Goran Šimić (2009), Zdravko Petanjek (2013) and Marijan Klarica (2014)

nagradu Hrvatske akademije znanosti i umjetnosti dobili su : Goran Šimić (2009.), Zdravko Petanjek (2013.) i Marijan Klarica (2014.).

Dosadašnji kompetitivni i međunarodno ocijenjeni projekti

Prvi znanstveni program HIIM-a (1997. – do 2006.) zvao se „Neurobiologija kognitivnog razvoja i kognitivnih poremećaja“ (direktor: Ivica Kostović), a obuhvaćao je 24 zasebna istraživačka projekta te još 5 poticajnih projekata za mlade istraživače (1997.-2000.), odnosno 41 istraživački projekt (2001.-2006.). Od 2007. do 2013. godine, na HIIM-u su izvođena tri velika istraživačka programa:

1. Razvojna neurobiologija kognitivnih, mentalnih i neuroloških poremećaja (Direktor: Ivica Kostović; ukupno 26 zasebnih istraživačkih projekata);
2. Cerebrospinalna patofiziologija i primjena ultrazvuka (Direktor: Marijan Klarica; ukupno 8 zasebnih istraživačkih projekata);
3. Regulacija staničnog rasta i dioba u fiziološkim i patološkim uvjetima (Direktor: Hrvoje Banfić; ukupno 5 zasebnih istraživačkih projekata).

U proteklom desetljeću, istraživači HIIM-a su također uspješno dovršili dva FP6 projekta (Neven Henigsberg, Srećko Gajović), tri UKF projekta (Ivica Kostović, Hrvoje Banfić, Srećko Gajović), tri COST projekta (Srećko Gajović, Neven Henigsberg), jedan Fogarty International Research Center Award projekt (Hrvoje Banfić) te niz drugih manjih domaćih projekata i projekata bilateralne međunarodne suradnje.

Treba istaknuti da je Fakultetsko vijeće Medicinskog fakulteta Sveučilišta u Zagrebu na svojoj 11. redovitoj sjednici održanoj 16. prosinca 2008. godine usvojilo „Prijedlog I. faze akcijskog plana Medicinskog fakulteta prema Istraživačkoj strate-

Previous competitive and internationally peer-reviewed research grants

The first CIBR's scientific program (1997 – 2006) was called “Neurobiology of cognitive development and cognitive disorders” (director: Ivica Kostović), and consisted of 24 individual research grants and 5 start-up grants of young investigators. Since 2007 – 2013 three large research programs were conducted at CIBR:

1. Developmental neurobiology of cognitive, mental and neurological disorders (Director: Ivica Kostović; in total 26 individual research grants);
2. Cerebrospinal pathophysiology and ultrasound application (Director: Marijan Klarica; in total 8 individual research grants);
3. Regulation of the cell growth and division in physiological and pathological conditions (Director: Hrvoje Banfić; in total 5 individual research grants).

During the past decade, CIBR researchers successfully completed two FP6 grants (Neven Henigsberg, Srećko Gajović); three Unity through Knowledge Fund (UKF) grants (Ivica Kostović, Hrvoje Banfić, Srećko Gajović); three COST grants (Srećko Gajović, Neven Henigsberg); one Fogarty International Research Center Award grant (Hrvoje Banfić), and a number of smaller domestic and/or bilateral research grants.

It should be emphasized that on the 11th regular session (16th December 2008) the School of Medicine Assembly adopted “Proposition of the 1st phase of the School of Medicine action plan according to the University of Zagreb Research Strategy”, which adopted research in the fields of basic, clinical and translational neuroscience as the crucial, international competitive research pathway of the School of Medicine.

giji Sveučilišta u Zagrebu“, kojim su istraživanja u području temeljne, kliničke i translacijske neuroznanosti prihvaćena kao bitan, međunarodno kompetitivan i prioritetan pravac istraživanja Medicinskog fakulteta.

Trenutno aktivni kompetitivni i međunarodno ocijenjeni projekti koji se izvode na HIIM-u

Trenutno aktivni kompetitivni i međunarodno ocijenjeni projekti koji se izvode na HIIM-u su (uz dva koji su netom dovršeni, to jest u fazi pisanja završnih izvješća):

Ivica Kostović: Subplate zona ljudskog mozga: neriješeni problemi (HRZZ projekt broj 4517)

Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (HRZZ projekt)

Mario Vukšić: Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (HRZZ projekt)

Zdravko Petanjek: Microcircuitry of higher cognitive functions (HRZZ projekt)

Goran Šimić: Otkrivanje i praćenje bioloških biljega radi rane terapijske intervencije u Alzheimerovoj bolesti (HRZZ projekt, dovršen u prosincu 2014.)

Goran Šimić: Hiperfosforilacija, agregacija i transsinaptički prijenos tau proteina u Alzheimerovoj bolesti: analiza likvora i ispitivanje potencijalnih neuroprotektivnih spojeva (HRZZ projekt broj 9730)

Neven Henigsberg: Multimodalni pristup liječenju i dugoročnom praćenju tijeka depresivnog poremećaja metodom magnetske rezonancije (HRZZ projekt broj 2979)

Nives Pećina-Šlaus: The role of Wnt signaling in epithelial to mesenchymal transition (WNT4EMT) (HRZZ projekt)

Currently active competitive and internationally peer-reviewed research grants at the CIBR

The following list presents currently active competitive and internationally peer-reviewed research grants at the CIBR (with two research grants which are just completed and are in a phase of submitting final report):

Ivica Kostović: Subplate zone of the human brain: unsolved problems. (CSF research grant)

Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (CSF research grant)

Mario Vukšić: Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (CSF research grant)

Zdravko Petanjek: Microcircuitry of higher cognitive functions (CSF research grant)

Goran Šimić: Tau protein hyperphosphorylation, aggregation and trans-synaptic transfer in Alzheimer's disease: CSF biomarker analysis and assessment of potential neuroprotective compounds in vitro (CSF research grant)

Goran Šimić: Detection and tracking of biological markers for early therapeutic intervention in sporadic Alzheimer's disease (CSF research grant, completed in December 2014.)

Neven Henigsberg: Multimodal approach to treatment and long-term follow-up of effects of depression by using MRI (CSF research grant)

Nives Pećina-Šlaus: The role of Wnt signaling in epithelial to mesenchymal transition (WNT4EMT) (CSF research grant)

Srećko Gajović: FP7 Capacities – REGPOT: Combining stem cells and biomaterials for brain repair – unlocking the potential of the

Srećko Gajović: FP7 Capacities – REGPOT: Combining stem cells and biomaterials for brain repair – unlocking the potential of the existing brain research through innovative in vivo molecular imaging: GLOWBRAIN

Dinko Mitrečić: Inovativni pristup liječenju moždanog udara presađivanjem živčanih matičnih stanica i inhibicijom molekularnog puta Hmgb1 – Tir2 – NfkB (HRZZ projekt uspostavne potpore, dovršen 2014.)

Nataša Jovanov-Milošević: Brain Extracellular Matrix in Health and Disease (EC-MNet)

Nataša Jovanov-Milošević: Komparativno histološko/MRI istraživanje u cilju poboljšanja dijagnostike perinatalnih oštećenja ljudskog mozga (projekt Zaklade Adris)

Kristina Mlinac: Neuroplastin i ganglioziidi u organizaciji sinaptičke membrane (DAAD Forschung projekt, 2014. – 2016.)

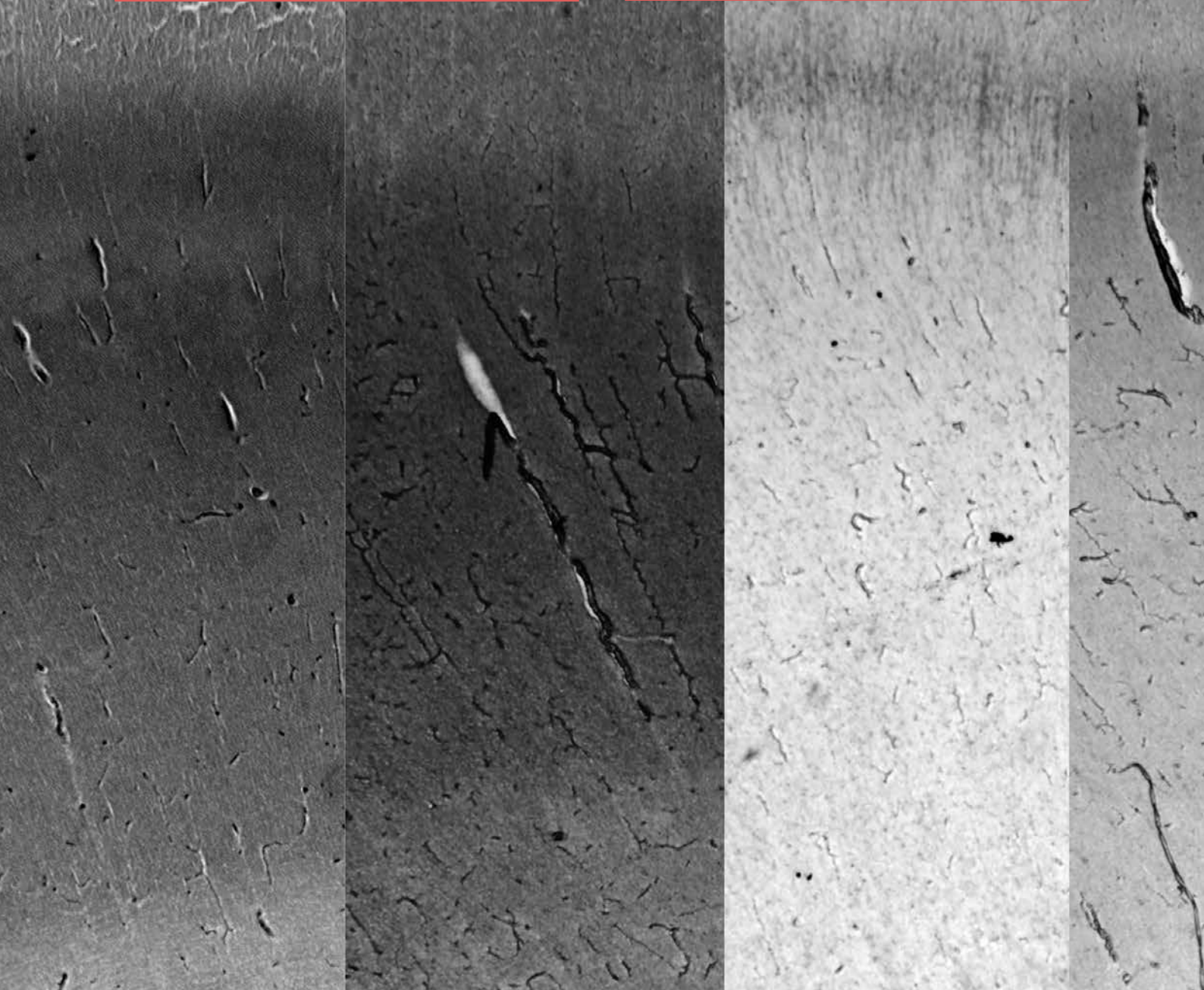
existing brain research through innovative in vivo molecular imaging: GLOWBRAIN

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PROGRAM RADA

Istraživački plan za razdoblje od 5 godina

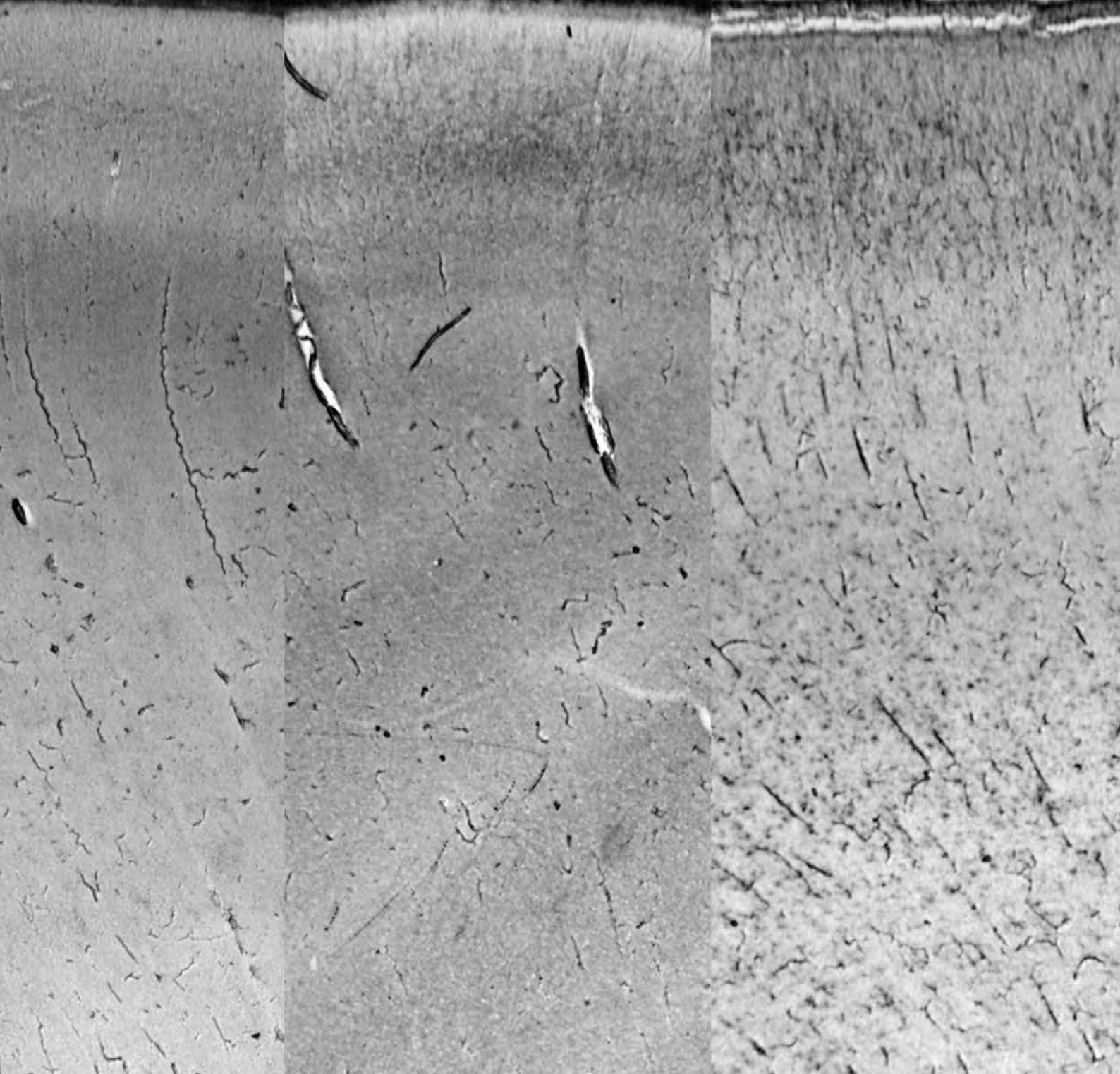
Novi istraživački program za uspostavu Centra izvrsnosti u kojem HIIM treba služiti kao središnja točka nacionalne mreže za integriranje, usmjeravanje i unapređenje inovativnog i translacijskog pristupa ranoj detekciji, liječenju, procjeni ishoda, te rehabilitaciji pacijenata koji su pretrpjeli hipoksijsko-ishemijske ili hemoragijske lezije mozga. Centra ima tri glavna cilja:

1) nastaviti tekuće kompetitivne projekte i

WORK PROGRAM

Research plan for a 5-year period

We present our new research program aimed to establish national Centre of Excellence – “Centre for basic, clinical and translational neuroscience” – with the CIBR serving as the hub of national network for integrating, focusing and advancing an innovative and translational approach to early detection, treatment, evaluation of outcome, and rehabilitation of patients suffering from hypoxic/ischaemic and haemorrhagic cerebral lesions. The Centre has



primijeniti rezultate u eksperimentalnom i kliničkom pristupu moždanom udaru i drugih poremećajima uzrokovanim hipoksijsko-ishemijskim lezijama moždane kore u odrasloj dobi i tijekom razvoja.

2) Razviti nove eksperimentalne modele (na glodavcima i mini-svinjama) i

3) Iskoristiti inovativne pristupe za ranu dijagnozu, praćenje, liječenje i rehabilitaciju djece i odraslih s hipoksijsko-ishemijskim lezijama mozga.

Ovaj program istraživanja kombinira temeljna

three major objectives: 1) To continue currently internationally evaluated research projects and implement results in the experimental and clinical approach to stroke and other entities caused by hypoxic/ischaemic and haemorrhagic lesions of the developing and adult cerebral cortex. 2) To develop new experimental models (in rodents and Göttingen mini-pigs), and 3) To use innovative approach for early diagnosis, follow-up, treatment and rehabilitation of children and adults suffering from hypoxic/ischaemic and haemorrhagic brain lesions.



i klinička istraživanja, a hipoksijsko-ishemijsko oštećenje mozga je ključna tema koja povezuje različite smjerove istraživanja. Prikazujemo šest

glavnih smjerova istraživanja (koje izvodi šest glavnih istraživačkih skupina):

- 1) Razvojno porijeklo neuropedijatrijskih poremećaja nakon perinatalne hipoksijsko-ishemijske lezije mozga (Skupina 1);
- 2) Novi biomarkeri starenja, Alzheimerove bolesti, vaskularne demencije i moždanih stanja s rezistencijom na inzulin (Skupina 2);
- 3) Klinička i eksperimentalna istraživanja cerebralnih hipoksijsko-ishemijskih i hemoragijskih lezija te njihovog odnosa s promjenama kretanja i tlaka intrakranijskih tekućina (Skupina 3);
- 4) Predkliničke studije hipoksijsko-ishemijskih lezija u eksperimentalnim modelima na glodavcima (Skupina 4);
- 5) Kognitivna i lingvistička analiza jezičnih poremećaja i oporavka nakon hipoksijsko-ishemijske lezije mozga (Skupina 5); i
- 6) Inovativni biomarkeri terapijskog odgovora u bolesnika s mentalnim poremećajima (Skupina 6).

Koristit ćemo zajedničku informacijsku platformu i tzv. matrix sustav (mrežu konstrukata i varijabli) da razjasnimo koji od naših prethodno otkrivenih biomarkera moždanog razvoja, građe i funkcije može biti dobro iskorišten za poboljšanje dijagnoze, prognoze i rehabilitacije poremećaja mozga. Naš istraživački program je dijelom interdisciplinaran/multidisciplinaran, jer kombinira različita polja temeljne neuroznanosti (neuroanatomija, neurohistologija, neuroembriologija, neuropatologija, molekularna neurobiologija, genetika i genomika, neurokemija, neurofarmakologija) te kliničke neuroznanosti (neurologija, pedijatrijska neurologija, neuroradiologija, psihijatrija, neurorehabilitacija, perinatologija), a dijelom je transdisciplinaran jer kombinira s jedne strane neuroznanost s veterinarskom medicinom, a s druge strane s društvenim i humanističkim znanostima (psihologija, logopedija, rehabilitacija, lingvistika). Usvojili smo sljedeće preporuke NIH Brain 2025 Inicijative:

- 1) usporedno izvoditi studije na ljudima i eksperimentalnim životinjama (naše studije na pacijentima, ljudskim mozgovima, eksperimentalnim glodavcima, mini-svinjama te rezus majmunima u suradnji sa sveučilištem Yale – Pasko Rakic, Nenad Sestan);
- 2) premostiti granice kroz interdisciplinarnu suradnju (naše istraživačke skupine su sastavljene od temeljnih i kliničkih neuroznanstvenika, kao i istraživača iz društvenih i humanis-

This research program combines basic and clinical investigations, with hypoxic/ischaemic & haemorrhagic cerebral lesions as an underlying topic in connecting various lines of research. We present six main lines of research (conducted by six major research groups):

- 1) The developmental origin of neuropediatric disorders after perinatal hypoxic/ischaemic brain lesion (Group 1);
 - 2) New biomarkers of ageing, Alzheimer's disease, vascular dementia and insulin resistant brain state (Group 2);
 - 3) Clinical & experimental studies of cerebral hypoxic/ischaemic & haemorrhagic lesions and their relation to alterations in movement and pressure of intracranial fluids (Group 3);
 - 4) Preclinical studies of hypoxic/ischaemic lesions in experimental rodent models (Group 4);
 - 5) Cognitive & linguistic analysis of language changes & recovery after stroke (Group 5); and
 - 6) Innovative markers in treatment response of patients with mental disorders. We will use a common information platform and matrix system (constructs & variables grid) to elucidate which of our previously discovered and described biomarkers of brain development, structure and function can be successfully used for improving diagnosis, prognosis and rehabilitation of brain disorders (see Table 1 at the end of this file). Our research program is partly interdisciplinary/multidisciplinary, combining different fields of basic neuroscience (neuroanatomy, neurohistology, neuroembryology, neuropathology, molecular neurobiology, genetics & genomics, neurochemistry, neuropharmacology) and clinical neuroscience (neurology, pediatric neurology, neuroradiology, psychiatry, neurorehabilitation, perinatology), and partly cross-disciplinary (combining neuroscience with veterinary medicine on one hand, and with social sciences & humanities on the other hand – psychology, speech therapy, rehabilitation, linguistics). We adopt the following recommendations from the NIH Brain 2025 Initiative:
- 1) to pursue human and non-human studies in parallel (our studies of patients, human brains, experimental rodents, Göttingen mini-pigs and rhesus monkey brain in collaboration with Yale University – Pasko Rakic & Nenad Sestan);
 - 2) to cross boundaries in interdisciplinary collaboration (our groups composed of both basic and clinical neuroscientists, as well as collaboration with researchers from social sciences & humanities);
 - 3) to integrate spatial and temporal scales (e.g., we analyze cerebral compartments and neuro-

tičkih disciplina);

3) integrirati pojave na vremenskoj i prostornoj ljestvici (npr. analiziramo cerebralne odjeljke i neurogenetska zbivanja u različitim stadijima razvoja; longitudinalno praćenje pacijenata s mentalnim poremećajima itd.);

4) uspostaviti platformu za zajedničku uporabu podataka (već postojeću platformu ćemo nadograditi i proširiti, da se uključe i multimodalne i multidisciplinarne podatke);

5) Validacija i diseminacija tehnologije (razvit ćemo nove MRI protokole, nove eksperimentalne modele, nove pristupe za aplikaciju matičnih stanica, nove kognitivne testove za procjenu jezičnih funkcija nakon moždanog udara);

6) Odgovorno se odnositi prema zdravstvenom sustavu, novcu poreznih obveznika te zajednici temeljnih, kliničkih i translacijskih neuroznanstvenika (predlažemo novi, izvorni pristup ranoj detekciji i liječenju, evaluaciji neurološkog, kognitivnog i behavioralnog ishoda nakon perinatalnog oštećenja mozga, kao i nove protokole za intervencijsku neuroradiologiju; to bi trebalo povoljno djelovati na prevenciju glavnih poremećaja i omogućiti uštede u procesu liječenja i rehabilitacije).

Skupina 1: Razvojno porijeklo neuropedijatrijskih poremećaja nakon hipoksično – ishemijskih oštećenja mozga (voditelj: Ivica Kostović i Miloš Judaš)

Nastavak, pozadina i umrežavanje: Ova skupina sastoji se od jezgre HIIM-ovih istraživača koji su dugoročno (više od tri desetljeća) uključeni u istraživanja strukturnog i funkcionalnog razvoja ljudskog mozga, s izvrsnim publikacijama, međunarodnom prepoznatljivošću i suradnjom, kao i s najvećim brojem kompetitivno dodijeljenih znanstvenih projekata. Predloženo istraživanje je nastavak i proširenje dosadašnjih znanstvenih projekata Hrvatske zaklade za znanost dodijeljenih: Milošu Judašu (Razvitak transkriptoma specifičnih populacija neurona u kortikalnim područjima ljudskog mozga bitnim za jezik i sustave zrcalnih neurona), Ivici Kostoviću (Subplate zona čovjeka – neriješena pitanja), Zdravku Petanjeku (Neuralna osnova viših spoznajnih funkcija), i Mariju Vukšiću (Histološka, MRI i analiza genske ekspresije reorganizacijskih procesa u medijalnom (limbičkom) zidu ljudskog mozga tijekom razvoja).

Nastavak i proširenje međunarodne suradnje: Ivica Kostović (u suradnji s Željkom Krsnik) nastaviti će dugogodišnju suradnju s Paškom Rakićem (Yale University – rhesus majmun kao model i komparativna analiza moždanih

genetic events at different developmental ages; longitudinal studies on patients with mental disorders, etc.);

4) to establish platform for sharing data (we will upgrade and expand our existing information platform, to incorporate multimodal and multidisciplinary data);

5) to validate and disseminate technology (we will develop new MRI protocols, new experimental models, new approaches to manipulate and deliver neural stem cells, new cognitive tests for language assessment after stroke);

6) to observe accountability to health system, the taxpayers and the basic, translational and clinical neuroscience community (we propose original and innovative approach to early detection and treatment in evaluation of neurological, cognitive and behavioural outcome after perinatal brain lesion, as well as for interventional neuroradiological protocols; this should have impact on prevention of major disorders and enable savings in treatment and rehabilitation processes).

Group 1: The Developmental Origin of Neuropediatric Disorders after perinatal Hypoxic/Ischaemic Brain Lesion (led by Ivica Kostović & Miloš Judaš)

Continuation, background & networking:

This group consists of CIBR's core-members involved in long-term (three decades) research on structural and functional development of the human brain, with excellent publication record, international visibility and international collaboration, as well as the largest number of competitively awarded grants. Here proposed research is continuation and extension of current Croatian Science Foundation grants awarded to: Miloš Judaš (Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network), Ivica Kostović (The Human Subplate Zone – unsolved problems), Zdravko Petanjek (Microcircuitry of higher cognitive functions), and Mario Vukšić (Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum).

Continuing and expanding international collaboration: Ivica Kostović (with Željka Krsnik) will continue his long-term collaboration with Pasko Rakic (Yale University – rhesus monkey model and comparative study of cerebral compartments in human and monkey); Miloš Judaš (with Goran Sedmak) will continue his long-term collaboration with his former stu-

zona kod čovjeka i majmuna); Miloš Judaš (u suradnji s Goranom Sedmakom) nastaviti će dugogodišnju suradnju sa svojim bivšim studentom i trenutačno redovitim profesorom u trajnom zvanju na Yale University, Nenadom Šestanom (transkriptom ljudske moždane kore tijekom razvoja i u odraslom mozgu); Zdravko Petanjek (u suradnji sa Sanjom Darmopil) nastaviti će suradnju s Monique Esclapez (INSERM, Marseille) i Svante Pääbo (Max Planck Institute). Željka Krsnik nastaviti će suradnju s Mladenom-Rokom Rašinom (Rutgers University, USA) na analizi transkriptoma kod glodavaca nakon prolazne intrauterine ishemije tijekom središnjeg razdoblja neurogeneze. Smatra se da je vremenski regulirano prepisivanje gena glavni regulator razvoja neokorteksa, ali također, pokazuje se da vremenski regulirana translacija mRNA je bitna kao regulatorni mehanizam. Rašin i Krsnik su nedavno otkrili da RNA vezujući proteini (RBP) mogu određivati proteine koji će postati dio ribosoma ili ribosomskog koda. Još uvijek je nejasno kako prenatalni događaji poput ishemije utječu na RBPi ili ribosomski kod. Nadalje, Ivica Kostović će nastaviti i proširiti svoja dosadašnja istraživanja o neurorazvojnom ishodu kod djece s perinatalnim oštećenjima mozga u suradnji s pedijatrijskim neurolozima (Nina Barišić, Vesna Benjak), psiholozima (Mirna Kostović Srzentić), neuroradiolozima (Marko Radoš, Milan Radoš, David Ozretić), kao i s međunarodnim partnerima na Montreal Neurological Institute (Alan Evans – zajednički projekt korelacije podataka o ekspresiji gena s MRI parametrima tijekom cijelog života), University of Geneva (Petra Hüppi i naš prijašnji doktorski student Lana Vasung) i University of Vienna (Daniela Prayer). Ove suradnje također imaju ulogu u koordiniranju i ujednačavanju protokola za snimanja živčanog sustava na HIIM-u (Poliklinika Neuron) i partnerskih institucija.

Uspostava novih znanstvenih suradnji i razvoj novih eksperimentalnih modela: Nataša Jovanov-Milošević i Mario Vukšić će uspostaviti novu suradnju s Dubravkom Hranilović (Prirodoslovno-matematički fakultet). Ivica Kostović i Miloš Judaš će uspostaviti novu suradnju s istraživačkim skupinama na Veterinarskom fakultetu (Tomislav Dobranić, Željko Grabarević, Miljenko Šimpraga, Marko Samardžija, Andrea Gudan-Kurilj i Dražen Vnuk) u svrhu uspostave novog eksperimentalnog modela (Göttingen mini-svinja – nedavno je pokazano da ovaj model predstavlja vrlo dobar model za proučavanje hipoksičnih promjena u mozgu tijekom razvoja – vidi Hou i sur. PLoS One 7/8, 2012; Bro i sru. Newslet-

ent and presently full professor at Yale University, Nenad Sestan (human cerebral cortical transcriptome in developing and adult brain); Zdravko Petanjek (with Sanja Darmopil) will continue his collaboration with Monique Esclapez (INSERM, Marseille) and Svante Pääbo (Max Planck Institute). Željka Krsnik will continue collaboration with Mladen-Roko Rašin (Rutgers University, USA) on rodent transcriptome analysis after transient intrauterine ischaemia during mid-neurogenesis. Time-dependent gene transcription is thought to be a major regulator of neocortical development, but time dependent regulation of mRNA translation is also emerging as a key control mechanism. Rašin & Krsnik recently discovered that RNA binding proteins (RBP) can determine proteins that will be part of the ribosome or the ribosome code. How RBPs or ribosome code are affected by prenatal insults like ischaemia is still unknown. In addition, Ivica Kostović will continue and expand his studies on neurodevelopmental outcome in children with perinatal brain lesions in collaboration with pediatric neurologists (Nina Barišić, Vesna Benjak), psychologists (Mirna Kostović Srzentić), neuroradiologists (Marko Radoš, Milan Radoš, David Ozretić) as well as international partners at Montreal Neurological Institute (Alan Evans – joint project to correlate gene expression data and MRI parameters using large datasets across the human life-span), University of Geneva (Petra Hüppi and our former PhD student Lana Vasung), and University of Vienna (Daniela Prayer). This collaboration also serves to coordinate and unify neuroimaging protocols at the CIBR (Polyclinic Neuron) and partnering clinical institutions.

Establishment of new research collaborations and development of new experimental models: Nataša Jovanov-Milošević and Mario Vukšić will establish new collaboration with Dubravka Hranilović (Faculty of Natural Sciences). Ivica Kostović & Miloš Judaš will establish new collaboration with research groups from Faculty of Veterinary Medicine (Tomislav Dobranić, Željko Grabarević, Miljenko Šimpraga, Marko Samardžija, Andrea Gudan-Kurilj, and Dražen Vnuk) to introduce new experimental model (Göttingen mini-pig, recently shown to represent quite appropriate model for studying hypoxic changes in developing brain – see Hou et al. PLoS One 7/8, 2012; Bro et al. Newsletter 38:8, 2012). In the first phase, we will explore development of transient cerebral compartments and white matter segments in mini-pigs. In the second phase, we will analyze

ter 38:8, 2012). U prvoj fazi projekta istražiti ćemo razvoj prolaznih moždanih zona i segmenata bijele tvari kod mini-svinja. U drugoj fazi analizirati ćemo razvojnu reorganizaciju i mijelinizaciju prolaznih moždanih zona nakon hipoksije izazvane podvezivanjem uterinih arterija kod skotnih mini-svinja (Dobranić, Samardžija, Vnuk). Fina histološka građa prolaznih zona (Kostović, Judaš) će se usporediti s općim patološkim strukturnim abnormalnostima (grupa Grabarević). Na kraju, Miloš Judaš i Maja Capanec će započeti pionirsku suradnju s grupom Ide Raffaelli (Filozofski fakultet Sveučilišta u Zagrebu, Odsjek za lingvistiku) u pokušaju premošćivanja trenutačnog jaza između neuroznanosti i humanističkih znanosti u Hrvatskoj (vidi opis istraživačkog plana Grupe 5).

Skupina 2. Novi biološki biljezi starenja, Alzheimerove bolesti, vaskularne demencije i moždanih stanja povezanih s inzulinskom rezistencijom (Voditelj skupine: Goran Šimić)

Nastavak prethodnih istraživanja, pozadina istraživanja i umrežavanje: Ova skupina nastavit će dosadašnja istraživanja kao i daljnje širenje dosadašnje suradnje koja je započela 2012. godine dobivanjem projekta Hrvatske zaklade za znanost (HRZZ) (Goran Šimić, voditelj; „Otkrivanje i praćenje bioloških biljega za ranu intervenciju u sporadičnoj Alzheimerovoj bolesti“ – <http://alzbiotrack.hiim.hr>), a osnažena nedavnom dodjelom novog HRZZ projekta Goranu Šimiću. Ova interdisciplinarna skupina čini mrežu od osam istraživačkih grupa (četiri koje već surađuju na HIIM-u plus četiri nove partnerske grupe u predloženom Centru) kako slijedi: 1) četiri grupe s HIIM-a koje vode: Goran Šimić (neuroanatomija i neuropatologija), Dora Višnjic i Hrvoje Banfić (fiziologija i molekulska stanična biologija), te Svjetlana Kalanj-Bognar (neurokemija); 2) Melita Šalković-Petrišić (Medicinski fakultet, Zavod za farmakologiju; prva nova grupa); 3) Marija Heffer i Jasenka Wagner (neurokemija i stanična biologija – Medicinski fakultet Sveučilišta u Osijeku; druga nova grupa); 4) Maja Jazvinščak-Jembrek (molekulska biologija – Institut Ruđer Bošković; treća nova grupa); 4) Domagoj Đikić i Nada Oršolić (biologija i animalna fiziologija – Prirodoslovno matematički fakultet Sveučilišta u Zagrebu; četvrta nova grupa). Skupina 2 će se uredotočiti na patogeneze mehanizme, biološke biljege, te razvitak novih dijagnostičkih i terapijskih pristupa neurodegeneraciji, napose u odnosu na Alzheimerovu bolest i vaskularnu demenciju. Istraživanje

developmental reorganization and myelination of transient cerebral compartments after hypoxia of pregnant mini-pigs caused by ligation of uterine arteries (Dobranić, Samardžija, Vnuk). The compartmental fine histological analysis (Kostović, Judaš) will be compared with general structural abnormalities, using pathological findings (Grabarević group). Finally, Miloš Judaš and Maja Capanec, will initiate pioneering collaboration with Ida Raffaelli group (University of Zagreb Faculty of Social Sciences & Humanities, Department of Linguistics) to bridge the currently existing gap between neuroscience and humanities in Croatia (see below the description of Research Plan of major Group 5).

Group 2. New Biomarkers of Ageing, Alzheimer's Disease, Vascular Dementia and insulin resistant brain state (Group Leader: Goran Šimić)

Continuation, background & networking:

This group will continue and expand collaborative research started in 2012, with competitive Croatian Science Foundation (CSF) grant awarded to G. Šimić (Detection and tracking of biological markers for early therapeutic intervention in sporadic Alzheimer's disease – <http://alzbiotrack.hiim.hr>) and strengthened by another recently awarded CSF grant to Goran Šimić. This interdisciplinary group network consists of eight individual research teams (four already collaborating at the CIBR plus four new partners to the proposed Centre), as follows: 1) Four teams from the CIBR: Goran Šimić (neuroanatomy & neuropathology), Dora Višnjic & Hrvoje Banfić (physiology & molecular cell biology), and Svjetlana Kalanj Bognar (neurochemistry); 2) new partnering group in the Centre Melita Šalković-Petrišić (School of Medicine, Department of Pharmacology); 3) second new partnering group in the Centre, team of Marija Heffer & Jasenka Wagner (neurochemistry & cell biology – University of Osijek School of Medicine); 4) team of Maja Jazvinščak-Jembrek (molecular biology – Institute Ruđer Bošković; third new partnering group in the Centre); 5) team of Domagoj Đikić & Nada Oršolić (biology & animal physiology – University of Zagreb Faculty of Natural Sciences; fourth new partnering group in the Centre). Group 2 will focus on pathogenetic mechanisms, biological markers and development of novel diagnostic and therapeutic approaches for neurodegeneration, particularly in relation to Alzheimer's disease and vascular dementia. Research is divided in four work

je podijeljeno u 4 radne skupine (RS): RS1 za proučavanje glikolipida i proteina (napose neuroplastina) u neurodegeneraciji; RS2 će nadalje karakterizirati eksperimentalni štakorski model Alzheimerove bolesti putem intracerebroventrikulskog davanja streptozotocina (STZ) te model moždanih stanja povezanih s inzulinskom rezistencijom; RS3 će analizirati mehanizme neurofibrilarne degeneracije i poremećaja prostorne orijentacije; te RS4 koja će zajedničnim naporima s RS3 pokušati bolje karakterizirati mehanizme neurodegeneracije in vitro i in vivo.

Skupina 3: Kliničke i eksperimentalne studije cerebralnih hipoksijsko ishemijskih i hemoragijskih lezija te njihov odnos sa promjenama tlaka i gibanja intrakranijskih tekućina (voditelji Marko Radoš i Marijan Klarica).

Kontinuitet, pozadina i umrežavanje: Skupina 3 uspostaviti će i razvijati istraživačku suradnju između kliničke skupine neuroradiologa i neurologa s bogatim iskustvom u liječenju pacijenata s aneurizmatском subarahnoidnom hemoragijom (aSAH), (Klinički bolnički centar Zagreb, Klinički Zavodi za neuroradiologiju i neurologiju; Marko Radoš, David Ozretić, Zdravka Poljaković) te neuroznanstvenika koji imaju 30-godišnje iskustvo u istraživanju patofiziologije cerebrospinalne tekućine na eksperimentalnim životinjama (mačke, psi) (Marijan Klarica na Hrvatskom institutu za istraživanje mozga i Darko Orešković na Institutu Ruđer Bošković). Pored toga, novo uspostavljena znanstvena grupa na Hrvatskom institutu za istraživanje mozga (Marija Renić, fiziolog i eksperimentalni neurolog, koja se nakon izuzetno uspješne karijere u Sjedinjenim američkim državama nedavno vratila u RH) proučavat će mehanizam vazokonstrukcije nakon subarahnoidne hemoragije na eksperimentalnim modelima vazokonstrukcije kod štakora. Grupe Marka Radoša i Zdravke Poljaković rade u vodećoj hrvatskoj bolnici (KBC Zagreb, bolnica nulte kategorije) i prvi su u Hrvatskoj uveli endovaskularne intrakranijske procedure u rutinsku kliničku praksu, uključujući i procedure endovaskularne embolizacije rupturiranih i nerupturiranih aneurizmi. Tijekom posljednjih 12 godina ove dvije kliničke grupe provele su više od 1000 endovaskularnih embolizacija aneurizmi od čega je polovica pacijenta bila sa akutnim aneurizmatским subarahnoidnim krvarenjem.

Istraživačka grupa Klarice i Oreškovića u seriji publikacija u časopisima sa visokim znanstvenim odjekom te u relevantnim neuroradi-

packages(WP): WP1 for studying glycolipids and proteins (esp. neuroplastin) in neurodegeneration; WP2 for further characterization of STZ-icv experimental rat model of Alzheimer's disease and insulin resistant brain state; WP3 analyzing mechanisms of neurofibrillary degeneration and impairment of spatial orientation; and WP4 to joint efforts with WP3 towards better characterization of neurodegeneration mechanisms in vitro and in vivo.

Group 3: Clinical & Experimental Studies of Cerebral Hypoxic/ischaemic & Haemorrhagic lesions and Their Relation to Alterations in Movement and Pressure of Intracranial Fluids (led by Marko Radoš & Marijan Klarica).

Continuation, background & networking:

Group 3 aims to establish and promote research collaboration between clinical groups of neuroradiologists and neurologists (Clinical Hospital Centre Zagreb – Departments of Neuroradiology and Neurology; Marko Radoš, David Ozretić, Zdravka Poljaković) involved in long-term studies of patients with aneurysmal subarachnoid haemorrhage (aSAH), and two basic neuroscience groups which have 30-years experience in investigating pathophysiology of cerebrospinal fluid (CSF) in experimental animal (cats, dogs) models (Marijan Klarica at the CIBR and Darko Orešković at the Institute Ruđer Bošković). In addition, newly established research group at the CIBR (Marija Renić, physiologist & experimental neurologist, who returned to Zagreb after pursuing research career in the USA) will study vasoconstriction after SAH in experimental rat model. Groups of Marko Radoš and Zdravka Poljaković work at the Croatia's leading teaching & research hospital, and were the first to introduce endovascular intracranial procedures in routine clinical practice, including patients with aSAH. Over the past 12 years, they performed more than 1.000 endovascular intracranial interventional procedures. Research groups of Klarica & Orešković, in a series of publications in high-impact journals and relevant neuroradiological and anesthesiology handbooks, introduced novel experimental animal models and developed a new concept of CSF pathophysiology. The proposed research is divided in three work packages: WP1 (Radoš & Poljaković), WP2 (Klarica & Orešković) and WP3 (Renić).

New conceptual approach to the analysis of intracranial fluids motion in states characterized by increase in intracranial pressure

ološkim i anesteziološkim knjigama uvela je novi eksperimentalni životinjski model i razvila novi koncept patofiziologije cerebroskopske tekućine. Predloženo istraživanje je podjeljeno u tri radne podskupine: RS1 (Radoš&Poljaković), RS2 (Klarica & Orešković) i RS3 (Renić). **Novi koncept analize kretanja intrakranijskih tekućina u stanjima karakteriziranim porastom intrakranijskog tlaka. (Marijan Klarica & Darko Orešković)**

Kontinuitet i osnove: Dugotrajni cilj našeg istraživanja je analiza mehanizama koji reguliraju gibanje intrakranijskih tekućina (intracelularne i ekstracelularne tekućine, likvora i plazme krvi). Prethodnim radovima smo pokazali kako klasična hipoteza fiziologije likvora (temeljena na aktivnoj sekreciji, cirkulaciji i resorpciji likvora) ne može objasniti brojne eksperimentalne nalaze i klinička stanja kod kojih se javlja porast intrakranijskog tlaka. (npr. edem mozga, ishemijski inzult). Mi smo razvili seriju originalnih eksperimentalnih modela; akutna i subakutna obstrukcija mezencefalnog akvedukta; akutna i kronična stenoza cervikalnog subarahnoidnog prostora; ventrikulo-akveduktalna perfuzija; mjerenje intrakranijskog tlaka na nekoliko pozicija u različitim položajima tijela sa ili bez blokade komunikacije između različitih dijelova likvorskih prostora; novi in vitro modeli kraniospinalnog sistema likvora. Za cjelovito razumijevanje poremećaja perfuzije mozga nije nam dovoljno poznavati samo patofiziologiju kardiovaskularnog sistema nego moramo poznavati mehanizme kontrole intrakranijskog tlaka. Nedavno smo pokazali (Klarica i sur. 2014, PLoS One) kako je intrakranijski tlak u uspravnom položaju tijela negativan (subatmosferski), što je primarno posljedica biofizičkih karakteristika intrakranijskog i spinalnog likvorskog prostora. Ovo je u suprotnosti sa prevladavajućim konceptom kako je intrakranijski tlak u subarahnoidnim prostorima pozitivan zbog stalnog lučenja i cirkulacije likvora. Razvojem originalnog in vitro modela koji svojim biofizičkim karakteristikama oponaša kranijalni i spinalni dio sustava uspjeli smo sukladno zakonima o dinamici fluida intrakranijski tlak likvora precizno definirati matematičkom jednadžbom u koju je po prvi puta uključena i varijabla g (gravitacija) te se time otvara mogućnost razumijevanja fiziologije tlaka likvora u ekstremnim uvjetima (svemirska istraživanja, zrakoplovna medicina, medicina ronjenja i sl.). Brojni neurološki poremećaji su praćeni porastom intrakranijskog tlaka (npr. neurotrauma, moždani udar) te je od iznimne važnosti razumijevanje kompenzatornih mehanizama koji

(Marijan Klarica & Darko Orešković)

Continuation and background: The long-term goal of our research is systematic analysis of mechanisms that regulate intracranial pressure and determine and regulate motion of intracranial fluids (intracellular and extracellular fluid, CSF, blood plasma). We have shown that the classical hypothesis of CSF physiology (based on active secretion, circulation and reabsorption of the CSF) cannot explain a number of experimental and clinical conditions accompanied with an increased intracranial pressure (e.g., brain oedema, stroke). We developed a series of original experimental models: acute and subchronic obstruction of mesencephalic aqueduct; acute and chronic stenosis of cervical subarachnoid space; ventriculo-aqueductal perfusion; measurement of intracranial pressure on several locations at different body positions, with or without blockade of communication between different parts of the CSF system; new in vitro model of craniospinal system. To completely understand perfusion impairments in the brain, we have to know not only pathophysiology of cardiovascular system but also mechanisms which regulate intracranial pressure. We recently demonstrated (Klarica et al. 2014, PLoS One) that intracranial pressure in the upright position is negative (subatmospheric), which is primarily a consequence of biophysical characteristics of cranial and spinal part of the CSF system. This in contrast with prevailing concept that intracranial pressure is positive due to the permanent CSF secretion and circulation. We succeeded in precise mathematical description of intracranial pressure using the law of fluid mechanics on our newly developed in vitro model. For the first time gravity (g) is incorporated in intracranial pressure calculation which opens new vistas in investigation and explanation of CSF physiology under extreme conditions (space exploration, air and diving medicine). Numerous neurological disorders are accompanied with increased intracranial pressure (e.g., neurotrauma, stroke) and it is of utmost importance to understand compensatory mechanisms which regulate intracranial pressure in order to be able to apply necessary therapy which will maintain intracranial pressure within physiological range. Our previous studies point toward the spinal part of the CSF system as a key factor in maintenance of CSF normotension, which is in contrast with prevailing assumption that normotension is maintained by increased reabsorption, decreased CSF secretion, vasoconstriction, etc. We noted that exhaustion of compensatory potential of spinal part of

reguliraju intrakranijski tlak, jer bi tako mogli prilagoditi adekvatnu terapiju za održavanje intrakranijskog tlaka unutar fiziološkog opsega. Naše prethodne studije su ukazale kako je spinalni dio likvorskog prostora od ključne važnosti u održavanju normalnog tlaka likvora što je u suprotnosti sa prevladavajućim mišljenjem kako se intrakranijska normotenzija održava pojačanom resorpcijom, smanjenjem lučenja likvora vazokonstrikcijom i sl. Iscrpljivanje kompenzatornih potencijala spinalnog dijela likvorskog sustava dovodi do naglog porasta intrakranijskog tlaka te posljedično i do pogoršanja neurološkog statusa.

U nastavku naših istraživanja ispitati ćemo slijedeće elemente vezane za patofiziologiju likovra:

1) redistribuciju likvora unutar kraniospinalnog sustava pri različitim položajima tijela u MR;

2) osjetljivosti na hipoksiju u različitim moždanim regijama (prednja i stražnja cirkulacija, korteks i bijela tvar i sl.) mjerenjem difuzijskih koeficijenata na MR prije, tijekom i nakon apneje kod posebne skupine profesionalnih ronilaca koji mogu provesti u apneji više od 5 minuta.;

3) na životinjskim modelima ćemo učiniti analizu kako različite metoda za sniženje intrakranijskog tlaka (i.v. primjena hiperosmolarnih otopina, hiperventilacija, vanjska likvorska drenaža i kranijektomija) utječu na volumen likvora zasebno u kranijском i spinalnom dijelu.

Skupina 4: Pretklinička istraživanja hipoksično/ishemičnih lezija u eksperimentalnim modelima na glodavcima (voditelji: Srećko Gajović i Dinko Mitrečić)

Nastavak prethodnih istraživanja, pozadina i umrežavanje: Istraživači skupine 4 nastaviti će i proširiti suradnju na istraživanjima koja su počela 2012. godine s FP7 REGPOT projektom GLOWBRAIN (voditelj: Srećko Gajović). Ta će skupina istraživača objединiti 4 istraživačke grupe iz HIIM-a (voditelji tih grupa su Srećko Gajović, Dinko Mitrečić, Aleksandra Sinđić i Nives Pećina-Šlaus) s još jednom grupom s Prehrambeno-biotehnoškog fakulteta Sveučilišta u Zagrebu (voditelj grupe je Reno Hrašćan). Skupina će također nastaviti i proširiti dosadašnju ekstenzivnu međunarodnu suradnju koju je uspostavila kroz FP7 GLOWBRAIN projekt. Grupa Aleksandre Sinđić nastaviti će suradnju s Eberhard Schlatterom (Sveučilišna bolnica Münster, Njemačka), Michaelom Kuhn (Sveučilište u Würzburgu, Njemačka), Scottom

CSF system leads to abrupt increase of intracranial pressure, which induces deterioration of neurological status. In this continuation of our research we will investigate the following aspects of CSF pathophysiology:

1) Redistribution of CSF within cerebrospinal system in different body positions, using MRI; 2) Perform MRI measurements (apparent diffusion coefficients) of different vulnerability to hypoxia in different brain regions (anterior and posterior circulation, white and grey matter, etc.) in special group of professional divers who can hold breath for longer than 5 minutes – measurements performed before, during, and after the apnoea;

3) Measurements of CSF volume changes (separately in cranial and spinal part of the CSF system) during the application of various methods for decreasing intracranial pressure (i.v. application of hyperosmolar solutions, hyperventilation, CSF drainage, craniotomy) in animal model.

Group 4: Preclinical studies of hypoxic/ischaemic lesions in experimental rodent models (led by Srećko Gajović & Dinko Mitrečić)

Continuation, background & networking: Researchers of Group 4 will continue and expand collaborative research started in 2012 with FP7 REGPOT project GLOWBRAIN (P.I.: Srećko Gajović). This group connects four research teams from the CIBR (Srećko Gajović, Dinko Mitrečić, Aleksandra Sinđić, Nives Pećina-Šlaus) with one research team from University of Zagreb Faculty of Food Technology & Biotechnology (Reno Hrašćan). It will also continue and expand collaboration within extensive international network established through FP7 GLOWBRAIN. The group of Aleksandra Sinđić will continue its collaboration with Eberhard Schlatter (University Hospital Münster, Germany), Michela Kuhn (University of Würzburg, Germany), Scott A. Waldman (Thomas Jefferson University Hospital, Philadelphia, USA), and Michael F. Romero (Mayo Clinic College of Medicine, Rochester, USA). The research of Group 4 is divided in three Work Packages (WP1 – WP3), as described below. The WP2 (Neuro-oncology group) is included to enable initial (3-5 years) period for communication, collaboration and integration with WP1 (Stem cells). Namely, cells with markers of tumor progression (such as N-cadherin, vimentin and fibronectin) can be (in future collaborative studies of WP1 and WP3) tagged with nanoparticles and transplanted into rodent brain (development of new exper-

A. Waldmanom (Sveučilišna bolnica Thomas Jefferson, Philadelphia, S.A.D.), te Michael F. Romerom (Mayo Clinic College of Medicine, Rochester, S.A.D.). Istraživanja u skupini 4 podjeljena su u tri Radne Skupine (RS1-RS3), kako slijedi. RS2 (Neuro-onkološka grupa) biti će u početnom razdoblju uključena u suradnju kroz povezivanje s RS1 (Matične stanice). Naime, stanice s biljezima progresije tumora (kao što su N-kadherin, vimentin i fibronektin) mogu se (u predviđenoj budućim istraživanjima RS1 s RS3) obilježiti nanočesticama i transplantirati u mozak glodavca (razvitak novih eksperimentalnih protokola za proučavanje tumora mozga u glodavaca), i ako se kroz ove pokuse ostvare obećavajući rezultati, buduća suradnja sa skupinom 3 (neuroradiologija) moći će poslužiti za razvitak tehnike kojom bi se intravaskularnim kateterom dostavljale stanice obilježene nanočesticama (ili biomaterijalima) radi in vivo praćenja tumorskih stanica i/ili pomicanja u mozgu čovjeka, odnosno za intrakranijalno davanje lijekova i biomaterijala za liječenje tumora.

Skupina 5: Kognitivna i lingvistička analiza jezičnih poremećaja i oporavka nakon hipoksijskoishemijskog oštećenja mozga (voditelji: Ida Raffaelli & Miloš Judaš).

Pozadina i umrežavanje: Ova istraživačka skupina predstavlja pionirski pothvat u Hrvatskoj da se premosti sadašnji jaz između neuroznanosti i humanističkih disciplina, tako što se u rad Centra uključuje vodeća hrvatska skupina lingvista (skupina Ide Raffaelli – Odsjek za lingvistiku, Filozofski fakultet Sveučilišta u Zagrebu). Ta skupina će započeti suradnju s nekoliko drugih, već interdisciplinarno povezanih, skupina iz glavne Skupine 1 (Miloš Judaš – neuroanatom, Maja Capanec – logoped, Mirna Kostović Srzentić – psiholog, Milan Radoš – neuroradiolog, fMRI) i glavne Skupine 3 (Zdravka Poljaković, neurolog). Ciljevi ove suradnje su:

- a) uspostaviti transdisciplinarni dijalog (prve 2-3 godine rada);
- b) omogućiti lingvistima pristup neurološkim pacijentima s jezičnim poremećajima nakon moždanog udara, tako da mogu početi razvijati odgovarajuće kognitivne i lingvističke testove za detektiranje za hrvatski jezik specifičnih problema u tih pacijenata;
- c) razviti kognitivne testove za analizu jezičnih funkcija tijekom fMRI pregleda pacijenata nakon moždanog udara (tijekom 4. i 5. godine). Na sličan način će se pristupiti i analizi jezičnog razvoja u djece s dokazanim perina-

mental protocols for studying brain tumors in rodents), and if such experiments provide promising results, future collaboration with Group 3 (neuroradiology) may serve to develop intravascular catheter-delivered nanoparticle tagged cells (or biomaterials) for in vivo tracing of tumor cell location and/or movement in the human brain, or for intracranial delivery of drugs and biomaterials for tumor treatment.

Group 5: Cognitive & Linguistic Analysis of Language Changes & Recovery after Stroke (led by Ida Raffaelli & Miloš Judaš).

Background & Networking: This Group represents a pioneering effort to bridge the gap between neuroscience and humanities in Croatia, by including Croatia's leading experts in linguistics (Ida Raffaelli group, Department of Linguistics, University of Zagreb Faculty of Social Sciences & Humanities). This research group will engage in collaboration with several other already interdisciplinary connected research groups from main Group 1 (Miloš Judaš - neuroanatomist, Maja Capanec – speech therapist; Mirna Kostović Srzentić – psychologist; Milan Radoš – neuroradiologist, fMRI) and main Group 3 (Zdravka Poljaković, neurologist). The aims of this collaboration are:

- a) to establish cross-disciplinary dialogue (first 2-3 years);
- b) to secure access of linguists to neurological patients with language impairments after stroke, so that they can start to develop appropriate cognitive and linguistic tests for detecting language-specific problems (Croatian vs. English);
- c) to develop cognitive tests for language assessment during fMRI investigations of post-stroke patients (during the 4. and 5. year). Another similar line of research will be pursued with respect to language development in children who suffered perinatal hypoxic/ischaemic brain lesion (collaboration with Maja Capanec and Mirna Kostović Srzentić).

Group 6: Inovative markers of therapeutic response in mental disorders (led by Neven Henigsberg)

Continuation, background & networking, competitiveness and methodological adequacy: This part of research is a continuation of long and productive interdisciplinary and international collaboration in studying genetic determinants which modify the onset and course of mental disorders and identification of biological markers of treatment outcome.

talnim hipoksijsko-ishemijskim oštećenjem mozga (suradnja s Majom Capanec i Mirnom Kostović Srzentić).

Skupina 6: Inovativni markeri terapijskog odgovora kod mentalnih poremećaja (voditelj skupine: Neven Henigsberg)

Nastavak, pozadina i umrežavanje; kompetitivnost i metodološka primjerenost: Ovaj dio programa je nastavak duge i produktivne interdisciplinarne i međunarodne suradnje na istraživanju genetskih determinanti koje modificiraju početak i tijek mentalnih poremećaja, te na identifikaciji biomarkera terapijskog ishoda. Ta je suradnja započela 2006. kad je skupina Nevena Henigsberga postala dio velikog europskog FP6 projekta u suradnji s Institute of Psychiatry – King’s College London (Peter McGuffin) s desetak drugih inozemnih partnera. To je trenutno najveći EU projekt usmjeren na analizu genomskih markera terapijskog odgovora u depresiji, a posljednjih godina istraživanje je prošireno i uporabom neuroimaging tehnika. Ovo je također dodatna razrada kompetitivnog HRZZ projekta koji je nedavno dobio Neven Henigsberg (Multimodal approach to treatment and long-term follow-up of effects of depression by using MRI). Svi profesionalni i tehnički uvjeti za provedbu istraživanja već postoje u HIIM-u i u drugim ustanovama uključenim u mrežu Centra. Glavni pristup se temelji na neuroimaging/genetičkim metodama, kako je opisano u našim radovima objavljenim u vodećim svjetskim časopisima. Mreža istraživačkih skupina u sklopu ovog ZCI sastoji se od istraživača u:

a) HIIM-u (Henigsberg, Hrabač),
b) Poliklinici Neuron (Petra Kalember),
c) KBC Zagreb (Marko Radoš, Milan Radoš, Darko Marčinko),
d) Kliničkoj bolnici Dubrava (Anđelko Vidović)
e) Psihijatrijskoj bolnici Vrapče (Vlado Jukić).
Prepoznavanje, o vremenu ovisnih, neurobioloških promjena u mozgu in vivo je ključno u razjašnjavanju uzroka i longitudinalnog tijeka mentalnih poremećaja. Prepoznavanje regionalno-specifičnih biokemijskih obrazaca i obrazaca funkcionalne povezanosti mozga u izravnoj je vezi s neurobiološkim mehanizmima koji su u podlozi promjena u mozgu koje se fenotipski ispoljavaju i neprecizno klasificiraju u određene dijagnostičke kategorije psihijatrijskih poremećaja. Naše istraživanje pokazalo je da, iako je genetski čimbenik u razvoju i liječenju depresije uveliko istraživano, genetski faktor promatran izolirano slab je pretskazatelj terapijskog odgovora u depresiji. Gleda-

This collaboration started in 2006 when group of Neven Henigsberg became part of FP6 project in collaboration with Institute of Psychiatry - King’s College London (Peter McGuffin) and a dozen of other international partners. This has been the largest EU contemporary project aimed to assay genomic markers of therapeutic response in depression, the research later being expanded with neuroimaging techniques. It will also expand the research of the Croatian Science Foundation grant recently awarded to Neven Henigsberg (Multimodal approach to treatment and long-term follow-up of effects of depression by using MRI). All professional and technical prerequisites for continuation of this research are already set in place at the CIBR and other institutions involved in the current Centre network. The main approach relies on neuroimaging/genetic methods as described in papers published in high impact journals. The network of research groups proposed in this Centre of Excellence consists of researchers located at:

a) the CIBR (Henigsberg, Hrabač),
b) Polyclinic Neuron (Petra Kalember),
c) Clinical Hospital Center Zagreb (Marko Radoš, Milan Radoš, Darko Marčinko),
d) Clinical Hospital Dubrava (Anđelko Vidović), and
e) Psychiatric University Hospital Vrapče (Vlado Jukić).

Recognition of temporal-dependent neurobiological changes in brain in vivo is crucial in elucidation of causes and longitudinal course of mental disorders. Identification of spatial-specific biochemical and connectivity patterns pinpoints neurobiological mechanisms underlying changes in brain expressed phenotypes vaguely grouped in categories of psychiatric disorders. Our previous studies demonstrated that genetic contribution per se is a weak predictor of treatment outcome in depression, although genetic susceptibility in depression is well grounded. In relation to broader class, genetic influence is not predictive for ADRs overall and, even in a huge sample, pharmacokinetics-related ADRs failed to be explained by P450 genotypes or by serum drug concentrations. In addition, biochemical, microstructural and functional connectivity changes after exposure to psychoactive medication are not class-specific, but sub-class or even substance-specific and confounded by other systemic state-specific variables. We showed that increase in neuronal density after treatment (as observed by 1-HMRS) may be related to particular substance in monotherapy, and that more than 10% of individual-level variance of

jući šire, genetski utjecaj nije niti pouzdan pretskazatelj nuspojava te se čak ni u velikom uzorku farmakokinetički determinirane nuspojave nisu uspjele objasniti genotipom P450 niti koncentracijom lijeka u serumu. Biokemijske i mikrostrukturane promjene te promjene funkcionalne povezanosti mozga nakon izloženosti psihoaktivnim lijekovima ne čine se povezane s pojedinom skupinom, nego vjerojatnije s podskupinom lijeka, a moguće je čak da su velikoj mjeri ovisni o pojedinoj supstanci sa specifičnim mehanizmom djelovanja i u vezi su i s drugim sistemskim, o stanju ovisnim varijablama. Naše je istraživanje pokazalo da povećanje neuronalne gustoće nakon terapije, primijećeno na spektroskopiji magnetskom rezonancom, može biti povezano za određenu supstancu u monoterapiji, kao što se pokazalo u shizofreniji i u depresiji. Više od 10% varijance na individualnoj razini terapijskog ishoda u depresiji moguće je objasniti isključivo interakcijom lijeka i sistemskog upalnog markera (CRP). Našim ćemo pristupom, prepoznavanjem međuovisnosti genetskih i okolinskih faktora, analizirati strukturne i vremenske promjene u mozgu u odnosu na multiaksijalnu ekspresiju psihometrijskih i psihopatoloških promjena putem sljedećih istraživanja:

1. Genetski, biokemijski i markeri funkcijske povezanosti mozga u prepoznavanju ranog terapijskog odgovora kod mentalnih poremećaja in vivo (u suradnji s Markom Radošem, Majom Bajs Janović i studentima posljediplomskog studija)
2. Kognitivni, emocionalni i perceptivni korelati posredovani acetilkolinom u učinkovitosti terapije mentalnih poremećaja (Mirna Kostović)
3. Oksidativni stres/hipoksija u nastanku i tijeku mentalnih poremećaja (u suradnji s Anđelkom Vidovićem, Viktorijom Erdeljić-Turk, Darkom Marčinkom, Helenom Šarac, Zrnkom Kovačić-Petrović, studentima posljediplomskog studija)
4. Epidemiološke, etičke i socioekonomske posljedice prepoznavanja markera ranog terapijskog odgovora u liječenju mentalnih poremećaja (u suradnji s Vladom Jukićem, Mladenom Lončarom)

Slika 1

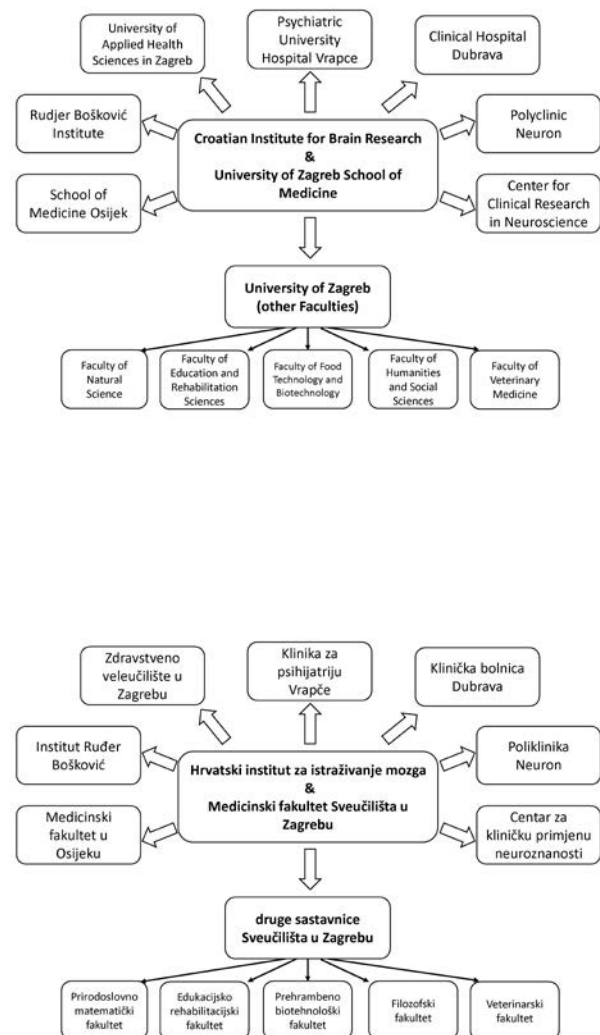
Hrvatski institut za istraživanje mozga i njegova ključna pozicija u širokoj mreži suradnih ustanova

treatment outcome in depression could be explained solely by medication vs. systemic inflammation marker (CRP) interaction. Therefore, our approach is to analyse spatial and temporal changes in brain in relation to multi-axial expression of behavioural pathology by evaluating:

- 1) Genetic, biochemical and connectivity time-leading in vivo brain markers of treatment response in mental disorders (in cooperation with Group 3 neuroimaging experts);
2. Acetylcholine-mediated cognitive, emotional and perceptual correlates of treatment effectiveness in mental disorders;
3. Oxydative stress/ hypoxia in onset and course of mental disorders; and
4. Epidemiological, ethical and socioeconomic impacts of recognition of treatment response markers in mental disorders.

Figure 1

Croatian institute for brain research and its key position in vast network of cooperating institutions





POPIS I RAD LABORATORIJA NA HIIM-u



LIST AND ACTIVITIES OF LABORATORIES AT THE CIBR

ZAVOD ZA NEUROZNANOST (Goran Šimić)
Odsjek za razvojnu neuroznanost (Miloš Judaš) –

*Laboratorij za neurohistologiju i
kemijsku anatomiju (Mario Vukšić)*

Voditelj:

Prof.dr.sc. Mario Vukšić
Izvanredni profesor neuroznanosti
Šalata 12, 10 000, Zagreb

Suradnici:

Akademik Ivica Kostović
Prof.dr.sc. Miloš Judaš
Prof.dr.sc. Zdravko Petanjek
Prof.dr.sc. Nataša Jovanov-Milošević
Doc.dr.sc. Željka Krsnik
Doc.dr.sc. Goran Sedmak
Vinka Kovačević, dr.med.
Danica Budinščak, lab. Ing.

Razvoj ljudskog mozga je vrlo složen i dugotrajan proces. U našem laboratoriju koristimo različite histološke metode kako bismo istraživali osobitosti razvoja ljudskog mozga. Neke od histoloških i histokemijski metoda koje koristimo su: Golgi i biocitin metode za prikaz cijelih neurona, AChE histokemija, NADPH histokemija, Nisslovo bojanje, Weigertovo bojanje, bojanje po Gallyas-u, srebrnu modifikaciju Nisslova bojanja, PAS-AB bojanje, itd.

Znanstveni interesi:

Razvoj subtalamičke zone i njezina uloga u patogenezi razvojnih poremećaja mozga.
Razvoj hipokampusa i povezanih struktura.
Morfološka i biokemijska analiza neurona bijele tvari.
Korelacija histoloških preparata s snimkama magnetske rezonance.
Razvoj asocijativnih (dugih i kratkih) putova u mozgu čovjeka.

Trenutno aktivni projekti u laboratoriju:

Ivica Kostović: Subplate zona ljudskog mozga: neriješeni problemi (HRZZ projekt broj 4517)
Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (HRZZ projekt)
Mario Vukšić: Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (HRZZ projekt)

DEPARTMENT OF NEUROSCIENCE (Goran Šimić)

Division of developmental neuroscience (Miloš Judaš)

Laboratory for neurohistology and chemical anatomy (Mario Vukšić)

Head:

Associate Professor Mario Vukšić
Professor of Neuroscience
Šalata 12, 10 000 Zagreb

Associates:

Professor emeritus Ivica Kostović
Professor Miloš Judaš
Associate Professor Zdravko Petanjek
Associate Professor Nataša Jovanov-Milošević
Assistant Professor Željka Krsnik
Assistant Professor Goran Sedmak
Vinka Kovačević, MD
Danica Budinščak, lab. Ing.

Development of the human brain is very complex and long process. In our laboratory, we use various histological methods in order to elucidate specificities of the human brain development. Histochemistry methods are still very useful methods in developmental neuroanatomy research. In this laboratory the following methods are performed: Golgi and biocytin methods for staining whole single neuron, AChE histochemistry, NADPH histochemistry, Nissl staining, Weigert staining, Gallyas staining, Ag-Nissl staining, PAS-AB staining, etc.

Scientific scope

Development of the subplate zone and its role in the pathogenesis of developmental brain disorders.
Development of the hippocampus and related structures.
Morphological and biochemical analysis of the interstitial neurons of the white matter.
Correlation of histological and MRI images.
Development of associative pathways (long and short) in the human brain.

Ongoing projects:

Ivica Kostović: Subplate zone of the human brain: unsolved problems. (CSF research grant)
Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (CSF research grant)
Mario Vukšić: Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (CSF research grant)

Popis izabranih, nedavnih publikacija / List of the selected recent papers:

1. Jovanov-Milosevic, N., Petanjek, Z., Petrovic, D., Judas, M. and Kostovic, I.; (2010); "Morphology, molecular phenotypes and distribution of neurons in developing human corpus callosum." European Journal of Neuroscience **32**(9): 1423-1432.
2. Kostovic, I., Jovanov-Milosevic, N., Rados, M., Sedmak, G., Benjak, V., Kostovic-Srzentic, M., Vasung, L., Culjat, M., Rados, M., Huppi, P. and Judas, M.; (2014); "Perinatal and early postnatal reorganization of the subplate and related cellular compartments in the human cerebral wall as revealed by histological and mri approaches." Brain Structure & Function **219**(1): 231-253.
3. Kostovic, I. and Judas, M.; (2010); "The development of the subplate and thalamocortical connections in the human foetal brain." Acta Paediatrica **99**(8): 1119-1127.
4. Kostovic, I., Judas, M. and Sedmak, G.; (2011); "Developmental history of the subplate zone, subplate neurons and interstitial white matter neurons: Relevance for schizophrenia." International Journal of Developmental Neuroscience **29**(3): 193-205.
5. Kostovic, I., Sedmak, G., Vuksic, M. and Judas, M.; (2015); "The relevance of human fetal subplate zone for developmental neuropathology of neuronal migration disorders and cortical dysplasia." CNS Neuroscience & Therapeutics **21**(2): 74-82.
6. Pogledic, I., Kostovic, I., Fallet-Bianco, C., Adle-Biassette, H., Gressens, P. and Verney, C.; (2014); "Involvement of the subplate zone in preterm infants with periventricular white matter injury." Brain Pathology **24**(2): 128-141.
7. Vasung, L., Huang, H., Jovanov-Milosevic, N., Pletikos, M., Mori, S. and Kostovic, I.; (2010); "Development of axonal pathways in the human fetal fronto-limbic brain: Histochemical characterization and diffusion tensor imaging." Journal of Anatomy **217**(4): 400-417.
8. Vasung, L., Jovanov-Milosevic, N., Pletikos, M., Mori, S., Judas, M. and Kostovic, I.; (2011); "Prominent periventricular fiber system related to ganglionic eminence and striatum in the human fetal cerebrum." Brain Structure & Function **215**(3-4): 237-253.

Laboratorij za razvojnu neuropatologiju (Goran Šimić)

Voditelj:

Prof. dr. sc. Goran Šimić, dr. med.
Redoviti profesor neuroznanosti i anatomije
Predstojnik Zavoda za neuroznanost i Pročelnik
Vijeća predmeta "Temelji neuroznanosti"
Zavod za neuroznanost, Hrvatski institut za
istraživanje mozga
Medicinski fakultet Sveučilišta u Zagrebu
Šalata 12, 10000 Zagreb, Republika Hrvatska
Translational Neuroscience, glavni i odgovorni
urednik <http://www.degruyter.com/view/j/tncsci>
gsimic@hiim.hr

Suradnici:

Mirjana Babić, mag.biol.mol.
Zavod za neuroznanost, Hrvatski institut za
istraživanje mozga
Medicinski fakultet Sveučilišta u Zagrebu
Šalata 12, 10000 Zagreb, Republika Hrvatska
mbabic@hiim.hr

Istraživački interesi:

Istraživački interesi Laboratorija za razvojnu neuropatologiju usmjereni su na proučavanje: (1) mehanizama starenja i neurodegeneracije, napose selektivne vulnerabilnosti neurona u Alzheimerovoj bolesti, (2) etiopatogeneze spinalnih mišićnih atrofija i drugih razvojnih neuromišićnih bolesti, te (3) ustrojstva, djelovanja i poremećaja moždane kore, te njezine kemijske neuroanatomije. U posljednjih nekoliko godina je glavni cilj laboratorija bilo određivanje bioloških biljega Alzheimerove bolesti iz cerebrospinalne tekućine i plazme, te usporedba dobivenih vrijednosti s rezultatima komplementarnih dijagnostičkih postupaka neuropsihološkog testiranja, evociranih potencijala, genetičkih i neuroslikovnih bioloških biljega (<http://alzbiotrack.hiim.hr/>). U našem laboratoriju također odnedavno rabimo inovativni neinvazivni test skrivenog objekta kojim se procjenjuje poremećaj prostorne orijentacije kao jedan od najranijih znakova Alzheimerove bolesti. Pored određivanja polimorfizama gena povezanih sa sporadičnom Alzheimerovom bolešću s kasnim početkom, te njihove uloge u patogenezi bolesti, naš je krajnji cilj postavljanje pouzdane rane dijagnoze bolesti u pacijenata s blagim spoznajnim poremećajem, ali također i njezino diferencijalno-dijagnostičko razlikovanje od drugih primarnih uzroka demencije. Koristeći nekoliko različitih kultura živčanih stanica istražujemo i učinke potencijalno neuroprotektivnih spojeva na patološke promjene tipične za Alzheimerovu bolest, posebice fosforilaciju tau proteina. Usporedno s navedenim istraživanjima demencije, pomoću mikropostrojbene analize i konfokalne imunofluorescencijske mikroskopije nedavno smo započeli istraživati i promjene izraženosti gena te podvrsti dopaminergičkih receptora na postmortalnim uzorcima mozgovca bolesnika sa shizofrenijom.

Laboratory for developmental neuropathology (Goran Šimić)

Head:

Goran Šimić, MD, PhD
Professor of Neuroscience and Anatomy
Chair, Department of Neuroscience
Croatian Institute for Brain Research
University of Zagreb Medical School
Šalata 12, HR-10000 Zagreb, Republic of Croatia
Translational Neuroscience, Editor-in-Chief and
Managing Editor <http://www.degruyter.com/view/j/tncsci>
gsimic@hiim.hr

Staff:

Mirjana Babić, mag.biol.mol.
Croatian Institute for Brain Research
University of Zagreb Medical School
Šalata 12, HR-10000 Zagreb, Croatia
mbabic@hiim.hr

Research interests:

The research interests of the Laboratory for Developmental Neuropathology are centered on (1) the mechanisms of brain aging and neurodegeneration, especially the study of selective neuronal vulnerability in Alzheimer's disease, (2) the etiopathogenesis of spinal muscular atrophy and other developmental neuromuscular diseases, and (3) the structure, function, and disorders of the human cerebral cortex and its chemical neuroanatomy. In recent years the main objective of the laboratory was the determination of early Alzheimer's disease biomarkers in cerebrospinal fluid and plasma, in the context of complementary diagnostic modalities, such as neuropsychological testing, evoked potentials, and genetic and neuroimaging biomarkers (<http://alzbiotrack.hiim.hr/>). We are also using an innovative non-invasive hidden-goal task to detect spatial orientation impairment, one of the earliest signs of Alzheimer's disease. Besides identification of gene polymorphisms associated with late-onset, sporadic Alzheimer's disease, and their role in disease pathogenesis, our ultimate goal is to establish reliable early diagnosis of the disease in patients with mild cognitive impairment, and to differentiate it from other primary causes of dementia. We are also using several neuronal cell lines to investigate the effects of potentially neuroprotective compounds on typical Alzheimer's disease pathological changes, particularly tau phosphorylation. In parallel to these studies of dementia, by using microarray analysis and a panel of novel monoclonal antibodies for immunofluorescence confocal microscopy we have initiated studies of changes in gene expression and localization of dopaminergic receptor subtypes in brains of patients with schizophrenia.

Projects:

1. 0108-1081870-1942 MZOŠ „Phosphorylation of tau proteins during development and Alzheimer's disease“

Projekti:

1. 0108-1081870-1942 MZOŠ „Fosforilacija tau proteina u razvitku I Alzheimerovoj bolesti“
2. 09/16 HRZZ „Otkrivanje i praćenje bioloških biljega radi rane terapijske intervencije u sporadičnoj Alzheimerovoj bolesti“
3. CMST COST Action CM1103 “Structure-based drug design for diagnosis and treatment of neurological diseases: dissecting and modulating complex function in the monoaminergic systems of the brain”

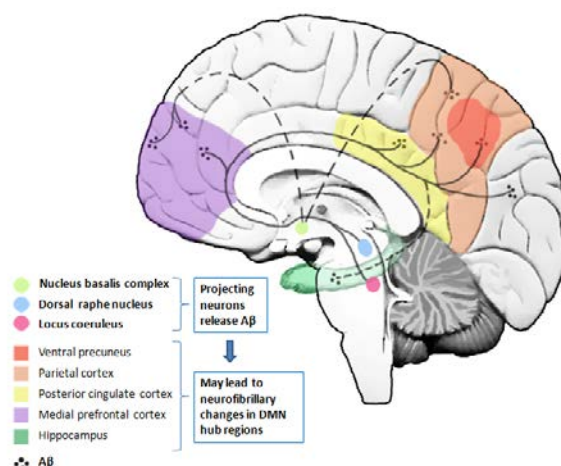
Znanstvena suradnja:

1. dr. Patrick R. Hof, prof., Mount Sinai School of Medicine, New York, Sjedinjene Američke Države
2. dr. Adrian Danek, prof., Großhadern Klinik, Ludwig-Maximilian Sveučilište, München, Njemačka
3. dr. Glenn E. Morris, prof., Robert Jones and Agnes Hunt Orthopedic Hospital, Oswestry, Keele Sveučilište, Ujedinjeno Kraljevstvo
4. Rohan de Silva, DPhil, University College London, Ujedinjeno Kraljevstvo
5. Andrea Diana, PhD, Zavod za biomedicinske znanosti Sveučilišta Cagliari, Italija

2. 09/16 CSF „ Detection and tracking of biological markers for early therapeutic intervention in sporadic Alzheimer’s disease “
3. CMST COST Action CM1103 “Structure-based drug design for diagnosis and treatment of neurological diseases: dissecting and

Scientific collaboration:

1. dr. Patrick R. Hof, prof., Mount Sinai School of Medicine, New York, NY, United States of America
2. dr. Adrian Danek, prof., Großhadern Klinik, Ludwig-Maximilian University, München, Germany
3. dr. Glenn E. Morris, prof., Robert Jones and Agnes Hunt Orthopedic Hospital, Oswestry, Keele University, United Kingdom
4. Rohan de Silva, DPhil, University College London, United Kingdom
5. Andrea Diana, PhD, Department for Biomedical Sciences, Cagliari, Italy

**10 odabranih publikacija 10 selected publications:**

1. Šimić G, Mladinov M, Šešo-Šimić Đ, Jovanov-Milošević N, Islam A, Pajtak A, Barišić N, Sertić J, Lucassen PJ, Hof PR, Krušlin B (2008) Abnormal motoneuron migration, differentiation, and axon outgrowth in spinal muscular atrophy. *Acta Neuropathol.* 115: 313-326.
2. Šimić G (2008) The pathogenesis of proximal autosomal recessive spinal muscular atrophy. *Acta Neuropathol.* 116: 223-234.
3. Šimić G, Stanić G, Mladinov M, Jovanov-Milošević N, Kostović I, Hof PR (2009) Does Alzheimer’s disease begin in the brainstem? *Neuropathol. Appl. Neurobiol.* 35: 532-554.
4. Rhaganti M-A, Šimić G, Watson S, Stimpson CD, Hof PR, Sherwood CC (2011) Comparative analysis of the nucleus basalis of Meynert in primates. *Neuroscience* 185: 1-15.
5. Petanjek Z, Judaš M, Šimić G, Rašin MR, Uylings HBM, Rakic P, Kostović I (2011) Extraordinary neoteny of synaptic spines in the human prefrontal cortex. *Proc. Natl. Acad. Sci.* 108: 13281-13286.
6. Boban M, Malojčić B, Mimica N, Vuković S, Zrilić I, Hof PR, Šimić G (2012) The reliability and validity of the mini-mental state examination in the elderly Croatian population. *Dement. Geriatr. Cogn. Disord.* 33: 385-392.
7. Jovanov-Milošević N, Petrović D, Sedmak G, Vukšić M, Hof PR, Šimić G (2012) Human fetal tau protein isoform: possibilities for Alzheimer’s disease treatment. *Int. J. Biochem. Cell Biol.* 44: 1290-1294.
8. Babić M, Švob Štrac D, Mück-Šeler D, Pivac N, Stanić G, Hof PR, Šimić G (2014) Update on the core and developing cerebrospinal fluid biomarkers for Alzheimer’s disease. *Croat. Med. J* 55: 347-365.
9. Šimić G, Babić M, Borovečki F, Hof PR (2014) Early failure of the default-mode network and the pathogenesis of Alzheimer’s disease. *CNS Neurosci. Ther.* 20: 692-698.
10. Šimić G, Hof PR (2015) In search of the definitive Brodmann’s map of cortical areas in human. *J. Comp. Neurol.* 523: 5-14.

**Laboratorij za neuromorfometriju
(Zdravko Petanjek)**

Voditelj:

prof. dr. sc. Zdravko Petanjek, dr. med.
redoviti profesor anatomije i neuroznanosti

Suradnici

doc. dr. sc. Sanja Darmopil, dipl. ing. biologije
Ana Hladnik, dr. med.
Domagoj Džaja, dr. med.
Ivana Bičanić, dr. med.
Dora Mandić, dr. med.

Istraživački interesi:

U laboratoriju se istražuju organizacija i molekularna svojstva neurona i njihovih veza s naglaskom na neuralne sustave i područja posebno razvijena kroz evoluciju čovjeka: frontalni asocijativni korteks, te asocijativni projekcijski neuroni i kalretininski interneuroni. Navedena područja i neuroni zbog svoje brojnosti predstavljaju glavni biološki elementi u procesuiranju najkompleksnijih kognitivnih funkcija kod čovjeka te stoga imaju glavnu ulogu u etiopatogenezi važnih psihijatrijskih i neuroloških poremećaja.

Iako su osnovni principi organizacije neuralne mreže kore velikoga mozga zajednički svim sisavcima, neke vrste neurona, kao što su veliki kortiko-kortikalni piramidni neuroni s paralelnim projekcijama prema više kortikalnih područja, ali i izrazito bogatim intra-arealnim projekcijama, jasno su izražene tek kod majmuna i čovjeka. Drugim skupinama, kao što su kalretininski GABA-ergički interneuroni, broj se eksponencijalno povećava i vjerojatno se unutar ove skupine pojavljuju strukturno i funkcionalno nove populacije neurona.

Glavne teme istraživanja:

1. Kvantitativna (utvrđivanje broja i distribucije) i kvalitativna (utvrđivanje morfoloških i molekularnih obilježja) analiza piramidnih neurona sloja III i GABA-ergičkih interneurona te regionalna komparativna analiza navedenih obilježja između multimodalnih, unimodalnih i primarnih kortikalnih područja. Također se provodi i komparativna analiza navedenih obilježja između čovjeka, majmuna i štakora.
2. Usporedba parametara stanične organizacije normalnog mozga čovjeka i makaki majmuna s mozgovima osoba oboljelih od psihijatrijskih i neuroloških poremećaja (npr. tkivo dobiveno prilikom operacija pacijenata s teškim oblicima epilepsije), kao i s podacima iz eksperimentalnih modela (model epilepsije frontalnog režnja majmuna). Ovaj dio istraživanja provodi se u suradnji s laboratorijem dr. Monique Esclapez u Marseilleu (Brain Dynamic Institute Marseille (BDI: <http://ins.medecine.univmed.fr/>).
3. Istraživanje genetički modificiranog ("humaniziranog") FoxP2 miša u svrhu utvrđivanja kako promjene u strukturi gena (koje su bile selekcionirane tijekom evolucije čovjeka i smatraju se

**Laboratory for neuromorphometry
(Zdravko Petanjek)**

Head:

Zdravko Petanjek, MD, PhD
Professor of Gross Anatomy and Neuroscience

Members:

Sanja Darmopil, PhD, MSc, Assistant Professor of Neuroscience
Ana Hladnik, MD, PhD student
Domagoj Džaja, MD, PhD student
Ivana Bičanić, MD, PhD student
Dora Mandić, MD, PhD student

The goal of our laboratory is to study organization and molecular properties of microcircuitry with an emphasis on neuronal elements that became particularly expressed during evolution of the human neocortex. Therefore, we specifically focus on the human associative frontal cortex as well as on the associative layer III of projecting neurons and calretinin expressing GABA-interneurons. Due to their expansion and unique features they are considered to be a main biological substrate of the most complex cognitive functions and involved in pathophysiology of various psychiatric and neurological disorders.

Despite common principles in connectivity, some neuron types are specific for monkey and human cerebral cortex, such as large cortico-cortical projecting neurons with parallel projection to several cortical areas and extremely reach local intra-areal connections. Also, a certain class of GABA-interneurons, calretinin expressing, shows a supralinear increase in number suggesting an appearance of new neuron types inside this group. These neurons are the key elements of human microcircuitry which molecular specificity and neuronal interaction need to be determined in order to assess how human cortex processes information.

RESEARCH TOPICS:

1. Quantitative (number and distribution) and qualitative (morphological and chemical properties) analysis of human specific neuron subclasses (layer IIIC pyramidal neurons, calretinin expressing GABA-interneurons) with comparative analysis of regional differences comparing multimodal, unimodal and primary cortical areas, as well as analysis of species differences (human, monkey and rat).
2. Comparison of cellular organization parameters in the normal human and monkey brain with morphology and chemical properties of specific neuron subclasses in various psychiatric and neurological disorders (analysis of cortical resections obtained after surgery of patients with severe epilepsy), including experimental models (model of frontal lobe epilepsy in monkey). This part of the research is performed in collaboration with dr. Monique Esclapez at the Brain Dynamic Institute Marseille (BDI: [— 76 —](http://ins.mede-</div><div data-bbox=)

jednom on najvažnijih promjena u razvoju govora) utječu na organizaciju kortikalnih veza. Ovaj dio istraživanja provodi se u suradnji s laboratorijem prof. Svante Paabo u Leipzigu (Max Planck Institute for Evolutionary Anthropology Leipzig; MPI-EVA: <http://www.eva.mpg.de/>).

4. Razvojne studije u majmuna i čovjeka usmjerene na istraživanja za primata specifičnih razvojnih događanja, kao što su obrazac rasta dendritičkog stabla asocijativnih piramidnih neurona, mjesto stvaranja kalretininskih neurona i specifični putovi migracije neurona.

METODOLOGIJA:

KVANTITATIVNA ANALIZA HISTOLOŠKIH PREPARATA; morfometrija i stereologija

U laboratoriju se koriste općeprihvaćene i dobro definirane kvantitativne metode analize obojenih histoloških preparata:

- stereologija (optički frakcionator)
- rekonstrukcija serijskih rezova i 3D mapiranje mozga
- rekonstrukcija neurona, anatomsko mapiranje
- morfometrija (rekonstrukcija i analiza grananja dendritičkog stabla i aksona te utvrđivanje broja i položaja dendritičkih trnova)

Kvantitativna analiza histoloških preparata provodi se uz korištenje Neurolucida i Stereoinvestigator programskih paketa (MicroBrightField, Williston, USA) na dva video-računarsko-mikroskopska sustava s 3D motoriziranim stolićem kontroliranih elektroničkim upravljačem. Stariji sustav sastoji se od Hitachi 3CCD video kamere u boji HV-C20M, Lucivid mikromonitora spojenog na Olympus BX50 mikroskop s 3D motoriziranim stolićem kontroliranim s elektroničkim upravljačem MAC 2000 (Ludl Electronic Products Ltd.). Noviji sistem (2010) sastoji se od MBF-DV-46 digitalne kamere koja se nalazi na Olympus BX61 mikroskopu motoriziranom za kretanje u dubinu, te motoriziranog stolića za pokretanje u x-y smjeru i koji je kontroliran MAC 5000 elektroničkim upravljačem (Ludl Electronic Products Ltd.).

HISTOLOŠKE TEHNIKE

- Golgi metode: Golgi-Cox, Rapid Golgi
- Histokemija: AchE, PAS-Alcian, NADPH
- Imunohistokemija za identifikaciju interneurona (GAD, kalretinin, somatostatin, parvalbumin, kalbindin), mapiranih neurona (SMI32, MAP2) te neurotransmitera i aksonskih završetaka (GABA, GAD; 65 i 67, VGAT, VGLUT1, VGLUT2). Imunohistokemijska bojenja provode se kao jednostruka bojenja korištenjem biotiniranih protutijela i metode označavanja bazirane na DAB-u, te kao višestruka obilježavanja korištenjem fluorescentnih protutijela.

[cine.univmed.fr/](http://www.cine.univmed.fr/)).

3. Examination of genetically modified mice model ("humanized" Foxp2 mice) in order to show how changes in the structure of a gene (that was positively selected during human evolution and related to the appearance of language) will affect the organization of cortical circuitry (this research is performed in collaboration with prof. Svante Paabo at the Max Planck Institute for Evolutionary Anthropology Leipzig; MPI-EVA: <http://www.eva.mpg.de/>).
4. Developmental studies in monkey and human with an emphasis on studying primate specific developmental events, as well as a pattern of dendritic growth in associative pyramidal neurons, place of origin of calretinin neurons and specific neuronal migratory routes.

TOOLS:

QUANTITATIVE ANALYSIS OF HISTOLOGICAL SECTIONS; morphometry and stereology

In our laboratory we are using well established qualitative methods for analysis of stained brain tissue:

- stereology (optical fractionator method),
- serial section reconstruction with three-dimensional brain mapping,
- neuron tracing, anatomical mapping and
- morphometry (reconstruction and analysis of branching pattern of the axon and dendrites together with spine counting).

These analyses are performed using Neurolucida and Stereoinvestigator software (MicroBrightField, Williston, USA) on two computer based automatic measuring microscope-video system connected to three-dimensional motorized stages controllers. An older system consists of Hitachi 3CCD color video camera HV-C20M placed on the Olympus BX50 microscope and connected to the MAC 2000 stage controller, (Ludl Electronic Products Ltd). A newer system (2010) is equipped with MBF digital camera placed on the Olympus BX61 microscope and connected to the MAC 5000 stage controller (Ludl Electronic Products Ltd).

TISSUE STAINING TECHNIQUES

Golgi methods: Golgi-Cox, Rapid Golgi method

- Histochemistry: AchE, PAS-Alcian, NADPH etc.
- Immunohistochemistry for identification of local circuit neuron markers (GAD, calretinin, somatostatin, parvalbumin, calbindin), pyramidal neuron markers (SMI32, MAP2) and markers of neurotransmitters and neurotransmitter terminals (GABA, GAD 65 and 67, VGAT, VGLUT1, VGLUT2). Immunohistochemistry is performed as a single labeling; using mostly biotinylated antibodies preceded by DAB protocol, and as multiple labeling using mostly fluorescent labels.
- Identification and morphological analysis of neurons label by tracing experiments and

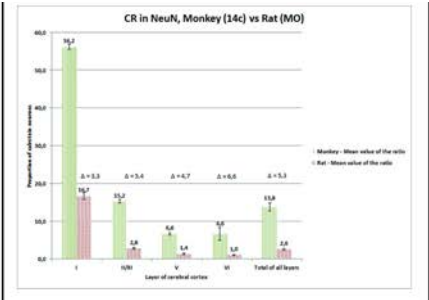
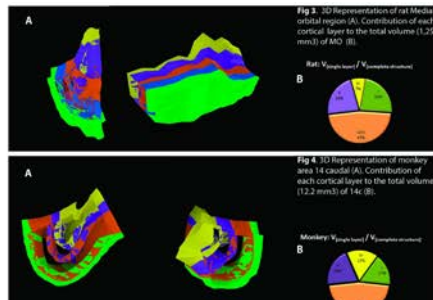
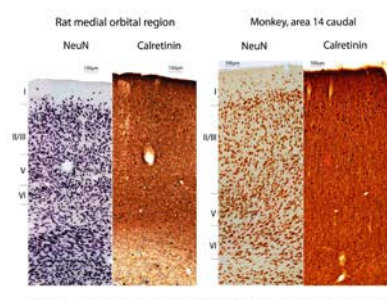
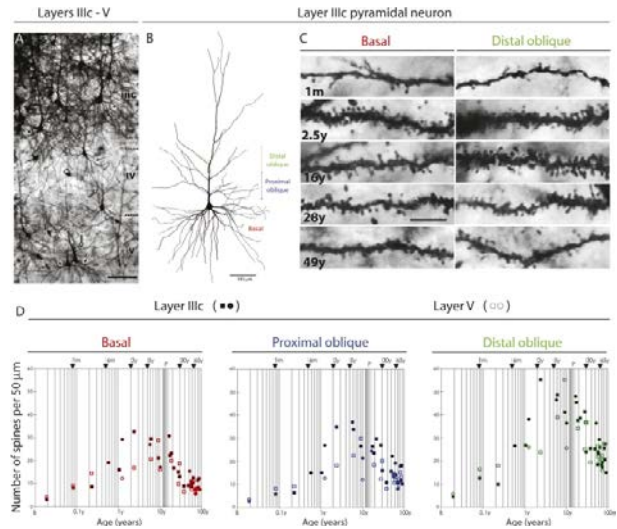
- Identifikacija i morfološka analiza neurona obilježenih tehnikama praćenja aksonskih projekcija te neurona obilježenih tijekom elektrofiziološkog eksperimenta: analiza neurona obilježenih tehnikama aksonskog transporta (biotin-dekstran-amin; pšenična klica konjugirana s aglutininom u koloidnom zlatu), uključujući i metode retrogradnog trans-sinaptičkog prijenosa biljega (rabies virus) te analiza morfologije neurona koji su po završetku elektrofiziološkog eksperimenta injicirani biocitinom.

Članovi Laboratorija za neuromorfometriju su Ana Hladnik, Dora Mandić, Sanja Darmopil, Ivana Bičanić, Domagoj Džaja i Zdravko Petanjek

Slika 1 (desno)

Mikrofotografija, rekonstrukcija i morfometrijska analiza dendritičkog stabla reprezentativnih piramidnih neurona IIIc i V sloja u dorsolateralnom prefrontalnom korteksu čovjeka impregniranih rapid Golgi-metodom dovelo je do otkrića o poruženoj maturaciji i post-adolescentnoj reorganizaciji neuralne mreže u čovjeka (Petanjek i sur 2011, Proc Natl Acad Sci USA 108(32):13281-6).

during electrophysiological recording; neurons labeled by axon transport methods (biotin dextran amine, wheat germ agglutinin-conjugated colloidal gold), including methods which allow retrograde transynaptic/transneuronal transfer (rabies virus), as well as neurons injected with biocytin at the end of the electrophysiological recording.

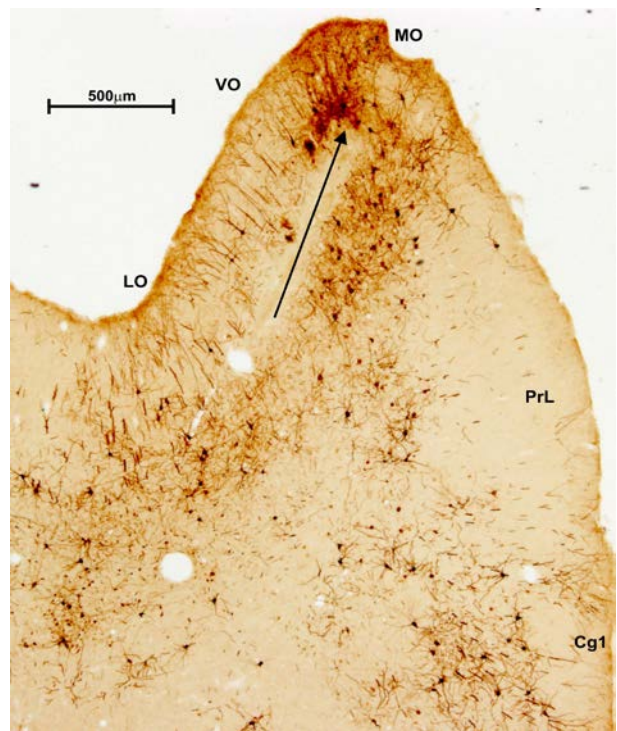


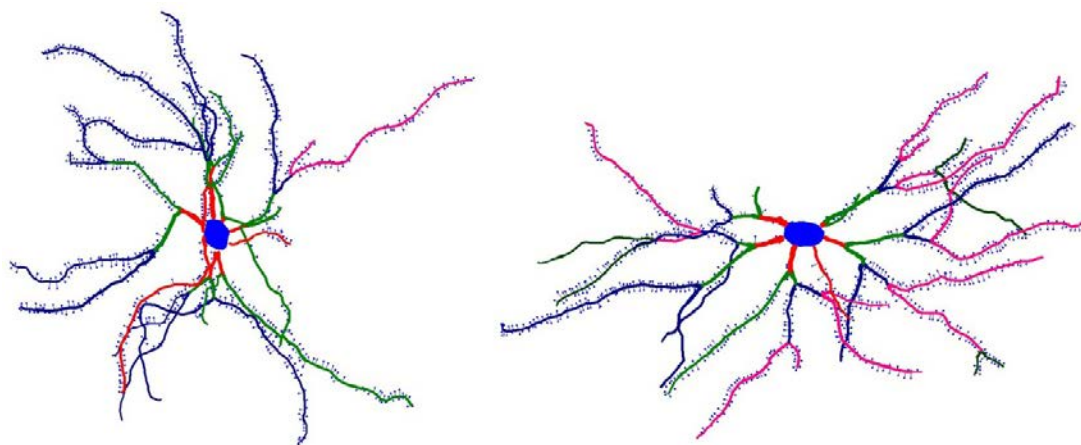
Slika 2 (u sredini)

Analiza distribucije kalretininskih neurona u orbitofrontalnom korteksu majmuna i štakora pokazuje dramatičan porast proporcije u asocijativnim područjima kod priamta (Džaja i sur 2014, Society for neuroscience).

Slika 3 (dolje)

Mikrofotografija koronarnog reza kroz rostralni dio mozga štakora u kojega je injiciran virus bjesnoće, obrađenog imunohistokemijski kako bi se prikazali neuroni koji su nakupili virus kroz retrogradni aksonski transport. Strelica prikazuje mjesto ulaska elektrode. (Džaja 2015, doktorska disertacija, suradnja Monique Esclapez, Brain Dynamic Institute, Marseille)



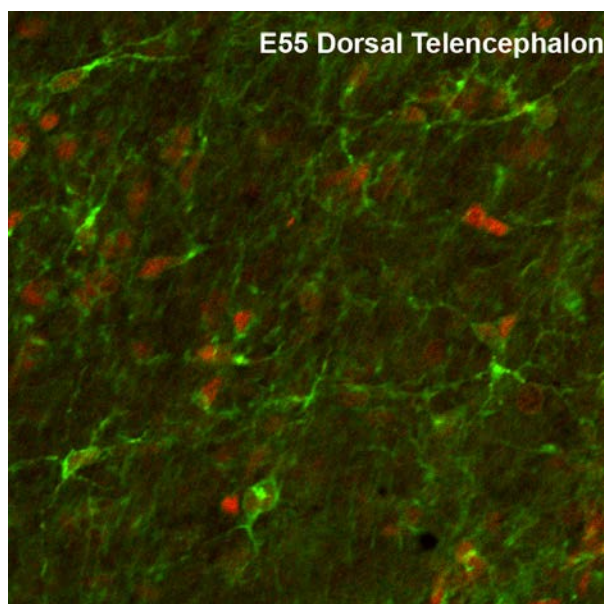


Slika 4 (gore)

Analiza morfologije trnastih neurona striatuma u miša s "humaniziranim" oblikom FoxP2 gena pokazuje kako promjene redoslijeda aminokiselina na dva mjesta dovela do značajnih promjena morfologije neurona (Bičanić i sur 2014, Society for neuroscience, suradnja Svante Paabo, Max Planck Institute for Evolutionary Anthropology, Leipzig)

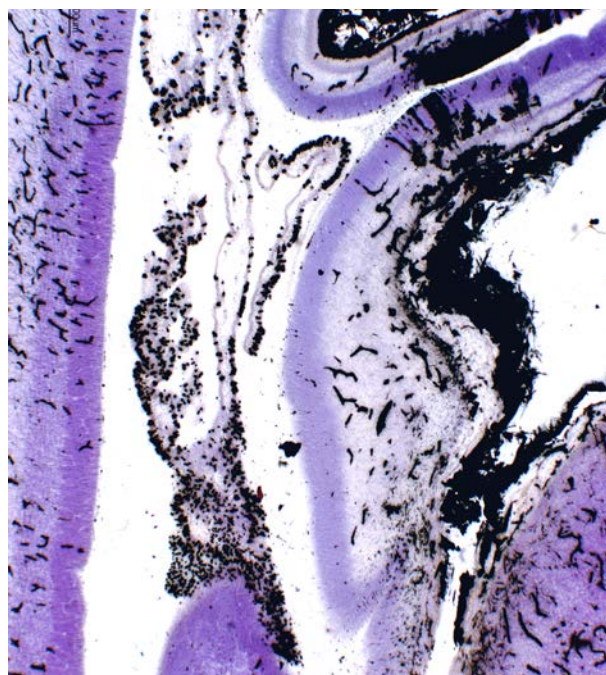
Slika 5 (u sredini)

Značajna produkcija GABA-ergičkih neurona je kod primata, za razliku od glodavaca, prisutna i u neokortikalnim proliferativnim zonama, a ne samo u ganglijskom brežuljku dorzalnom telencefalonu majmuna (dvostruko bojanje na biljeg proliferacije i glutamate dekarboksilazu 65 u majmuna embrionalni dan 55). U čovjeka postoji masivna tangencijalna migracija neurona kroz medijalni telencefalički zid (Golgi-Nissl bojanje, fetus 10 tjedana trudnoće). (Hladnik i sur. 2014, Frontiers in neuroanatomy 8:50).



Slika 6 (dolje)

Mikrofotografija preparata elektrofiziološki analiziranog piramidnog neurona hipokampusa miša ispunjenog biocitinom na kraju eksperimenta. Na fotografiji se nalaze rekonstrukcije dva interneurona koji imaju različiti afinitet pristupa na receptivnu površinu neurona: lijevo je košarsrasti koji se aksonom grana po piramidnom sloju, a desno OLM neuron koji akson pruža u stratum lacunosum moleculare. (Cossart, Petanjek, I sur 2006, Hippocampus 16).



**Laboratorij za imunohistokemiju i in situ
hibridizaciju**
(Nataša Jovanov Milošević)

Voditelj:

Prof.dr.sc. Nataša Jovanov-Milošević,
njovanov@hiim.hr

Osoblje:

Maja Horvat, ing.lab.diag.,
Božica Popović, lab.teh.

Laboratorij za imunohistokemiju i *in situ* hibridizaciju pruža histološka bojanja rezova tkiva različitih dijelova živčanog sustava čovjeka i animalnih modela (miš, štakor, mačka). Kombinirajući različite histološke tehnike prikazuje se ekspresija gena u citoarhitektonski očuvanim uzorcima tkiva. Fiksacija i uklapanje tkiva, vibratomski, parafinski i smrznuti rezovi, rezovi fiksirani na staklo ili "free-floating", jednostruka, višestruka bojanja i preko 20 različitih histoloških i histokemijskih bojanja specifičnih za neuroznanosti. Tehnička podrška laboratorija ima preko 20 godina iskustva u obradi moždanog tkiva fetusa i odrasla čovjeka i animalnih modela.

Znanstveni interes:

praćenje prostorne i vremenske distribucije specifičnih proteina u kontekstu razvitka čeonog i limbičkog režnja telencefalona čovjeka, njegove plastičnosti i degeneracije. Poseban interes su morfološko-kemijske značajke prolaznih razvojnih struktura i zona te kortikalnih veza, tijekom normalnog razvitka, nakon hipoksično-ishemičnog oštećenja mozga i u razvojnim anomalijama.

Znanstveni projekti u tijeku:

- 2013. - „Komparativni histološko –MRI istraživački pristup poboljšanju dijagnostike perinatalnih oštećenja mozga čovjeka“ (akronim HIMRICO od Histological-MRI COmparative research) (PI: N. Jovanov Milosevic)
- 2013. – Suradnik istraživač, „Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (PI: M. Vukšić)
- 2011.- 2014. COST BM1001: Brain Extracellular matrix in health an disease“ (MC N. Jovanov Milosevic, PI A. Dityatev)
- 2007.- UKF projekt: Neuroimaging, neurogenomics and pharmacogenomics of the frontal lobe connectivity: normal development and abnormalities in developmental disorders, (PI I. Kostović)
- 2006.-“Razvitak i plastičnost kortikalnih putova mozga čovjeka“, dio programa: Razvojna neurobiološka osnova kognitivnih, duševnih i neuroloških bolesti“ (PI I. Kostović)

**Laboratory for immunohistochemistry
and in situ hybridization**
(Nataša Jovanov-Milošević)

Head:

Associated professor Nataša Jovanov Milošević
njovanov@hiim.hr

Personnel

Božica Popović, lab. technician,
Maja Horvat, Bachelor of medical laboratory diagnostic maja@hiim.hr

Laboratory for Immunohistochemistry and In situ hybridization provides histological, immunohistochemical and in situ hybridization (non-radioactive) staining of human and animal nervous system tissue sections. The tissue fixation and embedding, resin, paraffin and frozen sectioning on-slides and free-floating, mono and double immuno-labelling, in situ (non-radioactive) hybridization, and more than 20 different histological and histochemical staining methods specific for neuroscience.

Core staff of the Laboratory has more than two decades of experience in processing fetal and adult human and animal brain tissue.

Scientific scope

Follow up study of spatial-temporal distribution of specific proteins in a context of frontal and limbic lobe development, plasticity and degeneration. Special emphasis is given to morphological-chemical phenotype characterization of the transient developmental features (zones, compartments and cells) and cortical connections of human fetal brain during normal development and in different developmental disorders.

Ongoing research projects

- 2013. –“Histological-MRI comparative research approach for improvement of diagnostic procedures for developmental disorders of the human brain, acronym HIMRICO, (PI: N. Jovanov Milosevic)
- 2013. – “Histological, MRI and gene expression analysis of the reorganizational processes in the medial (limbic) wall of developing human cerebrum (PI: Mario Vukšić)
- 2011.- COST BM1001: Brain Extracellular matrix in health an disease“ (PI A. Dityatev, MC, Jovanov Milosevic)
- 2007-2011,- “Neuroimaging, neurogenomics and pharmacogenomics of the frontal lobe connectivity“, Unity through Knowledge Fund, (PI: I. Kostovic)

Znanstveni članci (zadnjih 5 godina) Scientific papers (last 5 years):

1. Milosevic, Natasa Jovanov; Judas, Milos; Aronica, Eleonora; et al. Neural ECM in laminar organization and connectivity development in healthy and diseased human brain. *BRAIN EXTRACELLULAR MATRIX IN HEALTH AND DISEASE*, Progress in Brain Research, Volume: 214, Pages: 159-178, 2014
2. Kostovic, Ivica; Kostovic-Srzentic, Mirna; Benjak, Vesna; et al. Developmental dynamics of radial vulnerability in the cerebral compartments in preterm infants and neonates. *Frontiers in neurology*, Volume: 5, Pages: 139, 2014
3. Hladnik, Ana; Dzaja, Domagoj; Darmopil, Sanja; Jovanov Milosevic, Natasa; Zdravko Petanjek. Spatio-temporal extension in site of origin for cortical calretinin neurons in primates *FRONTIERS IN NEUROANATOMY*, Volume: 8, Article Number: 50 Published: JUN 26 2014
4. Mlinac K, Jovanov Milošević N, Heffer M, Smalla KH, Schnaar RL, Kalanj Bogнар S. [Neuroplastin expression in the hippocampus of mice lacking complex gangliosides](#). *J Mol Neurosci*.;48(1):161-6, 2012.
5. Jovanov-Milošević N, Petrović D, Sedmak G, Vukšić M, Hof PR, Simić G. Human fetal tau protein isoform: Possibilities for Alzheimer's disease treatment *Int J Biochem Cell Biol*. 44/8: 1290-4, 2012.
6. Jovanov-Milošević N, Petanjek Z, Petrović D, Judaš M, Kostović I. Morphology, molecular phenotypes and distribution of neurons in developing human corpus callosum. *Eur J Neurosci*. 32(9):1423-32, 2010.
7. Judaš M, Šimić G, Petanjek Z, Jovanov-Milošević N, Pletikos M, Vasung L, Vikšić M, Kostović I. The Zagreb Collection of human brains: A unique versatile but underexploited resource for the neuroscience community. *Ann N Y Acad Sci*. 1225 Suppl 1:E105-30. doi: 10.1111/j.1749-6632.2011.05993.x, 2011.
8. Vasung L, Jovanov-Milošević N, Pletikos M, Mori S, Judaš M, Kostović I. Prominent periventricular fiber system related to ganglionic eminence and striatum in the human fetal cerebrum. *Brain Struct Funct*. 215(3-4):237-53, 2011.
9. Jovanov-Milošević N, Petanjek Z, Petrović D, Judaš M, Kostović I. Morphology, molecular phenotypes and distribution of neurons in developing human corpus callosum. *Eur J Neurosci*. 32(9):1423-32, 2010.
10. Judaš M, Sedmak G, Pletikos M, Jovanov-Milošević N. Populations of subplate and interstitial neurons in fetal and adult human telencephalon. *J Anat*. 217(4):381-99., 2010.
11. Vasung L, Huang H, Jovanov-Milošević N, Pletikos M, Mori S, Kostović I. Development of axonal pathways in the human fetal fronto-limbic brain: histochemical characterization and diffusion tensor imaging. *J Anat*. 217(4):400-17, 2010.

**Laboratorij za konfokalnu mikroskopiju
(Mario Vukšić)**

Voditelj:

Prof.dr.sc. Mario Vukšić
Izvanredni profesor neuroznanosti & anatomije
Hrvatski institut za istraživanje mozga
Medicinski fakultet Sveučilišta u Zagrebu
Šalata 12, 10000 Zagreb

Laboratorij za konfokalnu mikroskopiju osnovan je 2008. godine a koristite ga svi znanstvenici zaposleni na Hrvatskom institutu za istraživanje mozga. Laboratorij je opremljen laserskim konfokalnim mikroskopom tvrtke Zeiss tipa LSM 510-META. Uređaj koristi lasere: Argon 458/477/488/514nm, HeNe 543 nm, HeNe laser 633 nm te posjeduje i META detektor koji omogućava razlikovanje različitih preklapajućih emisijskih signala. Sistem je nadograđen na invertirni mikroskop Axiovert 200M tvrtke Zeiss koji se također može koristiti za standardnu fluorescenciju te posjeduje slijedeće objektivne: 10x i 20x zračne; te 40x i 63x uljne.

Trenutno se uređaj koristi za: snimanje pojedinačnih konfokalnih slika, trodimenzionalnu rekonstrukciju pojedinačnih živčanih stanica koristeći konfokalni mikroskop i NeuroLucida sustav, dokazivanje prisutnosti i raspodjele različitih fluorescentnom bojom označenih struktura.

Istraživački interesi:

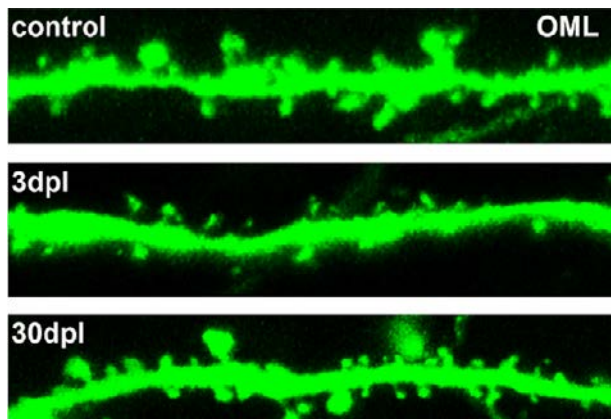
Procesi oporavka nakon moždane ozljede i prekidanja veza, plastičnost dendrita i dendritičkih trnova nakon lezije, pojava izrastanja aksonskih mladica.

Primjeri aplikacije:

Konfokalna slika prikazuje GFP-pozitivne zrnate stanice u girus dentatusu transgeničnog Thy-1 miša I trodimenzionalna rekonstrukcija iste stanice koristeći NeuroLucida sustav. (Vuksic i sur., Hippocampus 2008)

Entorinalna denervacija u transgeničnog Thy-1 miša uzrokuje brze i prolazne promjene gustoće dendritičkih trnova na zrnatim stanicama girus dentatusa.

(Vuksic i sur., Experimental Neurology 2011)



**Laboratory for confocal microscopy
(Mario Vukšić)**

Head:

Mario Vukšić, MD, PhD
Associate Professor of Neuroscience & Anatomy
Croatian Institute for Brain Research
School of Medicine University of Zagreb
Šalata 12, 10000 Zagreb, Croatia

The Laboratory of Confocal Microscopy was established in 2008. This is an open laboratory available to all scientists from Croatian Institute for Brain Research. The Lab basic equipment is a laser scanning microscope Zeiss LSM 510-META. The appliance uses Argon laser 458/477/488/514nm, HeNe laser 543 nm, HeNe laser 633 nm and the META detector which can spectrally separate overlapping emission signals. The system was coupled to inverted microscope Zeiss Axiovert 200M which is also equipped for standard epi-fluorescence imaging. The following objectives are available with the system: 10x air, 20x air, 40x oil and 63x oil.

Current applications include: single confocal images, 3D-reconstruction of single neurons using confocal microscopy and NeuroLucida system, colocalization and distribution of various fluorescently-tagged proteins.

Research interests:

Reorganizational processes following brain trauma and deafferentation, lesion-induced plasticity of dendrites and dendritic spines; axonal sprouting.

Example application:

Confocal image stack showing GFP-expressing granule cell in the fascia dentata of the Thy-1 GFP transgenic mouse and 3D reconstruction of the same cell using NeuroLucida system (Vuksic et al., Hippocampus 2008)

Entorhinal denervation of the Thy-1 GFP transgenic mouse induces fast and transient changes in spine densities of granule cells in the fascia dentata.

(Vuksic et al., Experimental Neurology 2011)

Figure 1 (left)

Confocal image stack showing GFP-expressing granule cell in the fascia dentata of the Thy-1 GFP transgenic mouse and 3D reconstruction of the same cell using NeuroLucida system (Vuksic et al., Hippocampus 2008)

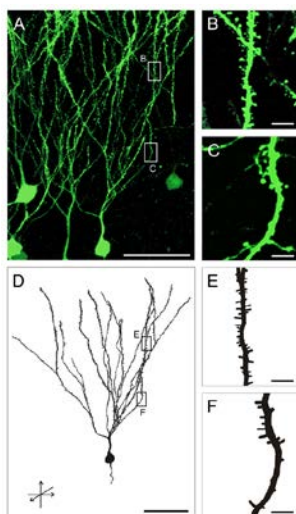
Figure 2 (right)

Entorhinal denervation of the Thy-1 GFP transgenic mouse induces fast and transient changes in spine densities of granule cells in the fascia dentata.

(Vuksic et al., Experimental Neurology 2011)

Odabrane publikacije:

1. Slade N, Zorić A, Horvat B, Vukšić M, Kostović I, Poljak L (2015) Suppression of Smad-1 mRNA expression level by Smad-2 likely control dichotomy of NF- κ B and Smads mediated activation. *Immunobiology*. 220(1):48-53
2. Kostović I, Sedmak G, Vukšić M, Judaš M (2015) The relevance of human fetal subplate zone for developmental neuropathology of neuronal migration disorders and cortical dysplasia. *CNS Neuroscience & Therapeutics* 21(2):74-82.
3. Kosi N, Alić I, Kolačević M, Vrsaljko N, Jovanov Milošević N, Sobol M, Philimonenko A, Hozak P, Gajović S, Pochet R, Mitrečić D. (2015): Nop2 is expressed during proliferation of neural stem cells and in adult mouse and human brain. *Brain Research* 1597:65-76.
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12. Schwarzacher SW*, Vukšić M*, Haas CA, Burbach GJ, Sloviter RS and Deller T (2006) Neuronal hyperactivity induces astrocytic expression of neurocan in the adult rat hippocampus. *Glia* 53:704-714. *equally contribution
13. Ghebremedhin E, Del Tredici K, Vukšić M, Rüb U, Thal DR, Burbach GJ, Rosenberger A, Bickeböller H, Deller T, Rob VAI, Jansen Steur ENH, Braak H (2006) Relationship of ApoE and age at onset to Parkinson's disease neuropathology. *Journal of Neuropathology & Experimental Neurology* 65:116-123.
14. Kienzler F, Jedlicka P, Vukšić M, Deller T, Schwarzacher SW (2006) Excitotoxic hippocampal neuron loss following sustained electrical stimulation of the perforant pathway in the mouse. *Brain Research* 1085:195-198.
15. Gierga K, Bürk K, Bauer M, Diaz Orozco G, Auburger G, Schultz C, Vukšić M, Schöls L, de Los RAI, Braak H, Deller T, Rüb U (2005) Involvement of the cranial nerves and their nuclei in spinocerebellar ataxia type 2 (SCA2). *Acta Neuropathologica* 109:617-631.
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Laboratorij za razvojnu molekularnu neurobiologiju (Miloš Judaš i Nenad Šestan)

Voditelji:

Prof.dr.sc. Miloš Judaš
Redoviti profesor neuroznanosti i anatomije
Hrvatski institut za istraživanje mozga
Šalata 12, 10 000 Zagreb, Hrvatska

Prof.dr.sc. Nenad Šestan
Redoviti profesor neurobiologije, komparativne medicine, genetice i psihijatrije
Department of Neurobiology
School of Medicine Yale University
333 Cedar Street, New Haven, CT, USA

Suradnici:

Doc.dr.sc. Goran Sedmak
Hrvatski institut za istraživanje mozga
Doc.dr.sc. Željka Krsnik
Hrvatski institut za istraživanje mozga
Mihovil Pletikos, dr.med.
School of Medicine Yale University
Ana Jaguš
Hrvatski institut za istraživanje mozga

Istraživanja u našem laboratoriju usmjerena su na otkrivanje kako promjene u ekspresiji gena utječu na strukturni i funkcionalni razvoj ljudskog mozga. U ovim nastojanjima, prije svega smo usredotočeni na prolazne fetalne strukture i s njima povezane stanične elemente. Nadalje, istražujemo i kako na ove procese utječu evolucijske promjene u nadi da ćemo barem dijelomično odgovoriti na pitanje „Što nas čini ljudima“. U ovu svrhu u našem laboratoriju koristimo slijedeće metodologije: analizu mikropostroja, PCR, qRT-PCR, itd.

Znanstveni interesi:

Morfološki i funkcionalni razvoj neurona u regijama bitnima za govor.
Promjene u ekspresiji gena u regijama bitnima za govor.
Klasifikacija subpopulacija neurona u subplate zoni čovjeka.
Praćenje molekularnog sazrijevanja prolaznih fetalnih zona.
Klasifikacija neurona bijele tvari na temelju molekularnih biljega.

Trenutačni projekti:

Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (CSF reserach grant)

Laboratory for developmental molecular neurobiology (Miloš Judaš & Nenad Šestan)

Heads:

Professor Miloš Judaš
Professor of Neuroscience and Anatomy
Croatian Institute for Brain Research
Šalata 12, 10 000 Zagreb, Croatia

Professor Nenad Šestan
Professor of Neurobiology, Comparative Medicine, Genetics and Psychiatry
Department of Neurobiology
School of Medicine Yale University
333 Cedar Street, New Haven, CT, USA

Associates:

Assistant Professor Goran Sedmak
Croatian Institute for Brain Research
Assistant Professor Željka Krsnik
Croatian Institute for Brain Research
Mihovil Pletikos, MD
School of Medicine Yale University
Ana Jaguš
Croatian Institute for Brain Research

Research in our laboratory investigates how changes in gene expression influence structural and functional development of the human brain. In pursuit of this goal we are focused on the transient fetal zones and related cellular structures. Furthermore, we explore evolutionary changes in order to understand the importance of above mentioned structure for "what makes us human". To explore these problems we use various molecular techniques such as; microarray analysis, PCR, qRT-PCR, etc.

Scientific scope:

Functional and morphological development of neurons in language related areas.
Changes in gene expression during development in language related areas.
Classification of neuronal subpopulations in the human subplate.
Molecular maturation of transient fetal structures.
Molecular classification of interstitial neurons of white matter.

Current projects.

Miloš Judaš: Development of cell-type specific expression of human transcriptome in language- and mirror neuron-system related cortical network (CSF reserach grant)

Izabrane nedavne publikacije / Selected recent publications

1. Huang, H., Jeon, T., Sedmak, G., Pletikos, M., Vasung, L., Xu, X. M., Yarowsky, P., Richards, L. J., Kostovic, I., Sestan, N. and Mori, S.; (2013); "Coupling diffusion imaging with histological and gene expression analysis to examine the dynamics of cortical areas across the fetal period of human brain development." *Cerebral Cortex* **23**(11): 2620-2631.
2. Judas, M., Sedmak, G. and Kostovic, I.; (2013); "The significance of the subplate for evolution and developmental plasticity of the human brain." *Frontiers in Human Neuroscience* **7**: 9.
3. Judas, M., Sedmak, G., Pletikos, M. and Jovanov-Milosevic, N.; (2010); "Populations of subplate and interstitial neurons in fetal and adult human telencephalon." *Journal of Anatomy* **217**(4): 381-399.
4. Ouyang, A., Jeon, T., Sunkin, S. M., Pletikos, M., Sedmak, G., Sestan, N., Lein, E. S. and Huang, H.; (2015); "Spatial mapping of structural and connectional imaging data for the developing human brain with diffusion tensor imaging." *Methods* **73**: 27-37.
5. Pletikos, M., Sousa, A. M. M., Sedmak, G., Meyer, K. A., Zhu, Y., Cheng, F., Li, M. F., Kawasawa, Y. I. and Sestan, N.; (2014); "Temporal specification and bilaterality of human neocortical topographic gene expression." *Neuron* **81**(2): 321-332.
6. Sedmak G., Jovanov-Milošević N., Puskarjov M., Ulamec M., Krušlin B., Kaila K., Judaš M.; (2015); "Developmental expression patterns of KCC2 and functionally associated molecules in the human brain." *Cerebral Cortex* *in press*.

**Laboratorij za neurorazvojnu analizu
RNA (Željka Krsnik)**

Voditeljica laboratorija:
Doc.dr.sc. Željka Krsnik

Suradnici:

Prof.dr.sc. Miloš Judaš,
prof.dr.sc. Mario Vukšić,
akademik Ivica Kostović,
Doc.dr.sc. Goran Sedmak,
Ana Jaguš

Inozemni suradnici:

Prof.dr.sc. Paško Rakić, Yale University,
Prof. Mladen-Roko Rašin, Rutgers University

U laboratoriju za neurorazvojnu analizu RNA bavimo se vremensko-prostornom analizom transkriptoma ljudskog mozga, u sklopu nekoliko domaćih projekata i inozemnih kolaboracija, koristeći rezultate mikročip tehnologije, in situ hibridizacije, imunitokemije, te neuroanatomske nalaze.

Projekti:

- IBRO RHF (2013/15) Doc.dr.sc. Željka Krsnik
- Zaklada HAZU (2014/15) "Digitalizacija Zagrebačke neuroembriološke zbirke" Doc.dr. Željka Krsnik
- WWN/SFN Kolaborativni istraživači program (2015): voditeljice kolaborativnog programa: dr. J.Zlatković, dr. D.Švob-Štrac i dr.Ž Krsnik
- HRZZ (2012/15) "Razvitak transkriptoma specifičnih populacija neurona u kortikalnim područjima ljudskog mozga bitnim za jezik i sustave zrcalnih neurona" (Prof.dr.sc.Miloš Judaš, voditelj projekta)
- HRZZ (2014/18) „Histološka, MRI i analiza ekspresije gena reorganizacijskih procesa u medijalnom (limbičkom) režnju ljudskog mozga tijekom razvitka“ (Prof. dr.sc. Mario Vukšić, voditelj projekta)

**Laboratory for developmental analysis of
RNA (Željka Krsnik)**

Head:
Željka Krsnik, PhD, Assistant Professor

Collaborators:

Prof. Miloš Judaš,
Prof. Mario Vukšić,
Prof. Ivica Kostović,
Prof. Goran Sedmak

Foreign Collaborators:

Prof. Paško Rakić (Yale University),
Prof. Mladen-Roko Rašin (Rutgers University)

Associate:

Ana Jagust

Research interest:

Focus of our research is spatio-temporal analysis of human brain transcriptome during development using different approaches, such as Affymetrix GeneChip Human Exon Array, in situ hybridization of selected candidate gene coupled to immunohistochemistry or immunofluorescence.

Funds:

IBRO RHF (2014/15): "Perinatal reorganization of the connectivity elements in the marginal zone of the human neocortex": Dr. Ž. Krsnik
Foundation of Croatian Academy of Science and Art (2014/15) "Digitalization of Zagreb Brain Collection": Dr. Ž.Krsnik
WWN/SFN Collaborative Research Program (2014/15): "Neurosteroids as therapeutic opportunities in ischemic brain in ischemic brain injury": collaborative research program between three institutions: Dr. J. Zlatkovic, Dr. D. Švob-Štrac & Dr. Ž.Krsnik
Croatian Science Foundation (2012/15): "Development of cell-type specific expression of human transcriptome in language and mirror neuron system related cortical network" (Prof. Miloš Judaš, P.I.)
Croatian Science Foundation (2014/18): (Prof. Mario Vukšić, P.I.) „Histological, MRI, and gene expression analysis of the reorganizational processes in the mdial (limbic) wall of developing human cerebrum“

Publikacije / Publications:

1. Kostović I, Sedmak G, Vukšić M, Judaš M. (2015) The relevance of human fetal subplate zone for developmental neuropathology of neuronal migration disorders and cortical dysplasia. *CNS Neurosci Ther.* 21(2):74-82
2. Kang H., Kawasawa Y., Cheng F., Zhu Y., Xu, X., Li M., Sousa A., Pletikos M., Meyer K., Sedmak G., Guennel T., Shin Y., Johnson M.B., Krsnik Z., Mayer S., Fertuzinhos S., Umlauf S., Lisgo S.N., Vortmeyer A., Weinberger D., Mane, S., Hyde T.M., Huttner A., Reimers M., Kleinmann J., Sestan N. (2011): Spatiotemporal transcriptome of the human brain. *Nature* 478(7370):483-9.
3. Johnson MB, Kawasawa YI, Mason CE, Krsnik Z, Coppola G, Bogdanovic D, Geschwind DH, Mane SM, State M, Sestan N (2009) Genetic complexity of human brain development and evolution revealed through global exon usage analysis. *Neuron* 62: 494-509.
4. Fertuzinhos S, Krsnik Z, Kawasawa YI, Rasin MR, Kwan KY, Chen JG, Judas M, Hayashi M., Sestan N (2009) Selective loss of cortical interneurons in human holoprosencephaly with striatal hypoplasia. *Cerebral Cortex* 19: 2196-207
5. Stillman A*, Krsnik Z*, Sun J, Rasin MR, State M, Sestan N, Louvi A (2009) Developmentally regulated and evolutionarily conserved expression of SLITRK1 in brain circuits implicated in Tourette syndrome. *Journal of Comparative Neurology* 513: 21- 37
6. Kwan KY, Lam MM, Krsnik Z, Kawasawa YI, Lefebvre V, Sestan N. (2008) SOX5 postmitotically regulates migration, postmigratory differentiation, and projections of subplate and deep-layer neocortical neurons. *PNAS* 105: 16021-6

Odsjek „Zagrebačka neuroembriološka zbirka i banka tkiva“ (Zdravko Petanjek)

*Laboratorij za digitalnu obradu preparata
Zagrebačke neuroembriološke zbirke
(Željka Krsnik)*

Voditelj

Doc.dr.sc. Željka Krsnik

Savjetnik

Akademik Ivica Kostović

Suradnici

Prof.dr.sc. Miloš Judaš

Prof.dr.sc. Mario Vukšić

Prof.dr.sc. Zdravko Petanjek

Prof.dr.sc. Goran Šimić

Prof.dr.sc. Nataša Jovanov-Milošević

Doc.dr.sc. Milan Radoš

Doc.dr.sc. Goran Sedmak

Pero Hrabač, dr.med.

Zagrebačku neuroembriološku zbirku osnovao je akademik Ivica Kostović 1974.godine. Do danas, zbirka je izrasla u jedinstvenu kolekciju od preko 1,300 mozgova - od najranijih stadija razvoja do odraslog doba. (Judas et al, 2011). Primarni cilj nam je digitalizacijom odabranih histoloških, imunohistokemijskih, te preparata *in situ* hibridizacije na skeneru visoke rezolucije (Hammamatsu NanoZoomer 2.0 RS), te osnivanjem jedinstvene baze podataka, omogućiti pristup podacima svim sastavnicama Hrvatskih sveučilišta, kao i kolegama znanstvenicima i kliničarima iz cijelog svijeta. Kao sljedeći korak, cilj nam je objediniti odabrane histološke preparate, te slikovni prikaz MRI u jedinstveni atlas mozga dostupan kolegama u edukacijske, znanstvene, te kliničke svrhe.

Za više informacija molimo kontaktirajte nas na: zkrsnik@hiim.hr, collection@hiim.hr

Web: <http://www.zagrebbraincollection.hr>

1.

Division “The Zagreb Neuroembryological Collection and Brain Bank” (Zdravko Petanjek)

*Laboratory for the digitization of the
Zagreb Neuroembryological Collection’s
slides (Željka Krsnik)*

Head:

Željka Krsnik, PhD, Assistant Professor

Consultant & Founder of the Zagreb Collection:
Academic Ivica Kostović

Collaborators:

Prof. Miloš Judaš,

Dr. Pero Hrabač,

Prof. Nataša Jovanov-Milošević,

Prof. Milan Radoš,

Prof. Mario Vukšić,

Prof. Zdravko Petanjek,

Prof. Goran Šimić,

Prof. Goran Sedmak

Research interest:

Zagreb Neuroembryological Collection was founded in 1974 by Professor Ivica Kostović and consists of more than 1,300 developing and adult human brains.

Currently, we are in a process of digitalizing and storing a large number of representative histological, immunohistochemical and *in situ* hybridization slides into an online database for sharing data and constructing slide libraries with distant facilities and institutes.

As the next step, our aim is to establish comparative MRI atlas throughout human neurodevelopment and make it available to the research and clinical community worldwide.

For further info please contact: zkrsnik@hiim.hr, collection@hiim.hr

Web: <http://www.zagrebbraincollection.hr>

Grants: IBRO (International Brain Research Organization) RHP 2014/15 (Ž. Krsnik)

Foundation of Croatian Academy of Sciences and Arts 2014/15 (Ž. Krsnik)

Croatian Science Foundation 2013/15 (M. Judaš)

Odabrane publikacije / Selected publications:

1. Judaš M, Šimić G, Petanjek Z, Jovanov-Milošević N, Pletikos M, Vasung L, Vukšić M, Kostović I. (2011) The Zagreb Collection of human brains: a unique, versatile, but underexploited resource for the neuroscience community. *Ann N Y Acad Sci.* 1225 Suppl 1:E105-30
2. Kostovic I, Judas M, Kostovic-Knezevic L, Simic G, Delalle I, Chudy D, Sajin B, Petanjek Z. (1991) Zagreb research collection of human brains for developmental neurobiologists and clinical neuroscientists. *Int J Dev Biol.* 35(3):215-30
3. Kang H, Kawasawa Y., Cheng F., Zhu Y., Xu X., Li M., Sousa A., Pletikos M., Meyer K., Sedmak G., Guennel T., Shin Y., Johnson M.B., Krsnik Z., Mayer S., Fertuzinhos S., Umlauf S., Lisgo S.N., Vortmeyer A., Weinberger D., Mane, S., Hyde T.M., Huttner A., Reimers M., Kleinmann J., Sestan N. (2011): Spatiotemporal transcriptome of the human brain. *Nature* 478(7370):483-9
4. Johnson MB, Kawasawa YI, Mason CE, Krsnik Z, Coppola G, Bogdanovic D, Geschwind DH, Mane SM, State M, Sestan N (2009) Genetic complexity of human brain development and evolution revealed through global exon usage analysis. *Neuron* 62: 494-509.
5. Fertuzinhos S, Krsnik Z, Kawasawa YI, Rasin MR, Kwan KY, Chen JG, Judas M, Hayashi M., Sestan N (2009) Selective loss of cortical interneurons in human holoprosencephaly with striatal hypoplasia. *Cerebral Cortex* 19: 2196-207
6. Stillman A*, Krsnik Z*, Sun J, Rasin MR, State M, Sestan N, Louvi A (2009) Developmentally regulated and evolutionarily conserved expression of SLITRK1 in brain circuits implicated in Tourette syndrome. *Journal of Comparative Neurology* 513: 21- 37 (*co-first authors)
7. Kwan KY, Lam MM, Krsnik Z, Kawasawa YI, Lefebvre V, Sestan N. (2008) SOX5 postmitotically regulates migration, postmigratory differentiation, and projections of subplate and deep-layer neocortical neurons. *Proceedings of the National Academy of Sciences* 105: 16021-6

Odsjek za slikovni prikaz mozga (Marko Radoš)

Laboratorij za funkcionalno oslikavanje mozga (Milan Radoš)

Voditelj:

Doc.dr.sc. Milan Radoš

Izuzetan razvoj medicinske tehnologije tijekom zadnjih nekoliko desetljeća značajno je unaprijedio dijagnostičke ali i istraživačke potencijale neuroradioloških metoda. Poseban iskorak je napravljen razvojem funkcijske magnetske rezonancije (fMRI) početkom 90-ih godina prošlog stoljeća koja je uz pomoć BOLD signala (od eng. Blood Oxygen Level Dependent signal) otvorila vrata razumijevanju funkcijskog ustroja mozga. Ova metoda je našla svoju primjenu kako u redovitoj kliničkoj praksi najčešće u sklopu predoperativne obrade neurokirurških pacijenata, tako i u brojnim istraživanjima mentalnih procesa napose u pacijenata kod kojih ne postoji jasno strukturno oštećenje u podlozi mentalnog poremećaja. Nadalje, razvojem difuzijskih traktografskih metoda snimanja (DTI, od eng. Diffusion Tensor Imaging) postalo je moguće jasnije i detaljnije proučavati bijelu tvar mozga, te odnose, tijek i morfologiju zasebnih aksonalnih putova. Uprkos svojoj nedvojbenoj dijagnostičkoj i istraživačkoj korisnosti ove metode još uvijek nisu široko prisutne prvenstveno stoga što su tehnički vrlo zahtjevne, a isto tako analiza snimljenih sekvenci traži kompleksnu multidisciplinarnu ekspertizu. Jedan od važnih ciljeva HIIM-a je održati i unaprijediti razinu izvrsnosti koja je dosegnuta u strukturnim MR snimanjima, no isto tako je od posebnog interesa uspostaviti i usavršiti funkcijske metode snimanja mozga. U skladu s tim nastojanjima je 2013.g u sklopu Odsjeka za slikovni prikaz mozga na HIIM-u osnovan i Laboratorij za funkcionalno oslikavanje mozga. Iako je je i prije ustroja Laboratorija postojala značajna aktivnost vezana za pokretanje i uspostavu funkcijskih metoda snimanja mozga upravo je njegovo osnivanje dalo formalni okvir i dodatni zamah ovim naporima. Nedugo nakon instalacije novog 3T MR uređaja u rujnu 2007.g. (Magnetom TrioTim, Siemens, Njemačka) počeli smo s testiranjem i podešavanjem sekvenci za funkcijska snimanja tako da smo već tijekom 2008.g. uspjeli standardizirati i uobličiti osnovne paradigme za lokalizaciju primarnog osjetnog, motoričkog, slušnog i vidnog korteksa. Isto tako uveli smo i funkcijsku paradigmu imenovanja predmeta koja se pokazala vrlo uspješna u lateralizaciji i lokalizaciji govornog korteksa. Spomenute metode nisu samo unaprijedile neuroradiološku dijagnostiku nego su dovele i do boljeg planiranja operativnih neurokirurških zahvata što je od presudnog utjecaja na smanjenje postoperativnih neuroloških ispada. S obzirom da se radi o specifičnim dijagnostičkim procedurama korisnici naših usluga u početku su bili ograničeni gotovo u cijelosti na pacijente koji su dolazili iz KBC Zagreb kao vodeće bolnice

Division for Brain imaging (Marko Radoš)

Laboratory for the functional magnetic resonance imaging (Milan Radoš)

Head:

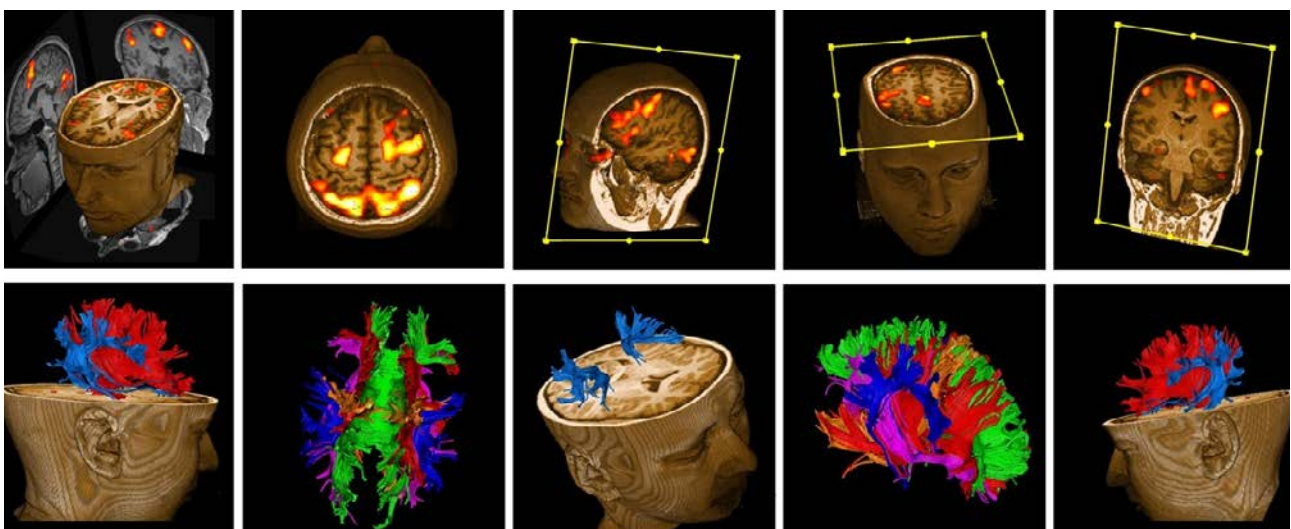
Assistant Professor Milan Radoš; MD, PhD

In the last decades a remarkable development in medical technology has significantly improved diagnostics and research potential in the field of neuroradiology. An outstanding step forward was the development of functional magnetic resonance imaging (fMRI) in the early 90s in which the BOLD signal (Blood Oxygen Level Dependent signal) is used for understanding the functional organization of the brain. This method has found its place in both clinical practice, usually as a part of preoperative treatment of neurosurgical patients, as well as in numerous studies of mental processes especially in patients with mental disorders but no clear underlying structural damage. Furthermore the development of diffusion tensor imaging tractography made possible to do clearer and more detailed studies of brain white matter and flow, interrelations and morphology of individual axonal pathways. Despite its undoubted diagnostic and research benefit these methods have not yet been commonly used while they require demanding technical support and recorded sequences postprocessing is a multidisciplinary field. One of the main goals of CIBR is to maintain and further develop achieved expertise in structural MRI, but also to reach the same for functional brain imaging. According to this in 2013 Laboratory for functional brain imaging was founded at the Division for brain imaging, CIBR. This was just a formal act to further encourage these efforts, since there was significant work with functional methods already in motion. Not long after the installation of new 3T MRI device in September 2007 (TrioTim, Siemens, Germany) we started testing and adjusting the sequences for functional imaging so in 2008 there were standardized and basic paradigms for the localization of primary sensory, motor, auditory and visual cortex. These methods have not only improved neuroradiological diagnosis but also lead to better planning of neurosurgical procedures, which led to less postoperative neurological impairments. Given that this is a highly specific diagnostic test our patients were in the beginning almost entirely the patients of the leading hospital in Croatia, University Hospital Centre Zagreb. Over time other centers were included and started to use functional brain imaging, so this year we organized a course entitled 'Clinical application of functional magnetic resonance' to inform potential users about this method's capabilities and limitations. Today the CIBR is the only place where functional brain imaging is performed, which is somewhat understandable since the establishment and application of these methods is possible only in highly specialized scientific and academic institutions. Apart from fMRI and DTI use in the clinic

u RH. No, vremenom su i drugi centri počeli koristiti mogućnosti funkcijskih snimanja mozga te smo stoga ove godine organizirali i tečaj pod nazivom „Klinička primjena funkcijske magnetske rezonancije“ s ciljem da potencijalne korisnike upoznamo s mogućnostima ali i ograničenjima ovih metoda. Trenutno je HIIM jedino mjesto u RH u sklopu kojeg je moguće napraviti funkcijska MR snimanja, što je donekle i razumljivo jer je pokretanje i kritička promjena ovih metoda moguća samo u ustanovama koje imaju snažno znanstveno i akademsko zaleđe.

Osim u klinici fMRI i DTI imaju i važnu primjenu znanosti kao iznimni istraživački alati. S obzirom na izvrsnost u klasičnoj neuroanatomiji po kojoj je HIIM prepoznat i u svijetu ne iznenađuje kako je DTI metoda vrlo brzo iskorištena za proučavanje putova u fetalnom mozgu što je dovelo i do nekoliko radova publiciranih u prestižnim časopisima. Na polju funkcijske magnetske rezonancije uspostavljena je suradnja s jednim od najprestižnijih centara (Yale University, SAD) s ciljem da se pokrene snimanje i analiza funkcijske MR u „mirovanju“ (resting state fMRI). Valja napomenuti kako je Laboratorij za funkcionalno oslikavanje mozga otvoren za suradnju sa svima drugim sastavnicama Medicinskog fakulteta i Sveučilišta s ciljem da se kroz interdisciplinarni pristup unaprijedi kvaliteta kliničke skrbi ali i znanstvenih istraživanja.

they are extraordinary research tools. Due to the CIBR widely known excellence in classical neuroanatomy it is not surprising that it wasn't long before DTI was used to for studying pathways in the fetal brain. This research papers were published in several leading journals. Collaboration with Yale University, USA, has been established in order to start the recording and analysis of functional brain imaging in resting state. Laboratory for functional brain imaging is open for collaboration with all departments in Medical School as well as the University to achieve the interdisciplinary approach and improve the quality of clinical and also scientific practice.



Odsjek za neurogenetiku, citogenetiku i razvojnu genetiku (Srećko Gajović)

Laboratorij za neurogenetiku i razvojnu genetiku (Srećko Gajović)

Voditelj:

Profesor Srećko Gajović
srecko.gajovic@hiim.hr

The GlowBrain djelatnici:

Boban Mirta, PhD
Brkić Lada, PhD
Ferhatović Hamzić Lejla, PhD
Lovrić Marija, PhD
Pavičić Josip, M.S.
Pochet Roland, Profesor
Pongrac Igor, PhD
Dr. Radmilović Marin
Renić Marija, PhD
Škokić Siniša, PhD.
Ulični Olja, M.S.

Moguća terapija bolesti mozga matičnim stanicama ovisi o njihovim mogućnostima opstanka i integracije u živčano tkivo. Inovativni biomaterijali podržavaju stvaranje 3D stanične mreže koje bi mogle poboljšati primjenu tkivnog inženjersva za bolesti mozga.

Pod okriljem projekta GlowBrain (Svjetleći mozak, <http://glowbrain.hiim.hr/>), istraživači kombiniraju bioluminiscentno snimanje (BLI) i magnetsku rezonanciju (MRI) mišjeg mozga. Oni razvijaju i optimiziraju aplikacije matičnih stanica i biomaterijala u popravaku oštećenja mišjeg mozga nastalog nakon moždanog udara.

Multimodalno snimanje BLI i MRI omogućuje vizualizaciju transplantiranih matičnih stanica koje su transplantirane u mozak miša preko biljega kao što su luciferaza i super paramagnetske čestice.

Projekt zapošljava sedam iskusnih znanstvenika koji razvijaju vještine uzgoja i primjene matičnih stanica, biomaterijala i in vivo snimanja. Osim organizacije radionica i sastanaka, ove osobe stječu potrebnu obuku u sedam partnerskih organizacija projekta. Za in vivo snimanje, istraživači su uređaj za MRI za male životinje (Bruker 7T), kao i uređaj za BLI snimanje (Spectrum, Perkin Elmer).

Paralelno, GlowBrain je zaposlio menadžera za inovacije. To olakšava suradnju s drugim sveučilištima i stručnjacima u području intelektualnog vlasništva. Ciljevi projekta i aktivnosti su vidljive putem web stranice projekta, Facebook, <https://www.facebook.com/GlowBrainCroatia> i YouTube profila, http://www.youtube.com/results?search_query=glowbrain. Osim toga, organizirana je Regionalna mreža za regenerativnu medicinu i terapiju matičnim stanicama, koja se zove RegMed, u kojoj sudjeluju stručnjaci iz različitih, ali komplementarnih disciplina.

Division for neurogenetics, cytogenetics and developmental genetics (Srećko Gajović) – Fig. 38.

Laboratory for neurogenetics and developmental genetics (Srećko Gajović)

Head:

Professor Srećko Gajović
srecko.gajovic@hiim.hr

The GlowBrain employees:

Boban Mirta, PhD
Brkić Lada, PhD
Ferhatović Hamzić Lejla, PhD
Lovrić Marija, PhD
Pavičić Josip, M.S.
Pochet Roland, Professor
Pongrac Igor, PhD
Dr. Radmilović Marin
Renić Marija, PhD
Škokić Siniša, PhD.
Ulični Olja, M.S.

Barriers to stem cell therapy include low survival and integration rate of cells. Innovative biomaterials that support formation of 3D cellular networks are required for applications in the brain.

Under the aegis of the GlowBrain (<http://glowbrain.hiim.hr/>) project, researchers are combining bioluminescent imaging (BLI) and magnetic resonance imaging (MRI) to image the brain. They develop and optimise stem cells and biomaterials applications to repair damages in the mouse brain occurring after a stroke.

Combining BLI and MRI enables visualisation of the transplanted stem cells that are integrated within the mouse brain through markers such as luciferase and super paramagnetic particles.

Project recruited seven experienced scientists which develop skills in stem cells, biomaterials and in vivo imaging. Besides organization of dedicated workshops and meetings, arrangements were made for these personnel to obtain necessary training at seven project partner organisations.

For in vivo imaging, researchers purchased a small animal MRI (Bruker 7T) as well as a BLI system (Spectrum, Perkin Elmer). The mouse facility was upgraded to maintain transgenic mice required for the study.

In parallel, GLOWBRAIN established an innovation office and employed an innovation manager. This helped facilitate collaborations with other universities and intellectual property experts.

Project objectives and activities have been widely disseminated through the project website, Facebook, <https://www.facebook.com/GlowBrainCroatia>, and YouTube profile, http://www.youtube.com/results?search_query=glowbrain. In addition, the team organized a regional network for regenerative medicine and stem cell therapies called RegMed, with experts from different but complementary disciplines participating.

GlowBrain has a long way to go towards devel-

GlowBrain još ima dug put prema razvoju potpuno funkcionalne platforme za praćenje transplantiranih matičnih stanica u mišjem modelu moždanog udara. Njegov uspjeh pomogao bi istraživanju bolesti mozga i osigurao bržu komercijalizaciju rezultata istraživanja, te osigurao prvenstvo HIIM-a u regenerativnoj medicini. Ova svestrana platforma može biti u budućnosti prilagođena za proučavanje osim moždanog udara i drugih bolesti mozga, kao što su primjerice Alzheimerova bolest.

Partnerske organizacije EU FP7 projekta GlowBrain:

1. Lund Stem Cell Center (LSCC), Lund University, Sweden,
2. Max Planck Institute for Neurological Research (MPINR), Cologne, Germany,
3. Paracelsus Medical University Salzburg (PMU), Salzburg, Austria,
4. Università Politecnica delle Marche (UNIVPM), Ancona, Italy,
5. Institute of Macromolecular Chemistry AS CR (PIMC), Prague, Czech Republic,
6. Semmelweis University (SEMU), Budapest, Hungary,
7. University of Minho, Portugal (UMINHO).

Pet odabranih publikacija / Five selected publications:

1. Kosi, N; Alić, I; Kolačević, M; Vrsaljko, N; Jovanov Milošević, N; Sobol, M; Philimonenko, A; Hozák, P; Gajović, S; Pochet, R; Mitrečić, D. Nop2 is expressed during proliferation of neural stem cells and in adult mouse and human brain. *Brain Res* 2014;1597:65-76.
2. Dobrivojević M, Bohacek I, Erjavec I, Gorup D, Gajović S. Computed microtomography visualization and quantification of mouse ischemic brain lesion by nonionic radio contrast agents. *Croat Med J.* 2013;54(1):3-11.
3. Winters, L; Winters, T; Gorup, D; Mitrečić, D; Križ, J; Gajović, S. Expression analysis of genes involved in TLR2-related signaling pathway, inflammation and apoptosis after ischemic brain injury. *Neuroscience.* 2013 Feb 10;238:87-96.
4. Curlin M, Kapuralin K, Muro AF, Baralle FE, Chowdhury K, Gajović S. Stam2 expression pattern during embryo development. *Gene Expr Patterns.* 2012 Jan-Feb;12(1-2):68-76.
5. Bohacek I, Cordeau P, Lalancette-Hébert M, Gorup D, Weng YC, Gajović S, Kriz J. Toll-like receptor 2 deficiency leads to delayed exacerbation of ischemic injury. *J Neuroinflammation.* 2012 Aug 8;9:191.

oping a fully functional platform for monitoring transplanted stem cells in a mouse model of stroke. Success could help brain research and ensure faster commercialization of research results, placing the CIBR ahead in the regenerative medicine sector. This versatile platform could also be adapted to study other brain diseases such as Alzheimer's disease in the future.

Partners of EU FP7 project GlowBrain:

1. Lund Stem Cell Center (LSCC), Lund University, Sweden,
2. Max Planck Institute for Neurological Research (MPINR), Cologne, Germany,
3. Paracelsus Medical University Salzburg (PMU), Salzburg, Austria,
4. Università Politecnica delle Marche (UNIVPM), Ancona, Italy,
5. Institute of Macromolecular Chemistry AS CR (PIMC), Prague, Czech Republic,
6. Semmelweis University (SEMU), Budapest, Hungary,
7. University of Minho, Portugal (UMINHO).

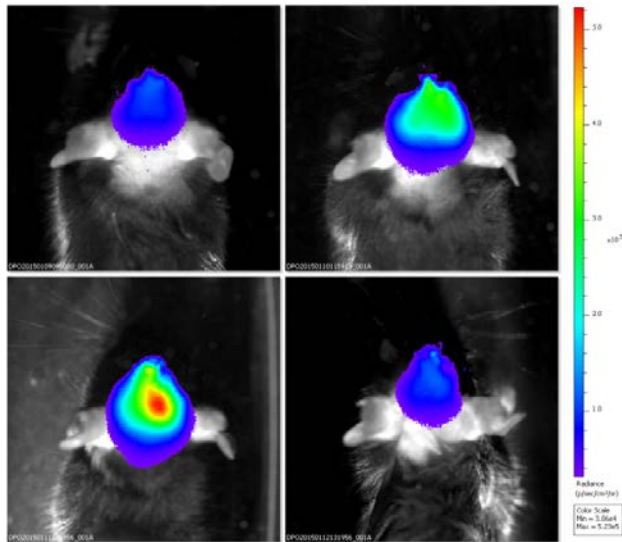


Figure 1.
Glowing mouse brain imaged by BLI modality after stroke

Slika 1.
Svijetleći mišji mozak snimljen tehnikom bioluminiscencije nakon moždanog udara



Figure 2.
Current construction work on setting up the Laboratory for Regenerative Neuroscience

Slika 2.
Trenutni radovi na postavljanju Laboratorija za regenerativnu neuroznanost

Laboratorij za molekularnu citogenetiku (Lukrecija Brečević)

Znanstveni interes:

Znanstveni interes usmjeren je na primjenu tehnika molekularne citogenetike u identifikaciji i karakterizaciji malih genomskih promjena (kriptične i suptilne submikroskopske kromosomske preraspodjele i varijacije u broju kopija (CNV)) u podlozi neurorazvojnih poremećaja (razvojni intelektualni poremećaj, zaostajanje u razvoju, poremećaji autističnog spektra). Laboratorij blisko surađuje s Institutom za humanu genetiku, Sveučilišne klinike u Jeni, Laboratorij za molekularnu genetiku (voditelj: PD, PhD Thomas Liehr) i Centrom za funkcionalnu genomiku, Medicinskog fakulteta Sveučilišta u Zagrebu (voditelj: Prof. dr. sc. Fran Borovečki).

Projekti:

- Molekularna citogenetika mentalne retardacije/razvojnog intelektualnog poremećaja nepoznate etiologije (Ministarstvo znanosti, obrazovanja i sporta, voditelj projekta prof. dr. sc. L. Brečević) (2007-2014)
- Ciljani arrayCGH čipovi za dijagnostiku neurorazvojnih poremećaja (Hrvatski Institut za tehnologiju, voditelj projekta prof. dr. sc. F. Borovečki) (2010-2013)
- Detection of cryptic chromosomal rearrangements in patients with idiopathic mental retardation (MZOŠ R. Hrvatske & DAAD Njemačka vlada, voditelji: Brečević L & Liehr T) (2008-2009)
- Kriptične kromosomske preraspodjele i mentalna retardacija (Ministarstvo znanosti, obrazovanja i športa RH 0220002, voditelj projekta prof. dr. sc. L. Brečević) (2002-2006)
- Identification and molecular characterization of cryptic subtelomeric rearrangements (NF 3200-045604.95/1: Swiss National Science Foundation; autor i glavni istraživač projekta prof. dr. sc. L. Brečević) (1996-1998)

Stručne vještine:

Iskustvo i rutinska primjena tehnika molekularne citogenetike. Kultura stanica s kariotipizacijom, sve postojeće tehnike fluorescentne in situ hibridizacije (FISH) i radu sa svim tipovima FISH DNA proba uključujući izradu long-range PCR lokus specifičnih proba, kultura i izrada BAC FISH proba. Primjena i izvođenje MLPA tehnike (Multiplex Ligation-dependent Probe Amplification). U sklopu suradnje s Institutom za humanu genetiku Univerziteta u Jeni; Njemačka (PD T. Liehr) rad sa MLPA specifičnim probama za leukemije. Uvođenje metilacijsko specifične MS-MLPA tehnike u dijagnostiku Prader-Will/Angelman sindroma i FRAX u Hrvatskoj. Prvi smo u Republici Hrvatskoj uveli aCGH (array komparativna genomika hibridizacija) tehniku u molekularno citogenetsku dijagnostiku neurorazvojnih poremećaja. U sklopu međunarodne suradnje (PD T. Liehr) rad na aCGH

Laboratory for molecular cytogenetics (Lukrecija Brečević)

Research interest:

Scientific interest is focused on molecular cytogenetics applications in the identification and characterization of small genomic changes (cryptic and subtle submicroscopic chromosomal rearrangements and variation in copy number – CNV) underlying neurodevelopmental disorders (intellectual disability, developmental delay, autism spectrum disorders). Laboratory works closely with the Institute of Human Genetics, University Clinic in Jena, Laboratory for Molecular Cytogenetic (Head: PD, PhD Thomas Liehr) and the Center for Functional Genomics, School of Medicine, University of Zagreb (Head: Prof. dr. Sc. Fran Borovečki).

Projects:

- Molecular cytogenetics of mental retardation/intellectual disability of unknown etiology (Ministry of Science, Education and Sports, project leader prof. Dr. Sc. L. Brečević) (2007-2014)
- Targeted arrayCGH chips for the diagnosis of neurodevelopmental disorders (Croatian Institute of Technology, project leader prof. Dr. Sc. F. Borovečki) (2010-2013)
- Detection of cryptic chromosomal rearrangements in patients with idiopathic mental retardation (Ministry of Science, Education and Sports & DAAD, project leaders: Brečević L & Liehr T) (2008-2009)
- Cryptic chromosomal redistribution and mental retardation (Ministry of Science, Education and Sport 0220002, project leader prof. Dr. Sc. L. Brečević) (2002-2006)
- Identification and molecular characterization of cryptic subtelomeric rearrangements (NF 3200-045604.95/1: Swiss National Science Foundation; author and principal investigator of the project prof. dr. sc. L. Brečević) (1996-1998)

Professional skills:

Experience and routine application of molecular cytogenetics techniques. Cell culture with karyotype analysis, all the existing fluorescence in situ hybridization techniques (FISH) and work with all types of FISH DNA probes including the construction of long-range PCR locus-specific probes, culture and production of BAC FISH probes. Application and performance of MLPA technique (Multiplex Ligation-dependent Probe Amplification). Within the cooperation with the Institute of Human Genetics at the University of Jena; Germany (PD T. Liehr) work with the MLPA probes specific for leukemia. The introduction of methylation specific MS-MLPA technique in the diagnosis of Prader-Will / Angelman syndrome and FRAX in Croatia. We were the first in the Republic of Croatia to introduce aCGH (array comparative genomic hybridization) technique in molecular cytogenetic diagnosis of neurodevelopmental disorders. Within the framework of international cooperation (PD T. Liehr) work on

čipovima modelnih organizma (transgenični miševi) za različita maligna oboljenja. Dizajn i bioinformatički dizajn „custom“ aCGH čipova, te dizajniranje „custom“ panela za sekvenciranje sljedeće generacije (Next-Gen Sequencing).

Publicistička aktivnost i članstvo u profesionalnim tijelima:

Prof. dr. sc. L. Brečević

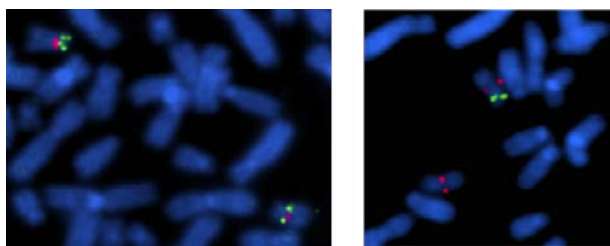
49 (36 peer recenzija: 29 CC, 5 SCI, 1 Medline, 1 Scopus; 9 non-peer recenzija, 3 rada u knjizi, 1 autorski rad); Citati: 637 (svibanj 2015, Current Contents, Web of Science)

Član uređivačkog odbora: „Molecular Cytogenetics“ (online peer-review casopis na BioMed Centralu)

Dr. sc. M. Rinčić

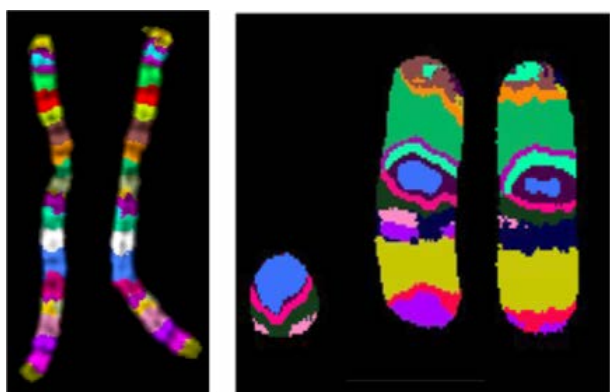
13 radova (5 CC, 7 SCI-Exp, 1 Medline); Citati: 44 (CC, SCI, svibanj 2015)

Stalni član odbora za „Clinical Laboratory Geneticists“ pri European Board of Medical Genetics (<https://www.eshg.org/clg.0.html>)



Slika 1

FISH s lokus specifičnim probama u dvije (recipročne) periferne neuropatije: duplikacija PMP22 gena u CMT1A (dup 17p11.2) i delecija PMP22 gena u HNPP (del17p11.2).



Slika 2

Višebojne MCB pruge. Normalan MCB2 (Sl.5a); identifikacija sSMC u prenatalnoj dijagnozi kao r(3q) (SL.5b).

aCGH chips for model organisms (transgenic mice) for different malignant diseases. The design and bioinformatics design of custom aCGH chips and designing of custom panel for next-generation sequencing (Next-Generation Sequencing).

Bibliography:

Prof. dr. sc. L. Brečević

49 papers (36 peer reviews: 29 CC, SCI 5, 1 Medline, Scopus 1; 9 non-peer review, 3 papers in the book, one author work); Citations: 637 (May 2015, Current Contents, Web of Science)

Editor of Molecular Cytogenetics (online peer-review journal in BioMed Central)

Dr. sc. M. Rinčić

13 papers (CC 5, 7 SCI-exp, 1 Medline); Citations: 44 (CC, SCI, May 2015)

Permanent member of the Clinical Laboratory Geneticists at the European Board of Medical Genetics (<https://www.eshg.org/clg.0.html>)

Figure 1

FISH with locus-specific probes in two (reciprocal) Peripheral neuropathy: PMP22 gene duplication in CMT1A (dup 17p11.2) and deletion of PMP22 genes in HNPP (del17p11.2).

Figure 2

Multicolor MCB banding. MCB2 normal (Fig.5a); identification of sSMC in prenatal diagnosis as r(3q) (Fig.6b).

Laboratorij za medicinsku genetiku (Nina Canki Klain – u mirovini od 2015.)

Voditelj:

Prof.dr.sc. Nina Canki-Klain
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Katedra za medicinsku Biologiju
Hrvatski institut za istraživanje mozga
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Suradnici:

Prof.dr.sc. Floriana Bulić-Jakuš
Prof.dr.sc. Sven Seiwerth
Dr.sc. Astrid Milić

Istraživački interes laboratorija predstavljaju različna istraživanja nastanka te molekularni aspekti najčešćih monogenih mišićnih i neuroloških poremećaja s naglaskom na epidemiološko stanje u Hrvatskoj. Ti podaci su neophodni kako bi se prošle usavršene mjere za sprječavanje, poboljšanje ili liječenje tih bolesti. Diferencijalna dijagnoza spomenutih poremećaja zahtijeva pomnu primjenu širokog opsega znanja: kliničku procjenu, istraživanje rodoslovlja, imunoblot analizu s upotrebom panela protutijela te opsežne molekularne genetske analize. Rad laboratorija je započeo sa širokim rasponom pristupa 1996. Bolesnici su se do 2009. odabirali u Neurogenetskoj ambulanti (Voditelj: Prof. dr. Nina Canki-Klain), Neurološka klinika, Klinički bolnički centar Zagreb. Danas se rad nastavlja u Neurogenetskoj ambulanti Hrvatskog Instituta za istraživanje mozga u okviru Medicinskog fakulteta Sveučilišta u Zagrebu.

Laboratorij je otkrio spektar mutacija nekih od najčešćih mišićnih bolesti u Hrvatskoj. Isto tako, radi se o laboratoriju koji jedini u zemlji obavlja slijedeće analize:

- Analiza genetskog povezivanja:
- Autosomnih recesivnih pojasnih mišićnih distrofija (LGMD2):
- Tip 2A – CAPN3 gen (Erbovjuvenilni oblik mišićne distrofije ili kalpainopatija (LGMD2A) (Slika 1.)
- Tip 2B – DYSF gen (disferlinopatija / Miyoshiyeva miopatija (LGMD2B) (Slika 2.)
- Tip 2C – SGCG (gamasarkoglikanopatija) (LGMD2C)
- Tip 2D – SGCA gen (alfasarkoglikanopatija) (LGMD2D)
- Tip 2I – FKRP gen (pojasna mišićna distrofija LGMD2I) (Slika 3a. i kongenitalna miš. distrofija MDC1D)
- Okulofaringealne mišićne distrofije (PABP2 gen) (OPMD) (Slika 4. i 5.)
- Direktna analiza
- Analiza šest mutacija CAPN3: 550delA i delFWSAL (egzon 4); P82LiR49H (egzon 1); R541WiY537 (egzon 13) koje pokrivaju 96% CAPN3 kromosoma našoj populaciji. (Tablica 1.)
- Analiza C826 – najčešće mutacije FKRP gena koja uzrokuje LGMD2I: (Slika 3b.)
- Analiza PABP2 gena uzročnika okulofaringealne

Laboratory for medical genetics (Nina Canki Klain – retired since 2015.)

Head:

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Pediatric-geneticist
Department of Medical Biology
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nina.canki-klain@mef.hr

Associates:

Prof.dr.sc. Floriana Bulić-Jakuš
Prof.dr.sc. Sven Seiwerth
Dr.sc. Astrid Milić

Laboratory research interests are basic research of formation and molecular aspects of the most common monogenic muscle and neurological disorders with an emphasis on the epidemiological situation in Croatia. These data are essential in order to find a sophisticated measures to prevent, improve or treat these diseases. The differential diagnosis of these disorders requires a careful application of broad-based knowledge: clinical assessment, genealogy research, immunoblot analysis with the use of wide range of antibodies and extensive molecular genetic analysis. The work of the laboratory began with a wide range of access in 1996. Until 2009. patients were selected in Neurogeneticist's office (Head: Prof.dr.sc. Nina Canki-Klain), Department of Neurology, University Hospital Center Zagreb. Today, work continues in Neurogeneticist's office of Croatian Institute for Brain Research at the Medical School, University of Zagreb.

Laboratory discovered spectrum of mutations of some of the most common muscle diseases in Croatia. Also, it is the only lab in the country that performs the following analysis:

- Genetic linkage analysis:
- Limb-girdle muscular dystrophy (LGMD2):
- Type 2A – CAPN3 gene (Erb's muscular dystrophy or calpainopathy (LGMD2A) (Figure 1.)
- Type 2B – DYSF gene (dysferlinopathy / Miyoshi myopathy (LGMD2B) (Figure 2.)
- Type 2C – SGCG (gamma-sarcoglycanopathy) (LGMD2C)
- Type 2D – SGCA gene (alpha-sarcoglycanopathy) (LGMD2D)
- Type 2I – FKRP gene (limb-girdle muscular dystrophy) (LGMD2I) (Figure 3a.) and congenital muscular dystrophy (MDC1D)
- Oculopharyngeal muscular dystrophy (PABP2 gen) (OPMD) (Figure 4. i 5.)
- Direct analysis:
- Analysis of six mutations of CAPN3: 550 delA and delFWSAL (exon 4); P82LiR49H (exon 1); R541WiY537 (exon 13) that make 96% CAPN3 chromosomes in our population (Table 1.)
- Analysis of C826 – most common mutation of FKRP gene that causes LGMD2I: (Figure 3b.)
- Analysis of PABP2 gene that causes oculopharyngeal muscular dystrophy (OPMD) (Figure 4.)

- mišićne distrofije (OPMD) (Slika 4.)
- Western blot analiza iz uzorka mišića:
- DMD gen (dystrophin)
- CAPN3 (calpain 3)
- SGCG (γ -sarkoglikan)
- SGCA (α -sarkoglikan)
- DYSF (disferlin).
- Neinvazivna Western blot analiza disferlina (DYSF) iz uzorka monocita periferne krvi (Slika 6.)

Projekt u tijeku:

- Genetika, priroda i epidemiologija značajnijih živčanih i mišićnih bolesti (ŽMB), Projekt br. 01080000003435 /2008 MZOS RHrvatske. Leader: Nina Canki-Klain

Završeni projekti napravljeni u laboratoriju

- Nacionalni genetički i epidemiološki studij mišićne distrofije u Hrvatskoj. Grant No 0108052/2002 od Ministarstva znanosti, obrazovanja i sporta Republike Hrvatske
- Genetički i epidemiološki studij mišićne distrofije u Hrvatskoj. Grant No 108041/1988 MZOS Hrvatske

Bilateralni francusko-hrvatski

- COGITO 2004/5 :L'étude clinico-génétique des dystrophies musculaires des ceintures (LGMD) en Croatie: analyse comparative des différents types. INSERM U 567, Paris, France, Pr. Jamel Chelly, direktor/ Pr.Nina Canki-Klain, haed, Zagreb University Medical School
- COGITO 2003/4: Correlation phénotype-génotype dans les dystrophies musculaires de l'enfant et de l'adulte. INSERM, U 582, Paris, France, Dr.Pascale GUICHENEY,direktor/ Pr. Nina Canki-Klain, haed, Zagreb University Medical School

Međunarodni

- ECO-NET 2004/5 Approche multiparamétrique pour la connaissance de l'histoire naturelle des calpainopathies visant à déterminer l'efficacité de thérapies potentielles, Généthon, UMR8115, CNRS, Evry, France Dr.Isabelle Richard
- AFM, MNM1 1999-Funding-groupe 4, No 7233 Canki-Klain N, Milić A, Zurak N., Šoštarko M., Pažanin L., Bonne G., Urtizberea J.A., Kaplan J.-C, Leturcq F., Recan D. Clinical and genetic study of limb-Girdle muscular dystrophies in Croatia.

- Western blot analysis from muscle tissue samples:
- DMD gene (dystrophin)
- CAPN3 (calpain 3)
- SGCG (γ -sarcoglycan)
- SGCA (α -sarcoglycan)
- DYSF (dysferlin).
- Noninvasive Western blot dysferline analysis (DYSF) from peripheral blood monocytes (Figure 6.)

Current project:

- Genetics, nature and epidemiology of major nervous and muscular disorders Grant number 01080000003435 /2008 MZOS. Leader: Nina Canki-Klain

Completed research grants

- Nacionalni genetički i epidemiološki studij mišićne distrofije u Hrvatskoj. Grant No 0108052/2002 od Ministarstva znanosti, obrazovanja i sporta Republike Hrvatske
- Genetički i epidemiološki studij mišićne distrofije u Hrvatskoj. Grant No 108041/1988 MZOS Hrvatske

Bilateral french-croatian

- COGITO 2004/5 :L'étude clinico-génétique des dystrophies musculaires des ceintures (LGMD) en Croatie: analyse comparative des différents types. INSERM U 567, Paris, France, Pr. Jamel Chelly, direktor/ Pr.Nina Canki-Klain, haed, Zagreb University Medical School
- COGITO 2003/4: Correlation phénotype-génotype dans les dystrophies musculaires de l'enfant et de l'adulte. INSERM, U 582, Paris, France, Dr.Pascale GUICHENEY,direktor/ Pr. Nina Canki-Klain, haed, Zagreb University Medical School

International

- ECO-NET 2004/5 Approche multiparamétrique pour la connaissance de l'histoire naturelle des calpainopathies visant à déterminer l'efficacité de thérapies potentielles, Généthon, UMR8115, CNRS, Evry, France Dr.Isabelle Richard
- AFM, MNM1 1999-Funding-groupe 4, No 7233 Canki-Klain N, Milić A, Zurak N., Šoštarko M., Pažanin L., Bonne G., Urtizberea J.A., Kaplan J.-C, Leturcq F., Recan D. Clinical and genetic study of limb-Girdle muscular dystrophies in Croatia.

Izabrane publikacije / Selected publications:

1. Milić A, Malnar M, Canki-Klain N. Non-invasive protein analysis in the first Translational Neuroscience. 2(3); 2011: 241-245
2. Alfirević-Ungarov T, Canki-Klain N, Handžić J, Jokić-Begić N, Kovač I, Kovač V, Richard J.L.F. LEMMERS, OZRETIĆ D, Sinanović O, Stiglmayer N, Štifter S, Vranješ D, Vukojević N. Novosti u kliničkoj genetici: Molekularna dijagnostika, terapija i prevencija facioskapulohumeralne mišićne distrofije (FSHD) / Canki-Klain, Nina (ur.). Best copy, Zagreb, 2011, 116 str.
3. Alfirević-Ungarov, Taida; Bilić, Erična; Canki-Klain, Nina; Guicheney, Pascale; Kosi, Damir; Kovač, Biserka; Kovač, Branislav; Milić, Astrid; Mitrović, Zoran; Sinanović, Osman; Šoštarko, Marija; Vranješ, Davorka. Novosti u kliničkoj genetici: genetske mišićne bolesti u svakodnevnoj praksi / Canki-Klain, Nina (ur.). Zagreb : Kolding, 2004., 161 str.
4. Canki-Klain, Nina; Fardeau, Michel; Jurčić, Dragan; Jurić, Gordana; Kovač, Ida; Ljubanović, Danica; Milić, Astrid; Sinanović, Osman; Stiglmayer, Neda; Tocilj-Šimunković, Gorana; Večerina, Santa; Vranješ, Davorka; Žagar, Marija. Novosti u kliničkoj genetici: multidisciplinarni pristup dijagnostici, terapiji i prevenciji okulofaringealne mišićne distrofije (OPMD) / Canki-Klain, Nina (ur.). Zagreb : Kolding, 2004. 99str.
5. Bushby, Kate; Canki-Klain, Nina; Stiglmayer, Neda; Fučić, Aleksandra; Jurić, Gordana; Mitrović, Zoran; Milić, Astrid. Novosti u kliničkoj genetici: dijagnostički postupci u bolesnika s kongenitalnim miopatijama i mišićnim distrofijama / Canki-Klain, Nina (ur.). Zagreb : Kolding, 2003., 74 str.
6. Milić A, Canki-Klain N. Calpainopathy (LGMD2A) in Croatia: Molecular and Haplotype Analysis. *Croat Med J* 2005; 46/4: 657-663.
7. Piluso G, Politano L, Aurino S, Fanin M, Ricci E, Ventriglia VM, Belsito A, Totaro A, Saccone V, Topaloglu H, Nascimbeni AC, Fulizio L, Broceto A, Canki-Klain N, Comi Li, Nigro G, Angelini C, Nigro V. Extensive scanning of the calpain-3 gene broadens the spectrum of LGMD2A phenotypes. *J Med Genet* 2005; 42:686-613.
8. Nina Canki-Klain, Astrid Milic, Biserka Kovac, Anuska Trlaja, Damir Grgicevic, Niko Zurak, Michel Fardeau, France Leturcq, Jean-Claude Kaplan, J Andoni Urtizberea, Luisa Politano, and Josue Feingold. Prevalence of the 550delA mutation in calpainopathy (LGMD 2A) in Croatia. *Am J Med Genet* 2004; 125A: 152-156.
9. Hecimovic S, Klepac N, Vlastic J, Vojta A, Janko D, Skarpa-Prpic I I, Canki-Klain N, Markovic D, Bozиков J, Relja M, Pavelic K. Genetic background of Huntington disease in Croatia: Molecular analysis of CAG, CCG, and Delta2642 (E2642del) polymorphisms. *Hum Mutat* 2002; 20/3:233-40.
10. N. Canki-Klain, D. Recan, D. Milicic, S. Lense, F. Leturcq, N. Deburgrave, J.C. Kaplan, M. Debevec, N. Zurak: Clinical Variability and Molecular Diagnosis in a Four-generation Family with X-linked Emery-Dreifuss Muscular Dystrophy. *Croat Med J* 2000; 41: 389-395.
11. Canki N, Tivadar I, Župančić N, Debevec M. Citogenetska študija sedmih bolnic z ataksijo-teleangiektazijo. *Zdrav Vestn* 1983; 52: 567-70.
12. Canki N, Dutrillaux B, Tivadar I. Dystrophie musculaire de Duchenne chez une petite fille porteuse d'une translocation t(X;3)(p21;q13) de novo. *Ann Génét* 1979; 22: 33-9.

Laboratorij za matične stanice (Dinko Mitrečić)

Voditelj:

Doc.dr.sc. Dinko Mitrečić, dr.med.

Djelatnici, doktorandi i suradnici:

Ivan Alić, dr.vet.
Prof.dr.sc. Ervina Bilić, dr.med.
Prof.dr.sc. Srećko Gajović, dr.med.
Dunja Gorup, dr.med.
Sandra Grgić, bacc.lab.med.
dr.sc. Katarina Kapuralin
Nina Kosi, dr.med.
Prof.dr.sc. Roland Pochet
Dora Polšek, dr.med.
dr.sc. Marija Renić, dr.med.
dr.sc. Tamara Stipčević

Laboratorij za matične stanice provodi istraživanja temeljena na regenerativnom potencijalu matičnih stanica. Idući u korak s brzim razvojem ovog novonastalog biomedicinskog područja, Laboratorij je uspostavio postupke izolacije stanica iz različitih izvora: u radu se koriste živčane matične stanice podrijetla telencefalona mišjeg zametka, mezenhimske matične stanice podrijetla koštane srži miša, te matične stanica iz subventrikularne zone i hipokampusa odraslih miševa. Istovremeno se razvijaju protokoli uzgoja ljudskih stanica podrijetla pulpe zuba i njušne sluznice te ljudskih induciranih pluripotentnih matičnih stanica. Osnovni smjerovi istraživanja obuhvaćaju *in vitro* i *in vivo* analize. *In vitro* analizama se proučava diferencijacijski i regenerativni potencijal stanica u ovisnosti od egzogenih čimbenika (npr. *in vitro* model ishemijske, ko-kultivacije), opažena se svojstva modificiraju transfekcijom - genetskim manipulacijama, te uzgojem stanica uz potporu biomaterijala (npr. alginat, biopolimeri). Jedan od osnovnih smjerova *in vivo* istraživanja je analiza regenerativnog potencijala matičnih stanica transplantiranih u mozak miša zahvaćen ishemijskim moždanim udarom. Koristeći brojne egzogene (razni stanični označivači, nanočestice) i endogene biljege (genetski modificirane stanice označene fluorescentnim bojama) Laboratorij se specijalizirao za praćenje sudbine stanica nakon transplantacije.

Slika 1 (slijedeća stranica, lijevo)

Zelena fluorescentna odgovara astrocitnom biljegu GFAP koji otkriva oštru granicu između zdravog tkiva i dijela motoričke kore mozga miša zahvaćene moždanim udarom. Crveni signal pokazuje živčane matične stanice koje nakon transplantacije migriraju i nakupljaju se u području tkivnog defekta.

Slika 2 (Slijedeća stranica, desno)

Diferencijacija živčanih matičnih stanica u kulturi nakon 6 dana: Crveni signal odgovara biljegu neurona MAP2. Zeleni signal otkriva sub-

Laboratory for Stem Cells (Dinko Mitrečić)

Head:

Assistant Professor Dinko Mitrečić, MD, PhD

Members, PhD students and main collaborators:

Ivan Alić, DVM
Prof. Ervina Bilić, MD, PhD
Prof. Srećko Gajović, MD, PhD
Dunja Gorup, MD
Sandra Grgić, Bacc.lab.med.
Katarina Kapuralin, PhD
Nina Kosi, MD
Prof. Roland Pochet, PhD
Dora Polšek, MD
Marija Renić, MD, PhD
Tamara Stipčević, PhD

Laboratory for Stem Cells is involved in research activities based on a regenerative potential of stem cells. Keeping the pace with a fast development of this new biomedical field, the Laboratory has established protocols for isolation of cells from various sources: we use neural stem cells from the telencephalon of mouse embryos, mesenchymal stem cells from the mouse bone marrow and stem cells from the adult mouse subventricular zone and hippocampus. Also, we are developing protocols for isolation of human stem cells from the tooth pulp and olfactory mucosa and human induced pluripotent stem cells. The basic directions of research include *in vitro* and *in vivo* analyses. *In vitro* analyses are used to get insight into differentiation and regenerative potential of stem cells in relation to exogenous factors (e.g. *in vitro* model of ischemia, co-cultivations) and observed features are improved by transfection-genetic manipulations and cultivation of cells using biomaterials (e.g. alginate, biopolymers). One of the major directions of *in vivo* research is analyses of regenerative potential of stem cells transplanted into the brain of mouse affected by ischemic stroke. Using various exogenous (cell markers, nanoparticles) or endogenous markers (genetically modified cells and fluorescent markers) the Laboratory has been specialized in cell tracing and analyses of cell fates after transplantation.

Using specific cell lines we can recognize differentiation stages (e.g. Nestin-GFP for multipotent stem cells or Thy1-YFP for neurons) or we can recognize some important events, like axonogenesis (Gap43-GFP). Using highly specific equipment for cell transfection (Magnefect Nano II, Nanotherics) and cell tracing equipment (bioluminescence IVIS Spectrum, Perkin Elmer; magnet resonance BIOSPEC 70/20 7T, Bruker) in combination with a whole battery of established morphological and behavioral analyses (morphology, histology, animal behavioral tests) the Laboratory is fully equipped for cell biology research and analyses of the impact of stem cell transplantation on experimental animals.

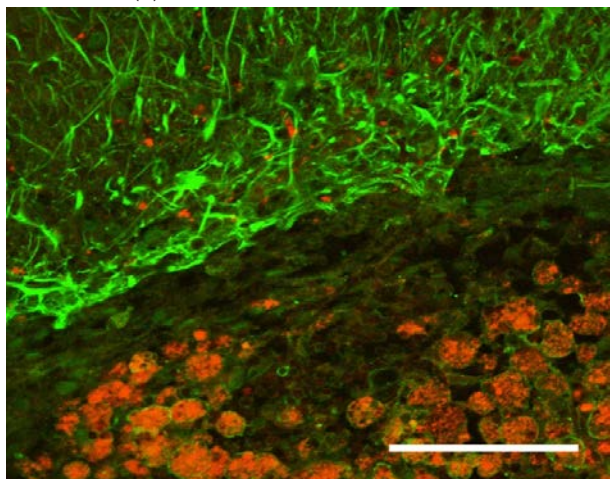
populaciju zrelih neurona prepoznatih pomoću konstrukta Thy1-YFP koji se aktivira samo u krajnje diferenciranim stanicama.

Korištenjem različitih staničnih linija se mogu prepoznati: stupanj diferencijacije (npr. nestin-GFP za prepoznavanje multipotentnih matičnih stanica ili Thy1-YFP za prepoznavanje zrelih neurona) ili ključna zbivanja, kao što je aksonogeneza (Gap43-GFP). Korištenjem visoko specifičnih uređaja za transfekciju matičnih stanica (Magnefect Nano II, Nanotherics) ili uređaja za praćenje stanica (bioluminiscencija IVIS Spectrum, Perkin Elmer; magnetna rezonancija BIOSPEC 70/20 7T, Bruker) u kombinaciji s cijelom baterijom uspostavljenih morfoloških i analiza zdravstvenog statusa (morfolologija i histologija, testovi zdravstvenog statusa eksperimentalnih životinja) Laboratorij istražuje biologiju matičnih stanica i njihove učinke na eksperimentalne modele neuroloških bolesti.

Temeljem brojnih međunarodnih suradnji sa centrima koji provode translaciju bazičnih rezultata u kliničke studije na pacijentima, Laboratorij tako sudjeluje u razvoju i unaprjeđenju tehnologije matičnih stanica u svrhu terapije ishemijskih i neurodegenerativnih bolesti živčanog sustava. U periodu od 2009 do 2015. članovi Laboratorija su bili koordinatori brojnih projekata (EU FP7 Regpot, HRZZ, MZOŠ, UKF, Adris, Bilateralni projekti sa Švedskom, Austrijom i Njemačkom), te je u istom periodu objavljeno 12 CC publikacija s tematikom matičnih stanica.

Pet odabranih publikacija / Five selected publications:

1. Kosi, N; Alić, I; Kolačević, M; Vrsaljko, N; Jovanov Milošević, N; Sobol, M; Philimonenko, A; Hozák, P; Gajović, S; Pochet, R; Mitrečić, D. Nop2 is expressed during proliferation of neural stem cells and in adult mouse and human brain. *Brain Res* 2014;1597:65-76.
2. Konig, N; Trolle, C; Kapuralin, K; Adamejko, I; Mitrečić, D; Aldskogius, H; Shortland, PJ; Kozlova, E. Murine neural crest stem cells and embryonic stem cell derived neuron precursors survive and differentiate after transplantation in a model of dorsal root avulsion *J Tissue Eng Regen Med.* 2014 Apr 21.
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4. Nicaise, C; Mitrečić, D; Pochet, R. Brain and spinal cord affected by amyotrophic lateral sclerosis induce differential growth factors expression in rat mesenchymal and neural stem cells. *Neropath Appl Neuro:* 2011 Feb;37(2):179-88.
5. Mitrečić, D; Nicaise, C; Gajovic, S; Pochet, R. Distribution, differentiation and survival of intravenously administered neural stem cells in a rat model of amyotrophic lateral sclerosis. *Cell Transplantation* 2010;19(5):537-48.



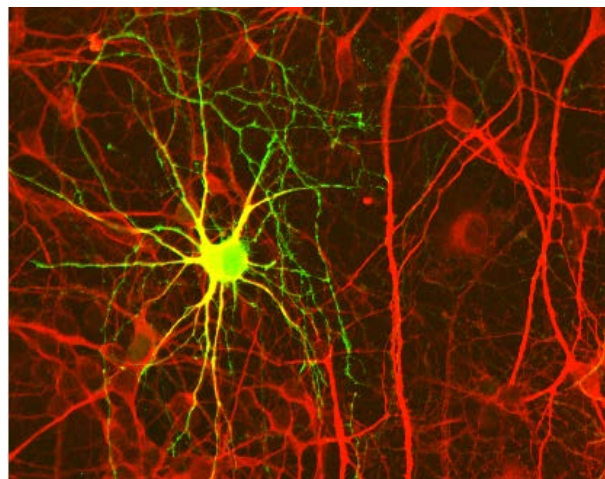
Based on international collaborations with centers which are performing clinical trials, the Laboratory is involved in development and improvement of technology of stem cells for therapeutic applications in ischemic and neurodegenerative diseases. In the period 2009 – 2015 members of the Laboratory have been coordinators of several projects (EU FP7 Regpot, HRZZ, Adris, Bilateral projects with Sweden, Austria and Germany) and in that period 12 CC publications based on stem cells have been published.

Figure 1 (left)

Green signal corresponds to astrocytic marker GFAP which sharply demarcates border between healthy tissue and a part of motoric cortex of the mouse brain affected by stroke. Red signal corresponds to neural stem cells which after transplantation migrate and accumulate in the region of tissue defect.

Figure 2 (right)

Differentiation of neural stem cells in the culture after 6 days: red signal corresponds to neuronal marker MAP2. Green signal reveals sub-population of branched cells recognized by using construct Thy1-YFP which is activated only in fully differentiated neurons.



Odsjek za elektronsku mikroskopiju (Dinko Mitrečić)

Odsjek za biokemiju i molekularnu biologiju (Hrvoje Banfić)

Laboratorij za druge glasnike (Hrvoje Banfić)

Voditelj:

Prof.dr.sc Hrvoje Banfić

Nakon preseljenja laboratorija u zgradu Hrvatskog instituta za istraživanje mozga nastavili smo s istraživanjem inozitol lipidnog signaliziranja u staničnoj jezgri. U modelu kompenzacijskog rasta jetre pokazali smo da nakon parcijalne hepatektomije dolazi do porasta fosfatidil-inozitol 3-fosfata u jezgri zbog aktivacije fosfoinozitol 3-kinaze C2 bete (1) koja se nalazi u jezgrinom matriksu (2) i koja se aktivira cijepanjem enzima pomoću calpaina. Nadalje pokazali smo da u C2 domeni enzima postoji nuklearni lokalizacijski signal koji nužan za lokalizaciju enzima u staničnoj jezgri (3). U stanicama koje sinkrono prolaze kroz stanični ciklus enzym se aktivira tijekom G2/M faze staničnog ciklusa (4), dok diferencijacija stanica s pomoću sve-trans retinoične kiseline aktivira enzym putem tirozinske fosforilacije (5).

Također smo proučavali nazočnost i mehanizme aktivacije fosfolipaze C (PLC) u staničnoj jezgri. U modelu kompenzacijskog rasta jetre pokazali smo da su u jezgri nazočna tri izooblika. PLC-b1b i PLC-g1 nalaze se u jezgrinom matriksu, dok je izooblik PLC-d1 nazočan u kromatinu (6). U HL-60 stanicama koje sinkrono prolaze kroz stanični ciklus enzym se aktivira na početku G1 faze, potom na kraju G1 faze, te konačno tijekom G2/M faze staničnog ciklusa. Uvijek se radi o PLC-b1b izoobliku koji se aktivira fosforilacijom enzima na serinskom ostatku ato je posredovano MEK kinazom (7, 8). S obzirom da se prilikom izolacije jezgara rabe deterenti pa nije moguće u jezgrama određivati inozitolske fosfate zadnjih nekoliko godina počeli smo studirati njihov metabolizam u modelu pupajućeg kvasca *Saccharomyces cerevisiae*, jer je u kvascu mehanizam inozitolskog signaliziranja sličan onom u staničnim jezgrama (9). Inozitolski fosfati i pirofosfati su drugi glasnici koji nastaju postupnom fosforilacijom iz inozitol-1,4,5-trifosfata. Brojni radovi ukazuju na njihovu ulogu u regulaciji različitih staničnih procesa u eukariota, ali mnogi detalji su slabo poznati. Naaa nedavna studija dokazala je genetsku, metaboličku i biokemijsku vezu da sinteza inozitolskih pirofosfata putem aktivacije PLC i enzima odgovornog za stvaranje inozitolskih pirofosfata (Kcs-1) igra važnu ulogu u signalnom slijedu neophodnom za progresiju staničnog ciklusa u kvascu sinkroniziranom s pomoću alfa-čimbenika (10). Međutim, nepoznato je koji je od inozitolskih pirofosfata odgovoran za taj učinak, te je isto tako nepoznato koja je veza izme u porasta inozitolskih pirofosfata putem aktivacije

Division for electron microscopy (Dinko Mitrečić)

Division for biochemistry and molecular biology (Hrvoje Banfić)

Laboratory for second messengers (Hrvoje Banfić)

Head:

Professor Hrvoje Banfić

After we have moved laboratory in the building of Croatian Institute for Brain Research we have continue to investigate mechanisms of inositol lipid signaling in the cell nuclei. In the model of compensatory liver hypertrophy we have shown that following partial hepatectomy there is increase in phosphatidylinositol 3-phosphate level in the liver nuclei as consequence of phosphoinositide 3-kinase C2beta activation (1) which is localized in the nuclear matrix (2) and is activated due to enzyme cleavage by calpain. Furthermore, we have shown that C2 domain of the enzyme contains nuclear localization signal which is crucial for nuclear localization of the enzyme (3). In synchronized cells the enzyme is activated during G2/M phase of the cell cycle (4), while in cells which are differentiated by all-trans-retinoic acid enzyme is activated via tyrosine phosphorylation (5).

Also we have investigated presence and mechanisms of activation of nuclear phospholipase C (PLC). In the model of compensatory liver growth we have shown that nuclei contains three isoforms of PLC. PLC-b1b and PLC-g1 are localized in the nuclear matrix while PLC-d1 isoform is localized in the chromatin (6). In synchronized HL-60 cells the enzyme is activated at the beginning of G1 phase, then in the late G1 and finally during G/M phase of the cell cycle. The isoform which is activated is PLC-b1b isoform and activation is due to serine phosphorylation caused by MEK kinase (7, 8). Because detergents are used during nuclei isolation and therefore inositol phosphate determination is impossible in the nuclei, in the last couple of years we have started to study inositol phosphate metabolism in budding yeast *Saccharomyces cerevisiae*, since in yeast inositol lipid signaling is similar to signaling in the cell nuclei (9). Inositol phosphates and pyrophosphates are second messengers generated by the sequential phosphorylation of inositol 1,4,5-trisphosphate (InsP3). Several recent studies pointed to their role in the regulation of different cellular processes in eukaryotes, yet in many instances direct mechanistic roles remain elusive. Our recent study provided genetic, metabolic and biochemical evidence that synthesis of inositol pyrophosphates through activation of PLC and Kcs-1 play an important role in the signaling response required for cell cycle progression after mating pheromone arrest in the budding yeast (10). However, it is still uncertain which of the inositol pyrophosphates increased is/are responsible for Kcs-1-mediated effects, and it is unclear what might be the

enzima Kcs-1 i progresije stanica kvasca kroz S fazu staničnog ciklusa. Cilj budućih istraživanja je razjasniti mehanizme putem kojih inozitolski pirofosfati reguliraju stanični ciklus. Uporabit ćemo niz delecijских mutanti kvasca kako bi:

- a) pokazali koji je od inozitolskih pirofosfata odgovoran za prolaz stanica kroz S fazu staničnog ciklusa,
- b) testirali mogućnost da inozitolski pirofosfati koji se stvaraju u S fazi staničnog ciklusa reguliraju duljinu telomera,
- c) testirali mogućnost da je porast inozitolskih pirofosfata u stanicama sinkroniziranim s pomoću alfa-čimbenika odgovoran za pirofosforilaciju staničnih bjelančevina i/ili njihov izražaj odnosno modifikaciju i
- d) odredili promjene staničnog metabolizma u alfa-čimbenikom sinkroniziranim stanicama, te ih usporedili s promjenom razine inozitolskih pirofosfata.

possible link between the Kcs-1-mediated increase in the level of pyrophosphates and the progression of yeast cells through the S phase of the cell cycle. The aim of the future research will be to define the mechanism of inositol pyrophosphates-mediated regulation of cell cycle progression. We will use a set of yeasts deletion mutants to define a) the particular pyrophosphate responsible for S phase-associated effects, b) to test for the possibility that inositol pyrophosphates generated during S phase progression regulate telomere length, c) to test the possibility that the increase in the level of pyrophosphates in alpha-factor synchronized cells is associated with an increase in pyrophosphorylation of the proteins and/or protein expression or modification, and d) to determine the changes in metabolism in alpha-factor synchronized cells and to correlate them with the changes in the level of inositol pyrophosphates.

Odabrane publikacije Selected publications:

1. A. Sindić, A. Aleksandrova, A.P. Fields, S. Volinia and H. Banfić: Presence and activation of nuclear phosphoinositide 3-kinase C2b during the compensatory liver growth. *J. Biol. Chem.* 276: 17754-17761, 2001.
2. A. Sindić, V. Crljen, K. Matković, V. Lukinović-Škudar, D. Višnjić and H. Banfić: Activation of phosphoinositide 3-kinase C2b in the nuclear matrix during compensatory liver growth. *Adv. Enzyme Regul.* 46: 280-287, 2006.
3. H. Banfić, D. Višnjić, N. Miše, S. Balakrishnan, S. Deplano, Y.E. Korchev and J. Domin: Epidermal growth factor stimulates translocation of the class II phosphoinositide 3-kinase PI3K-C2-beta to the nucleus. *Biochem. J.* 422: 53-60, 2009.
4. D. Višnjić, J. Čurić, V. Crljen, D. Batinić, S. Volinia and H. Banfić: Nuclear phosphoinositide 3-kinase C2b activation during G2/M phase of the cell cycle in HL-60 cells. *Biochim. Biophys. Acta* 1631: 61-71, 2003.
5. D. Višnjić, V. Crljen, J. Čurić, D. Batinić, S. Volinia and H. Banfić: The activation of nuclear phosphoinositide 3-kinase C2b in all-trans-retinoic acid-differentiated HL-60 cells. *FEBS Lett.* 529: 268-274, 2002.
6. V. Crljen, D. Višnjić and H. Banfić: Presence of different phospholipase C isoforms in the nucleus and their activation during compensatory liver growth. *FEBS Lett.* 571: 35-42, 2004.
7. V. Lukinović-Škudar, L. Đonlagić, H. Banfić and D. Višnjić: Nuclear phospholipase C-b 1b activation during G2/M and late G1 phase in nocodazole synchronized HL-60 cells. *Biochim. Biophys. Acta*, 1733: 148-156, 2005.
8. V. Lukinović-Škudar, K. Matković, H. Banfić and D. Višnjić: Two waves of the nuclear phospholipase C activity in serum-stimulated HL-60 cells during G phase of the cell cycle. *Biochim. Biophys. Acta* 1771: 514-521, 2007.
9. D. Višnjić and H. Banfić: Nuclear phospholipid signaling: phosphatidylinositol-specific phospholipase C and phosphoinositide 3-kinase. *Pflugers Arch.* 455: 19-30, 2007.
10. H. Banfić, A. Bedalov, J. York and D. Višnjić: Inositol pyrophosphates modulate S phase progression after pheromone-induced arrest in *Saccharomyces cerevisiae*. *J. Biol. Chem.* 288: 1717-1725, 2013.

**Laboratorij za radioaktivne nuklide
(Vladiana Crljen)**

Voditeljica:

Doc. dr. sc. Vladiana Crljen

Članovi:

Prof. dr. sc. Hrvoje Banfić

Marijana Andrijašević, laboratorijski tehničar

Naziv projekta: Inozitol lipidno signaliziranje u staničnim jezgrama

U laboratoriju se upotrebom radioaktivnih nuklida obilježavaju inozitol fosfati čija razina se mijenja tijekom staničnog ciklusa kao posljedica aktivacije fosfolipaza kako na staničnoj membrani tako i u jezgri. Radioaktivno obilježeni inozitol fosfati se upotrebom HPLC-a razdvajaju i njihova prisutnost određuje pomoću scintilacijskog brojača. Članovi laboratorija imaju iskustvo od dvadeset godina u radu s radioaktivnim nuklidima.

Odabrane publikacije / Selected publications:

1. Banfić H, Višnjić D, Mise N, Balakrishnan S, Deplano S, Korochev YE, Domin J. Epidermal growth factor stimulates translocation of the class II phosphoinositide 3-kinase PI3K-C2beta to the nucleus. *Biochem J.* 2009; 422(1):53-60.
2. Sindić A, Crljen V, Matković K, Lukinović-Škudar V, Višnjić D, Banfić H. Activation of phosphoinositide 3-kinase C2 beta in the nuclear matrix during compensatory liver growth. *Adv Enzyme Regul.* 2006; 46:280-287.
3. Crljen V, Višnjić D, Banfić H. Presence of different phospholipase C isoforms in the nucleus and their activation during compensatory liver growth. *FEBS Lett* 2004; 571(1-3):35-42.

Laboratory for radioactive nuclides (Vladiana Crljen)

Head:

Assistant Professor Vladiana Crljen

Associates:

Professor Hrvoje Banfić

Marijana Andrijašević, lab. tech.

Project title: Inositol lipid signalling in cellular nucleus.

In our laboratory we are using radioactive labelled inositol phosphate and measure its levels during the cell cycle. The concentration of inositol phosphate changes during the cell cycle as an effect of the activation of phospholipases in the cell membrane and in the nucleus. Radioactive inositol phosphate is separated using HPLC, and its presence is detected using scintillating counter. The laboratory members have more than 20 years of experience with radioactive nuclides.

Laboratorij za stanične kulture i kulture tkiva (Dora Višnjić)**Voditelj:**

prof.dr.sc. Dora Višnjić
Zavod za fiziologiju i imunologiju
Hrvatski institut za istraživanje mozga
Medicinski fakultet Sveučilišta u Zagrebu
Kontakt: visnjic@mef.hr

Suradnici:

prof.dr.sc. Hrvoje Banfić
doc.dr.sc. Vesna Lukinović-Škudar
doc.dr.sc. Vladiana Crljen
Hrvoje Lalić, dr.med.
Vilma Dembitz, dr.med.
Dunja Tanković, laboratorijski tehničar

Istraživački interes ovog laboratorija je proučavanje signalnih putova tijekom proliferacije i diferencijacije leukemijskih staničnih linija.

Laboratory for cell and tissue cultures (Dora Višnjić)**Head:**

Professor Dora Višnjić,
Department of physiology and immunology
Croatian Institute for Brain Research
School of Medicine University of Zagreb
Contact: visnjic@mef.hr

Associates:

Professor Hrvoje Banfić
Assistant Professor Vesna Lukinović-Škudar
Assistant Professor Vladiana Crljen
Hrvoje Lalić, MD, PhD
Vilma Dembitz, MD
Dunja Tanković, lab. tech.

Scientific scope of this laboratory is the study of signalling pathways during proliferation and differentiation of leukemic cells.

Odabrane publikacije / Selected publications:

- Lalic H, Dembitz V, Lukinovic-Skudar V, Banfic H, Visnjic D. 5-Aminoimidazole-4-carboxamide ribonucleoside induces differentiation of acute myeloid leukemia cells. *Leuk Lymphoma*. 2014 doi:10.3109/10428194.2013.876633
- Banfic H, Bedalov A, York JD, Visnjic D. Inositol pyrophosphates modulate S phase progression after pheromone-induced arrest in *Saccharomyces cerevisiae*. *J Biol Chem* 288:1717-1725, 2013.
- Lalic H, Lukinovic-Skudar V, Banfic H, Visnjic D. Rapamycin enhances dimethyl sulfoxide-mediated growth arrest in human myelogenous leukemia cells. *Leuk Lymphoma* 53:2253-2261, 2012.
- Mise J, Dembitz V, Banfic H, Visnjic D. Combined Inhibition of PI3K and mTOR Exerts Synergistic Antiproliferative Effect, but Diminishes Differentiative Properties of Rapamycin in Acute Myeloid Leukemia Cells. *Pathol Oncol Res*. 17:645-656, 2011.
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- Banfic H, Visnjic D, Mise N, Balakrishnan S, Deplano S, Korchev YE, Domin J. Epidermal growth factor stimulates translocation of the class II phosphoinositide 3-kinase PI3K-C2beta to the nucleus. *Biochem J*. 422:53-60, 2009.
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- Lukinovic-Skudar V, Matkovic K, Banfic H, Visnjic D. Two waves of the nuclear phospholipase C activity in serum-stimulated HL-60 cells during G₁ phase of the cell cycle. *Biochim Biophys Acta*. 1771:514-21, 2007.
- Matkovic K, Brugnoli F, Bertagnolo V, Banfic H, Visnjic D. The role of the nuclear Akt activation and Akt inhibitors in all-trans-retinoic acid-differentiated HL-60 cells. *Leukemia*. 20:941-51, 2006.
- Lukinovic-Skudar V, Donlagic L, Banfic H, Visnjic D. Nuclear phospholipase C-β_{1b} activation during G₂/M and late G₁ phase in nocodazole-synchronized HL-60 cells. *Biochim Biophys Acta*. 1733:148-56, 2005.
- Visnjic D, Kalajzic Z, Rowe DW, Katavic V, Lorenzo J, Aguila HL. Hematopoiesis is severely altered in mice with an induced osteoblast deficiency. *Blood*. 103:3258-64, 2004.
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- Visnjic D, Crljen V, Curic J, Batinic D, Volinia S, Banfic H. The activation of nuclear phosphoinositide 3-kinase C2β in all-trans-retinoic acid-differentiated HL-60 cells. *FEBS Lett*. 529:268-74, 2002.
- Visnjic D, Kalajzic I, Gronowicz G, Aguila HL, Clark SH, Lichtler AC, Rowe DW. Conditional ablation of the osteoblast lineage in Col2.3Δtk transgenic mice. *J Bone Miner Res*. 16:2222-31, 2001.
- Dacic S, Kalajzic I, Visnjic D, Lichtler AC, Rowe DW. Col1a1-driven transgenic markers of osteoblast lineage progression. *J Bone Miner Res*. 16:1228-36, 2001.
- Visnjic D, Batinic D, Banfic H. Different roles of protein kinase C α and δ isoforms in the regulation of neutral sphingomyelinase activity in HL-60 cells. *Biochem J*. 344:921-8, 1999.
- Visnjic D, Batinic D, Banfic H. Arachidonic acid mediates interferon-gamma-induced sphingomyelin hydrolysis and monocytic marker expression in HL-60 cell line. *Blood*. 89:81-91, 1997.
- Visnjic D, Batinic D, Lasić Z, Knotek M, Marusić M, Banfić H. Phorbol 12-myristate 13-acetate-mediated signalling in murine bone marrow cells. *Biochem J*. 310:163-70, 1995.

**Laboratorij za molekularnu
neurobiologiju i neurokemiju (Svjetlana
Kalanj Bognar)**

Voditeljica:

prof. dr. sc. Svjetlana Kalanj Bognar, dr. med.

Istraživački tim:

dr. sc. Kristina Mlinac (postdoktorant),
Katarina Ilić, dr. med. (doktorand)

Suradnici:

dr. sc. Željka Vukelić,
dr. sc. Dragana Fabris,
dr. sc. Marija Heffer, dr. med. (Medicinski fakultet
Osijek),
dr. sc. Koraljka Bačić Baronica,
dr. med. (neurolog, Odjel neurologije, Klinička
bolnica "Sveti Duh", Zagreb)

Dugoročni ciljevi naše grupe su istražiti:

- ulogu membranskih lipida u razvoju središnjeg živčanog sustava i u neurodegenerativnim procesima.
- utjecaj promjena sastava i strukture lipida na ekspresiju i specifičnu funkciju membranskih proteina.
- ulogu specifičnih interakcija između membranskih lipida i proteina u organizaciji sinaptičke membrane.

Područje za koje smo posebno zainteresirani su membranski glikosfingolipidi/gangliozidi kojih se u izobilju mogu naći u središnjem živčanom sustavu sisavaca. Gangliozidi nisu ravnomjerno raspoređeni kroz staničnu membranu neurona, već koncentrirani u lipidnim nakupinama unutar membrane aksona gdje su uključeni u specifične interakcije s molekulama ekstracelularnog matriksa. Do sada je u životinjskim stanicama pokazano da gangliozidi imaju brojne uloge: uključeni su u proliferaciju, diferencijaciju stanica, apoptozu, prijenos signala, adheziju stanica i međustaničnu komunikaciju. Gangliozidi u središnjem živčanom sustavu omogućuju odgovarajuće interakcije aksona i glija stanica, te također sudjeluju u molekularnim mehanizmima učenja i pamćenja. Rezultati naših istraživanja dosad su pokazali određene promjene u količini i sastavu gangliozida u moždanom tkivu bolesnika s Alzheimerovom bolešću, kao i povećanu aktivnost lizosomalnih enzima uključenih u razgradnju sfingolipida u ekstraneuralnim stanicama (leukociti, kožni fibroblasti) u pacijenata s Alzheimerovom bolešću. Naši rezultati, zajedno s rezultatima ostalih skupina, potvrđuju da su promjene u koncentraciji, sastavu i metabolizmu, a posebno razgradnja glikosfingolipida, doprinosi složenoj patogenezi neurodegeneracije.

Naša posljednja istraživanja usmjerena su na analizu učinka promjene u sastavu i strukturi membranskih lipida na ekspresiju i specifičnu funkciju membranskih proteina u središnjem živčanom sustavu sisavaca. Lipidni okoliš i interakcije lipida i proteina unutar membrane su od ključne važnosti

**Laboratory for molecular neurobiology
and neurochemistry (Svjetlana Kalanj
Bognar)**

Head:

Associate Professor Svjetlana Kalanj Bognar; MD, PhD

Team:

Kristina Mlinac, PhD (postdoctoral researcher);
Katarina Ilić, MD (PhD student)

Collaborators:

Željka Vukelić, PhD;
Dragana Fabris, PhD;
Marija Heffer, MD, PhD (School of Medicine
University of Osijek),
Koraljka Bačić Baronica, MD, PhD (neurologist;
Department of Neurology, Clinical Hospital "Sveti
Duh", Zagreb)

Long-term interests of our group are to investigate:

- The role of membrane lipids in the central nervous system development and neurodegeneration
- The influence of changes in lipid composition and structure on the expression and specific functions of membrane proteins
- The role of specific interactions between membrane lipids and membrane proteins in the organization of synaptic membrane.

We are particularly interested in membrane glycosphingolipids/gangliosides which are especially abundant in mammalian central nervous system. Gangliosides are not evenly distributed throughout the membrane, but rather more concentrated in lipid rafts within axonal membranes where they engage in specific interactions with molecules in the extracellular matrix. Gangliosides have numerous roles in animal cells: they are involved in proliferation, differentiation, apoptosis, signal transduction, cell adhesion and intercellular communication. Gangliosides in the nervous system enable proper axon-glia interactions, as well as participate in the molecular mechanism of learning and memory. The results of our studies so far showed the specific changes in quantity and composition of gangliosides in brain tissue of patients with Alzheimer's disease, as well as increased activity of lysosomal enzymes involved in the breakdown of sphingolipids in extraneural cells (leukocytes, skin fibroblasts) of patients with Alzheimer's disease. Our results, in conjunction with the results of other groups, confirm that changes in concentration, composition and metabolism, especially degradation of glycosphingolipids, contribute to complex pathogenesis of neurodegeneration.

Our recent research is focused on the analysis of the effect of changes in membrane lipid composition and structure on the expression and specific functions of membrane proteins in mammalian central nervous system. Lipid environment and lipid-protein interactions within the membrane are crucial

za pravilno pozicioniranje i funkciju membranskih proteina te stoga iznimno važni za organizaciju sinaptičkih membrana. Naši rezultati pokazuju da su u moždanom tkivu miša s promijenjenom biosintezom proteina (mišji model *knocked out* gena za diferencijaciju enzima za biosintezu gangliozida) prisutne različite modifikacije strukture gangliozida koje još nisu opisane u tkivu miša divljeg tipa, a mogu ulaziti u interakcije s drugim membranskim molekulama. Također smo uočili značajne promjene u ekspresiji gena i proteina na istim mišjim modelima. Promjene u ekspresiji su najistaknutije za gene koji kodiraju membranske proteine i koji su uključeni u interakcije s drugim proteinima. Od niza gena s promijenjenom ekspresijom posebno nas je zainteresirao gen za neuroplastin zbog poznatih uloga neuroplastina u živčanom sustavu.

Neuroplastin je transmembranski protein koji pripada staničnim adhezijskim molekulama i uključen je u sinaptičku plastičnost te modulaciju neuritogeneze. Opisana je vrlo specifična raspodjela neuroplastina u središnjem živčanom sustavu, osobito u mozgu glodavaca. Međutim, lokalizacija i uloga neuroplastina u ljudskom mozgu nije sustavno istražena. Stoga je jedan od ciljeva naše grupe sistematično ispitati ekspresiju neuroplastina u ljudskom mozgu. Osim toga, cilj nam je potvrditi našu hipotezu na temelju preliminarnih rezultata koji pokazuju da je neuroplastin uključen u sinaptičku plastičnost tijekom kritičnih faza razvoja ljudskog mozga kao i u neurodegenerativnim procesima.

Projekti:

1. Uloga membranskih lipida u moždanom razvoju, starenju i neurodegeneraciji (MZOS, 2007.-2014., PI: S. Kalanj Bognar)
2. Neuroplastin i gangliozidi u organizaciji sinaptičke membrane (Hrvatsko-Njemački bilateralni projekt, 2014., PI: K. Mlinac)
3. Ekspresija neuroplastina u ljudskom hipokampusu (projekt financiran od strane Sveučilišta u Zagrebu, 2014., PI: S. Kalanj Bognar)

Međunarodna suradnja:

Leibniz Institute for Neurobiology, Magdeburg, Germany - dr. Rodrigo Herrera Molina, dr. Karl-Heinz Smalla, dr. Dirk Montag

for proper positioning and function of membrane proteins and therefore exceptionally important for the organization of synaptic membranes. Our results show that in brain tissue of mice with altered ganglioside biosynthesis (mouse models with knocked out genes for different ganglioside biosynthetic enzymes) different modifications of ganglioside structures are present not yet described in tissue of wild-type mice which can influence the interactions with other membrane molecules. We also observed significant changes in gene and protein expression in the same mouse models, the changes in expression being most prominent for genes coding for membrane proteins involved in interactions with other proteins. From the array of genes with differential expression, we became especially interested in neuroplastin due to known roles of neuroplastin in the nervous system.

Neuroplastin is a transmembrane protein belonging to cell adhesion molecules and it is involved in synaptic plasticity and modulation of neuritogenesis. A very specific distribution of neuroplastin in the central nervous system has been described, especially in rodent brain. However, the localization and roles of neuroplastin in human brain have not been systematically investigated. Therefore, one of the goals of our group is to systematically examine the expression of neuroplastin in human brain. Additionally, we aim to confirm our hypothesis based on preliminary results that neuroplastin is involved in synaptic plasticity in critical phases in human brain development as well as in neurodegeneration.

Projects:

1. The role of membrane lipids in brain development, aging and neurodegeneration (MZOS, 2007.-2014., PI: S. Kalanj Bognar)
2. Neuroplastin and gangliosides in organization of synaptic membrane (Croatian-German bilateral project, 2014., PI: K. Mlinac)
3. Expression of neuroplastin in human hippocampus (project financed by the University of Zagreb, 2014., PI: S. Kalanj Bognar)

International collaboration:

Leibniz Institute for Neurobiology, Magdeburg, Germany - dr. Rodrigo Herrera Molina, dr. Karl-Heinz Smalla, dr. Dirk Montag

Izabrane publikacije / Selected publications:

1. Bačić Baronica K, Mlinac K et al: [Progression of multiple sclerosis is associated with gender differences in glutathione S-transferase P1 detoxification pathway](#). Acta Neurobiol Exp, 74(3):257-265, 2014.
2. Mlinac K, Fabris D, Vukelić Ž, Rožman M, Heffer M, Kalanj Bognar S: [Structural analysis of brain ganglioside acetylation patterns in mice with altered ganglioside biosynthesis](#). Carbohydrate Res, 382:1-8, 2013.
3. Mlinac K, Jovanov Milošević N, Heffer M, Smalla KH, Schnaar RL, Kalanj Bognar S: [Neuroplastin Expression in the Hippocampus of Mice Lacking Complex Gangliosides](#). J Mol Neurosci. 48(1):161-166, 2012.
4. Mlinac Kristina, Fon Tacer K, Heffer M, Rozman D, Kalanj Bognar S: [Cholesterogenic genes expression in brain and liver of ganglioside-deficient mice](#). Molecular and cellular biochemistry, 369(1/2):127-133, 2012.
5. Mlinac K and Kalanj Bognar S: Role of gangliosides in brain aging and neurodegeneration. Translational Neuroscience, 1(4):300-307, 2010.
6. [Vukelić Ž, Bognar SK, Froesch M, et al](#): Human gliosarcoma-associated ganglioside composition is complex and distinctive as evidenced by high-performance mass spectrometric determination and structural characterization. Glycobiology 17(5):504-15, 2007.
7. Kalanj Bognar S: Ganglioside catabolism is altered in fibroblasts and leukocytes from Alzheimer's disease patients. Neurobiol Aging. 27(9):1354-6, Sep 2006.
8. Kalanj Bognar S et al: Leukocyte Lysosomal Enzymes in Alzheimer's Disease and Down's Syndrome. J Gerontol A Biol Sci Med Sci 57A (1):B16-B21, 2002.
9. Vukelić Ž and Kalanj Bognar S: Cell density-dependent changes of glycosphingolipid biosynthesis in cultured human skin fibroblasts. Glycoconjugate J, 18:429-437, 2001
10. Kračun I, Kalanj S, Talan-Hranilović J, Čosović Č: Cortical distribution of gangliosides in Alzheimer's disease. Neurochem Int 20, 3:433-438, 1992.

**Laboratorij za neuroonkologiju
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Voditelj:

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School of medicine, University of Zagreb, Hrvatska

Prof.dr.sc. Denys Neville Wheatley

Director of BioMedES

Studenti:

Leon Marković, MF

Petar-Krešimir Okštajner, MF

Anamarija Varošaneć, MF

**Laboratory for neurooncology
(Nives Pećina Šlaus)**

Head:

Associate Professor Nives Pećina-Šlaus

School of Medicine University of Zagreb;
Croatian Institute for Brain Research;
Šalata 12, 10 000 Zagreb,
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Team members

Ljiljana Šerman, MD, PhD, Associate professor
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sity of Zagreb,

Reno Hrašćan, PhD, Associate professor
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Food Technology and Biotechnology, University of
Zagreb,

Professor Vesna Kušec

Clinical department for laboratory diagnostics
University Clinical Hospital Zagreb, School of Med-
icine, University of Zagreb

Tamara Nikuševa Martić, PhD, Assistant professor
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Davor Tomas, MD, PhD, Assistant professor
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ty Hospital "Sisters of Charity"

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Department of neurosurgery University Clinical
Hospital Centre Zagreb, School of Medicine, Uni-
versity of Zagreb

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Petar-Krešimir Okštajner, MF

Anamarija Varošaneć, MF

Monika Logara, PMF

Mateja Bačić, PMF

Josip Skoko, PMF

Marina Morić, PMF

The Laboratory for Neurooncology is studying the molecular basis of human brain tumors. The research focuses on genetic abnormalities in brain tumors with emphasis on genes that are key components of the wnt signaling pathway. The labora-

Monika Logara, PMF
Mateja Bačić, PMF
Josip Skoko, PMF
Marina Morić, PMF

Laboratorij za neuroonkologiju bavi se istraživanjima molekularnih osnova humanih tumora mozga. Znanstvena istraživanja fokusirana su na genetičke promjene u tumorskom tkivu središnjeg živčanog sustava s naglaskom na gene i proteine sudionike signalnog puta wnt. Laboratorij je osnovan 2004. godine, te su se u laboratoriju provodili slijedeći znanstveni projekti: 2002-2005 Ministarstvo znanosti i tehnologije RH, "Uloga gena signalnog puta wnt u neoplazijama čovjeka" (0108 215), 2007-2013 MZOŠ, projekt "Uloga signalnog puta wnt u tumorigenezi i embriogenezi mozga" (108-1081870-1905), 2013-2014. Sveučilište u Zagrebu, Potpora istraživanju, „Signalni put Wnt od membrane do jezgre tumorskih stanica mozga“ (1.2.1.19). Trenutno se provode istraživanja u sklopu projekta Hrvatske zaklade za znanost „Uloga signalnog puta Wnt u epitelno-mezenhimskej tranziciji“ (WNT4EMT6625). Put prijenosa signala wnt, nazvan po sekretornim signalnim proteinima wnt, često je promijenjen u tumorigenezi, a od izuzetnog je značaja u normalnom embrionalnom razvoju čovjeka, pa tako i ljudskog mozga. Najveći interes ovog laboratorija leži upravo u istraživanjima uloge gena Dishevelled, TCF/LEF, APC, beta- katenina, E-kadherina i aksina u tumorima mozga i procesu epitelno-mezenhimske transzicije. Cilj je razumijevanje molekularnih mehanizama koji upravljaju nastankom i progresijom različitih histološki tipova tumoramozga. Laboratorij također uključuje rad na prikupljanju materijala tumorskog i zdravog tkiva za potrebe Banke tumora mozga u suradnji sa Kliničkim bolničkim centrima Zagreb i Sestre milosrdnice. Treba spomenuti i edukativnu dimenziju laboratorija i banke kao vrijedan izvor ideja i materijal za izradu znanstvenih diplomskih radova, magisterija i doktorata. U laboratoriju je do sada izrađeno ukupno 15 kvalifikacijskih radova. Voditeljica laboratorija diplomirala je 1990. godine, magistrirala 1992. na Prirodoslovno-matematičkom fakultetu Sveučilišta u Zagrebu, a doktorirala 1998. na Medicinskom fakultetu Sveučilišta u Zagrebu. Usavršavala se na Cold Spring Harbor Laboratorija, SAD i Georgetown University u Washingtonu D.C. U znanstvenog savjetnika izabrana je 2005, 2007. u izvanrednog profesora, a 2012. godine u redovitog profesora na Zavodu za biologiju, Medicinskog fakulteta Sveučilišta u Zagrebu. Područja kojima se bavi su genetika karcinoma, put prijenosa signala wnt, tumorigeneza, tumor supresorski geni, onkogeni, genetičke osnove tumora mozga čovjeka, RNA izrezivanje, sinteza oligonukleotida, metode molekularne biologije. Vodila je ukupno 5 znanstvenih projekata i sudjeluje na međunarodnom projektu FP7-REGPOT GlowBrain. Istraživanja u kojima je sudjelovala rezultirala su s ukupno preko 100 publikacija od čega 51 znanstvenih radova objavljenih u časopisima s međunarodnom

tory was founded in 2004, and following research projects were conducted in the laboratory: 2002-2005 Ministry of Science and Technology, "The role of the wnt signaling pathway genes in human neoplasms" (0108 215), 2007- 2013 Ministry of Science, entitled "The role of the wnt signaling pathway in tumorigenesis and embryogenesis of the brain "(108-1081870-1905), 2013-2014. University of Zagreb, support for research, "Wnt signaling pathway from the membrane to the nucleus of tumor cells of the brain" (1.2.1.19). We are currently conducting research project funded by Croatian Science Foundation "The role of the Wnt signaling pathway in epithelial to mesenchymal transition" (WNT4EMT6625). Wnt signaling, named after the secretory signaling proteins wnt, is often changed in tumorigenesis, and is also critical in human brain developmental processes. Our particular interest lies in studying changes in Dishevelled, TCF/LEF, APC, beta-catenin and E-cadherin and Axin genes in order to understand molecular and genetic mechanisms that govern the formation and progression of different types of brain tumors and in the process of epithelial to mesenchymal transition. The goal is to understand the molecular mechanisms that govern the initiation and progression of different histological types of brain tumors. The Laboratory of Neurooncology is also involved in the formation of the bank of brain tumor tissues. In collaboration with the Clinical Hospital Centers Zagreb and Sisters of Mercy we collected and stored an extensive Brain tumor bank resource and encourage young scientists and students to research in neurooncology. We should mention the educational dimension of laboratory and Brain tumor bank as a valuable source of ideas and materials to produce graduate, master and PhD thesis. The lab has so far produced a total of 15 theses. Nives Pecina-Slaus Head of the Laboratory is full professor at the department of biology Medical School University of Zagreb. She has received her B.S. in 1990. her M.S. in 1992. from the University of Zagreb, Faculty of Math and Sciences, and her Ph.D. in the field of molecular oncology in 1998. from Medical School University of Zagreb. She was trained at Cold Spring Harbor Laboratory, New York, and at Georgetown University, Washington DC, USA. She was granted as principal investigator 5 scientific projects. She is a collaborator on the international project FP7-REGPOT GlowBrain. Her research has led to publication of more than 100 publications – 51 scientific papers, a book, abstracts, 7 book chapters and professional papers. She was cited 385 times in Web of Science and 417 in Scopus. Her main fields of research are cancer genetics, Wnt signaling pathway, brain tumorigenesis, tumor suppressor genes, oncogenes, genetic profiles of brain tumors. She acts as a reviewer for many scientific peer-reviewed journals and is a member on editorial boards of *Frontiers in Bioscience*, *Acta Clinica Croatica*, *Cancer Cell International*, *Croatian Medical Journal*. She teaches Medical biology and was mentor on numerous theses (13 theses) and mentor on four papers re-

recenzijom. Sudjelovala je na 43 znanstvena skupa od čega 8 puta s pozvanim predavanjima. Također je objavila 4 poglavlja u inozemnim znanstvenim monografijama. Citirana je do sada ukupno 385 puta u Web of Science i 417 u Scopusu. Mentorica je na ukupno 13 obranjenih radova, 3 doktorata, 3 magisterija, 7 diplomskih i 5 studentskih radova nagrađenih Rektorovom i Dekanovom nagradom. Članica je European Society of Human Genetics, Hrvatskog biološkog društva, Hrvatskog društva za istraživanje raka, European Society for Cancer Research, Hrvatskog liječničkog zbora i Hrvatskog društva za neuroznanost. Recenzent je za MZOŠ, HAZU, Slovensku agenciju za znanost, Fonda za razvoj Sveučilišta, te brojnih međunarodnih časopisa. 2010. godine imenovana je urednicom časopisa *Frontiers in Bioscience*, časopisa *Cancer Cell International* i *Acta Clinica Croatica*, a 2011. članicom uredničkog odbora *Croatian Medical Journala*. Dobitnica je 4 znanstvene nagrade od kojih je jedna Državna nagrada za znanost.

warded by Rector's award. She was awarded four scientific awards, among which is National Science Award in 2011. She is a member of Croatian Society of Human Genetics, Croatian Medical Association, Croatian Biological Society, European Society for Human Genetics, European Association for Cancer Research, Croatian Society for Neuroscience. She acts as a reviewer for Ministry of Science, Education and Sports Croatia, for Slovenian Research Agency (ARRS) for National council for university education, many scientific peer-reviewed journals. She is a member on editorial boards of scientific journals *Frontiers in Bioscience*, *Acta Clinica Croatica*, *Cancer Cell International*, *Croatian Medical Journal* and *Journal of Cancer Science and Therapy*

Odabrane publikacije / Selected publications:

1. Pećina-Šlaus N, Majić Ž, Musani V, Zeljko M, Čupić H. Report on mutation in exon 15 of the APC gene in a case of brain metastasis. *J Neurooncol.* 97; 143-148; 2010.
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8. Pećina-Šlaus, N. Kafka, A. Tomas, M. Marković, L. Okštajner, P.K. Sukser, V. Krušlin, B. Wnt signaling transcription factors TCF-1 and LEF-1 are upregulated in malignant astrocytic brain tumors. *Histol Histopathol*, 29: 1557-1564, 2014.
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Odsjek za neurofiziologiju (Marijan Klarica)

Laboratorij za neurofiziologiju i „whole cell patch-clamp“ (Aleksandra Sindić)

Voditelj:

Prof.dr.sc. Aleksandra Sindić
Zavod za fiziologiju
Hrvatski institut za istraživanje mozga
asindic@mef.hr

Suradnici:

Dr.sc. Marina Dobrivojević
Nikola Habek, dr.med.

Naslov projekta: Povoljni učinci natriuretskih peptida u različitim patološkim zbivanjima

Natriuretski peptidi reguliraju krvni tlak i volumena te izlučivanje soli i vode. Članovi ove obitelji su atrijski natriuretski peptid (ANP), natriuretski peptid izoliran iz mozga (BNP), C-tip natriuretskog peptida (CNP) te urodilatin (URO) koji je bubrežna izoforma ANP. Njihova fiziološka uloga se većinom zasniva na aktivaciji receptora vezanih uz enzim guanilat ciklazu te posljedično porast unutarstanične koncentracije cGMP-a. ANP, BNP i URO su agonisti guanilat ciklaze (GC) -A (poznata i kao receptor za natriuretske peptide tip A, NPR-A) dok guanilat ciklaza (GC) - B (receptor za natriuretske peptide tip B, NPR-B) posjeduje veliku specifičnost za CNP. Svi navedeni natriuretski peptidi su agonisti za receptor tip C, poznat i kao receptor koji odstranjuje natriuretske peptide iz cirkulacije (clearance receptor) koji ne posjeduje guanilat ciklaznu aktivnost. Poznato je da natriuretski peptidi imaju povoljan učinak na razvoj edema nakon moždanog infarkta no mehanizam tog učinka je još uvijek nepoznat. Jedan od mogućih mehanizama je interakcija između natriuretskih peptida i bradikininskog (BK) signalnog puta. Da bismo ispitali ovu hipotezu koristili smo HEK293 stanice koje posjeduju sve potrebne dijelove signalnog sustava i za bradikinin i za natriuretske peptide. (rezultat nije prikazan).

Svi prikazani rezultati natriuretskih peptida na B2R-PLC-Ca²⁺ ovisan signalni sustav BK-a su dodatno potvrđeni mjerenjem unutarstanične koncentracije Ca²⁺. Iako je cijeli sustav za izvedbu ovih pokusa donirao Prof dr E Schlatter, University of Munster, Germany te je smješten na našoj ustanovi, ova mjerenja su radi nedostatka novca napravljena na PHARIS Biotec GmbH, Hannover, Germany. BK depolarizira HEK293 stanice (tablica 1.) aktivacijom bradikininskog receptora tipa 2 (B2R - Ca²⁺ signaling put) te kloridnih kanala ovisnih o Ca²⁺ (rezultati nisu prikazani). Učinak BK se može inhibirati svim natriuretskim peptidima koji su agonisti GC-A receptora te cGMP-om (Sl.1.) (aktivacijom protein kinaze G (sl 2)) dok CNP kao agonist GC-B nema učinak. Vežanje bradikinina za B2R receptor dovodi do aktivacije fosfolipaze C (PLC) (Sl 3.). Poznato je da PKG može inhibirati PLC te kada smo inhibirali PLC specifičnim inhibitorom U-73122 (10 μM), depolarizacija nastala djelovanjem BK je inhi-

Division for neurophysiology (Marijan Klarica)

Laboratory for neurophysiology and „whole cell patch-clamp“ (Aleksandra Sindić)

Project title: Effects of natriuretic peptides in physiological and pathological conditions in the brain

Natriuretic peptides regulate blood pressure-volume homeostasis, salt excretion and diuresis. Even they are showing physiological and pathophysiological effects in the brain their function is not well investigated. Members of the human natriuretic peptide family are the atrial natriuretic peptide (ANP), the brain natriuretic peptide (BNP), the C-type natriuretic peptide (CNP), urodilatin (URO - the kidney isoform of ANP), guanylin (GN) and uroguanylin (UGN). They exert their biological functions mainly through activation of guanylate cyclase receptors and subsequently, through an increase in intracellular cGMP. Guanylate cyclase (GC)-A selectively binds ANP, BNP and URO, the GC-B has a high affinity towards CNP while GN and UGN activates GC-C. Additional natriuretic peptide receptor type C (NPR-C) known as clearance receptor binds ANP, URO, BNP and CNP has no guanylate cyclase activity. The function of GC-A and B agonists are more investigated there is almost no research of GN and UGN in the brain. We investigate effects of natriuretic peptides on the primary culture of neurons and astrocytes (table 1.) and their signaling pathways.

Natriuretic peptides depolarized neurons similar to membrane permeable cGMP (8 Br cGMP) which is their well know second messenger. To definitely confirm that GCs are receptors for natriuretic peptides in neurons need further investigation. In astrocytes, ANP and in some cases URO (agonists of GC-A) as well as cGMP lead to cell hyperpolarization. However, natural agonists of GC-B (CNP) and GC-C (GN and UGN) depolarized astrocytes which are opposites of cGMP effects suggesting existence of GC independent signaling pathway.

In neurons all natriuretic peptides depolarized cells (dose dependence curve shown at figure 1). That depolarization was inhibited when BaCl₂, an inhibitor of K⁺ channels is used suggesting that natriuretic peptides as well as cGMP depolarized cells by inhibiting K⁺ channels (figure 2.).

Lab equipment:

- Set-up for electrophysiological experiments (NAPI) (includes air table, microscope. Amplifier, temperature regulator, AD/DA converter, computer with Tida software for patch-clamp measurements, patch clamp puller for pipette preparation.
- Additional equipment for patch-clamp measurements (donation by prof dr Eberhard Schlatter, University of Münster, Germany): WeKa Graph thermo printer, 2x patch-clamp amplifiers, one pulse generator with control units, pH-meter, spectrophotometer.

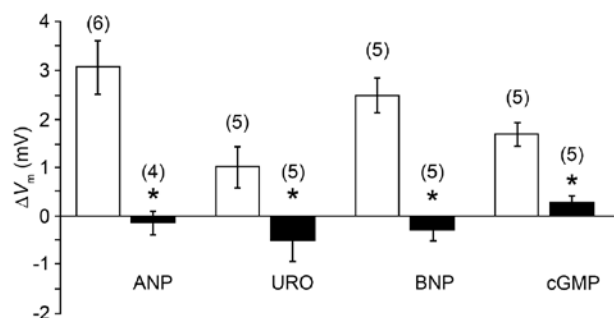
birana na isti način kako i djelovanjem natriuretski peptida, dovodeći do zaključka da je PLC protein od interesa u istraživanju interakcija između signalnog sustava natriuretskih peptida i bradikininu (rezultati nisu prikazani). Ovaj projekt pokazuje da natriuretski peptidi djelovanjem PKG mogu utjecati na PLC ovisan signalni sustav bradikininu te mogu djelovati kao prirodni inhibitori edema uzrokovanog bradikininom u raznim patološkim stanjima kao što su nasljedni angioedem te moždani udar.

Oprema u laboratoriju:

1. Jedan set up za elektrofiziološka istraživanja (NAPI) (uključuje stol na zračnim jastucima, mikroskop, amplifier, regulator temperature, AD/DA jedinica, kompjuter sa Tida software-om za patch-clamp mjerenja, patch clamp puller za izradu elektroda.
2. Ostala operma za elektrofiziološka istraživanja (donacija prof dr Eberhard Schlatter, University of Münster, Germany): WeKa Graph termo pisač, 2x patch-clamp amplifier-a, jedan puls generator s vanjskom jedinicom za upravljanje, pH-metar, spektrofotometar)
3. Vaga, eppendorf grijači blok te sve potrebno za western blotting, Microforge MF 900 za poliranje pipeta za patch-clamp – nabavljeno povratničkim projektom NZZ-a.

Objavljeni radovi u posljednje 3 godine / Papers published in the last 3 years:

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5. Sindić A, Dobrivojević M, Hirsch JR. *Natriuretic peptides in brain physiology. Translational Neuroscience*, 2(3); 246-251, 2011.
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- scale, Eppendorf thermal block and all equipment for western blotting, Microforge MF 900 for pipette polishing for patch-clamp – financed by the National Foundation for Science, Higher Education and Technological Development of the Republic of Croatia.

Figure 1

Effects of ANP, URO, BNP (10 nM each), and 8-Br-cGMP (100 μM) (white bars) were blocked by K⁺-channel inhibitor, 1 mM BaCl₂ (black bars). Results are presented as mean ± SEM. * indicates a statistically significant effect compared to control.

Slika 1

Učinci ANP, URO, BNP (10 nM svaki), i 8-Br-cGMP (100 μM) (bijeli stupići) su nestali djelovanjem inhibitora K⁺ kanala, 1 mM BaCl₂ (crni stupići). Rezultati su prikazani kao aritmetička sredina ± SEM * statistička značajnost učinka u odnosu na kontrolu.

**Laboratorij za neuropatofiziologiju
likvora (Marijan Klarica)**

Voditelj:

Prof.dr.sc. Marijan Klarica
Redoviti profesor farmakologije
Šalata 8, 10 000 Zagreb

Suradnici:

Dr.sc. Darko Orešković
Institut Ruđer Bošković
Dr.sc. Ivana Jurjević
Goran Ivkić, dr.med.

U laboratoriju se odvijaju istraživanja fiziologije i patofiziologije likvora i intrakranijskog tlaka.

U tijeku su sljedeći projekti:

Sudbina moždanih metabolita i lijekova u likvorskom sustavu

- Utvrđeno je da cerebralne kapilare djeluju kao glavni put za otklanjanje moždanih metabolita i anionskih lijekova putem aktivnog transporta
- Likvorski sustav je zatvoreni sustav koji komunicira s krvi uglavnom preko cerebralnih kapilara, ali ne u smislu cirkulacije i apsorpcije likvora u duralne venske sinuse kako postulira klasična hipoteza o sekreciji likvora, cirkulaciji i apsorpciji

Patofiziologija hidrocefalusa

- U novom modelu akutne okluzije Sylvijevog akvadukta u mačaka, veličina izoliranih moždanih komora i promjene tlaka likvora u komorama i subarahnoidnom prostoru istražuju se kako bi se razjasnila patofiziologija akutnog hidrocefalusa
- Rezultati pokazuju da za dilataciju izoliranih komora mehanička opstrukcija sama po sebi nije dovoljna

Mehanizam regulacije intrakranijskog tlaka

- Po prvi puta registrirano je da se tlak u moždanim komorama, cervikalnom i epiduralnom prostoru te spinalnom i subarahnoidnom prostoru mijenja istodobno tijekom promjena položaja tijela i tijekom infuzija u likvorski sustav

Mehanizam djelovanja osmotskih lijekova na intrakranijsku hipertenziju

- Naši rezultati ukazuju da intravenska primjena hiperosmolarnih otopina osmotskih lijekova uzrokuje pad tlaka likvora u intaktnom kraniju smanjenjem volumena likvora u spinalnom dijelu, ali ne dehidracijom moždanog tkiva, smanjenjem intrakranijskog volumena likvora ili smanjenjem sekrecije likvora, kako se općenito pretpostavlja

**Laboratory for neuropathophysiology of
CSF (Marijan Klarica)**

Head:

Professor Marijan Klarica,
Professor of pharmacology
Šalata 8, 10 000 Zagreb

Associates:

Darko Orešković, PhD
Institute Ruđer Bošković
Ivana Jurjević, MD, PhD
Goran Ivkić, MD, PhD

Our laboratory is involved in the research about physiology and pathophysiology of the cerebrospinal fluid and intracranial pressure.

Following lines of investigations are currently being pursued:

Fate of the brain metabolites in medications in the cerebrospinal fluid's system

- It has been shown that cerebral capillaries are the main pathway, via active transport, for the removal of brain metabolites and anionic medications.
- Cerebrospinal fluid's system is a close circuit system which is communicating with the blood mainly through cerebral capillaries. However, this communication is not done by the circulation and absorption of the CSF into sinuses of the dura mater, as postulated by the classical theory of secretion, circulation and absorption of the CSF.

Pathophysiology of the hydrocephalus

- We are investigating the size of the isolated brain ventricles and changes in the CSF pressure (within the brain ventricles and subarachnoid space) on the new model of acute occlusion of the cerebral aquaducte (aqueductus Sylvii) in order to elucidated pathophysiology of the hydrocephalus.
- Results have shown that mechanical obstruction itself is not sufficient to cause the hydrocephalus.

Regulation mechanisms of the intracranial pressure

- For the first time it has been shown that the pressure in the brain ventricles, cervical, epidural and spinal and subarachnoid space change simultaneously during changes in the body posture and application of the infusion in the CSF system.

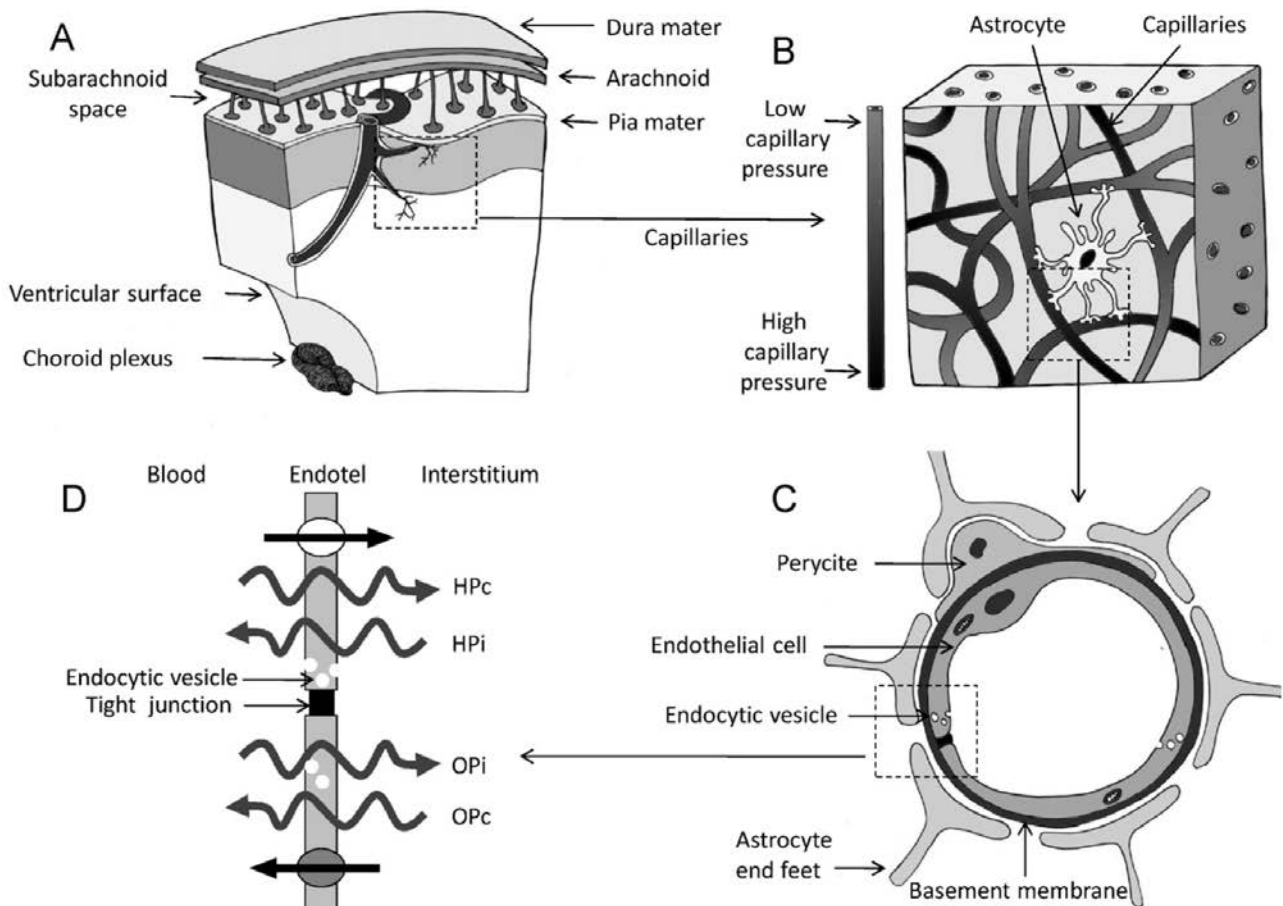
Effect of osmotic drugs on the intracranial hypertension

- Our results have shown that the application of the hyperosmolaric solutions of osmotic drugs causes drop of the intracranial pressure within the intact cranium. However, this effect is not accomplished by the dehydration of the brain tissue, reduction in the intracranial CSF volume,

or reduction of CSF secretion, as have been believed before, but through the reduction of the CSF volume in the spinal part of the system.

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10. Orešković D, Klarica M. Development of hydrocephalus and classical hypothesis of cerebrospinal fluid hydrodynamics: facts and illusions. *Progress in Neurobiology* 94: 238-258, 2011.



Slika 1
Shematski prikaz nove radne hipoteze hidrodinamike CSL (referenca 10 u gornjem popisu).

Figure 1
Schematic representation of the new working hypothesis of CSF hydrodynamics (reference 10 in the list above).

**Odsjek za neuropsihofarmakologiju
i farmakologiju ponašanja (Neven
Henigsberg)**

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Hrvatski institut za istraživanje mozga
Šalata 12, 10000 Zagreb

Odsjek za psihofarmakologiju i neurobiologiju ponašanja je posvećen etičkoj studiji i sudjelovanju u pronalaženju novih lijekova za psihijatrijske poremećaje kroz klinička istraživanja. Ciljevi Odjela su da stimulira kvalitetu kliničkih ispitivanja, da usmjeri istraživačke procese, od dizajna do objavljivanja protokola, te da educira istražitelje o dobroj kliničkoj praksi, regulatornim pitanjima i menadžmentu. Hrvatski institut za istraživanje mozga (HIIM) je osnovao Institucionalni odbor za recenziju svih predloženih istraživanja na ljudima kako bi se osiguralo da ispitanici i njihova prava i dobrobiti budu adekvatno zaštićeni. Odsjek za psihofarmakologiju i neurobiologiju ponašanja je multidisciplinarna skupina, koja je uključena u integrativna neuroznanstvena istraživanja moždanih mehanizama psihijatrijskih poremećaja. Odjel je odgovoran za istraživanje, obrazovanje i liječenje koje uključuje kliničku psihofarmakologiju, ali nije samo na nju ograničeno.

Danas je HIIM poticajno okruženje u kojem akademska istraživanja i nastava dolaze zajedno kako bi unaprijedili znanje o terapijskim mogućnostima u duševnim smetnjama. Glavna snaga HIIM-a je kapacitet za proučavanje mozga pomoću kombiniranih perspektiva - kliničkih i temeljnih istraživanja. Ovo istraživačko okruženje aktivno potiče suradnju između istraživača koji imaju različita područja stručnosti. Više od 50 članova nastavnog osoblja pridonose svojim istraživačkim i kliničkim kapacitetom u multidisciplinarnim timovima. Studije na ljudima koriste bihevioralnu, spoznajnu, i elektrofiziološku metodologiju, kao i slikovni prikaz mozga.

ORGANIZACIJA

Odsjek za psihofarmakologiju i neurobiologiju ponašanja funkcionalno je integriran s Odjelom za kliničko ispitivanje Poliklinike "Neuron", zdravstvenoj ustanovi koja pruža usluge specijalista u svim srodnim područjima poremećaja centralnog živčanog sustava. Osim svojih obveza pri HIIM-u, istraživači su svojim istraživanjima povezani sa svim sveučilišnim zavodima i klinikama. U cilju promicanja integrativne suradnje između najpriznatijih institucija u kliničkim istraživanjima, Odsjek koordinira "Mrežu kliničkih istraživanja pri HIIM-u", kao multi-partnersku inicijativu za promicanje kliničkih istraživanja u Hrvatskoj, izgradnjom istraživačke infrastrukture i profesionalnih resursa, te pojednostavljenjem upravljanja i regulatornih procesa. Četiri vodeće institucije pridružile su se Mreži, s ukupnim kapacitetom od 2.000 bolničkih kreveta, što

**Division of neuropsychopharmacology
and pharmacology of behaviour (Neven
Henigsberg)**

Head:

Prof. Neven Henigsberg, MD, PhD
Croatian Institute for Brain Research
Šalata 12, HR-10000 Zagreb

The Department of Psychopharmacology and Neurobiology of Behaviour is dedicated to ethical studies and participation in finding new drugs for psychiatric disorders through clinical trials. The goals of the Department are the stimulation of the quality of clinical trials, directing the research processes from design to protocol finalization and education of researchers about Good clinical practice in regulatory issues and management. Croatian Institute for Brain Research (CIBR) has founded The Institutional Board for the review of all proposed research on humans as to ensure the adequate protection of research subjects, their rights and their well-being. The Department for Psychopharmacology and Neurobiology of Behaviour is a multidisciplinary team that is involved in integrative neuroscientific research of brain mechanisms of psychiatric disorders. The Department is responsible for research, education and treatment which includes clinical psychopharmacology but is not limited to it.

Today, CIBR is a stimulating environment in which academic research and teaching come together to advance the knowledge about therapeutic possibilities in mental disorders. CIBRS's main strength is the capacity to study brain through combined perspectives - clinical and basic research. This research environment actively encourages collaboration between researchers of different areas of expertise. More than 50 members of teaching staff contribute with their research and clinical capacity in multidisciplinary teams. Studies conducted on humans utilise behavioural, cognitive and electrophysiological methodology, as well as brain imaging techniques.

ORGANIZATION

The Department of Psychopharmacology and Neurobiology of Behaviour is functionally integrated with the Department for Clinical Trials of Polyclinic "Neuron", medical institution which provides the services of the specialists related to central nervous system disorders. The researchers are associated to all university departments and clinics, as well as CIBR. Aiming to promote integrative cooperation between most recognized institutions in clinical trials, the Department is coordinating "The Network of Clinical Trials at CIBR" as a multi-partner initiative for promoting clinical trials in Croatia by establishing research infrastructure and professional resources together with the simplification of governing and regulatory processes. Four of the leading institutions have joined The Network with the combined capacity of almost 2000 hospital beds which represents considerable potential for quick activation of research in almost every area related to

predstavlja znatan potencijal za brzu aktivaciju istraživanja u gotovo svakom području vezanom za središnji živčani sustav, a s ciljem poboljšanja brzine, kvalitete i integracije kliničkih istraživanja.

ZNANSTVENI INTERESI

Znanstveni interesi Odsjela su uglavnom usmjereni na:

1. Prepoznavanje neurobioloških prediktora, kao i parametara u slikovnom prikazu mozga za učinkovitost i sigurnosti psihoaktivnih lijekova;
2. Sudjelovanje u razvoju genomske terapije u depresiji, shizofreniji i progresivnoj demenciji. Kao jedino kliničko mjesto izvan zemalja Europske unije, Odsjek za psihofarmakologiju i neurobiologiju ponašanja, sudjelovao je u razdoblju između 2004. i 2008. kao punopravni član Europske komisije u znanstvenom projektu "Genomic-based therapies for depression /GENDEP/", financiranom putem FP6, koji je uključivao 12 kliničkih centara u 9 europskih zemalja. Poštujući sva etička načela, znanstvena ispitivanja u psihijatrijskoj genetici dodatno su osnažena suradnjom s Hrvatskim zavodom za javno zdravstvo, koji održava jedan od najstarijih registara psihijatrijskih bolesnika u Europi.

SURADNJA S INDUSTRIJOM

Istraživači Odsjeka imaju više od 70 multicentričnih, međunarodnih kliničkih ispitivanja te proučavaju mnoge nove metode liječenja koje će se naknadno odobriti za kliničku primjenu kako u djece, odraslih i adolescenata, tako i u gerijatrijskoj populaciji s dijagnozom različitih duševnih smetnji. Odsjek za psihofarmakologiju i neurobiologiju ponašanja nudi svojim partnerima niz usluga vezanih uz regulatornu prijavu ispitivanja, njegovo izvođenje i praćenje, uključujući:

- Izradu izvješća i ostale potrebne dokumentacije regulatornim tijekima
- Razvoj protokola u kliničkim ispitivanjima
- Pregled izvedivosti novih studija
- Odgojno-obrazovnog mogućnosti za kliničke istražitelje/koordinatore
- Koordinacija i izvođenje kompletnih studija,
- Kompletnaklinička, laboratorijska i tehnička podrška, uključujući i pripremuuzoraka, obradu i dostavu
- Računalno upravljanje i vođenje ispitivanja
- Analizapodatakai izradaizvješćapoj edinihstudijaimeta-analize kliničkih ispitivanjaFarmakoekonomskeanalize
- Edukacija pacijenata
- Odsjek jamči osiguranje kvalitete, s ciljemjačanja i poštivanja dobre kliničke prakse izakonskih zahtjeva u vođenju ispitivanja.

BUDUĆI RAZVOJ

Integracija kliničke psihofarmakologije s predkliničkom psihofarmakologijom istraživanja predstavlja jedan od glavnih interesa istražitelja unutar Odsjeka. Istraživači imaju veliko iskustvo

centralnog nervnog sustava, s ciljem poboljšanja brzine, kvalitete i integracije kliničkih istraživanja.

SCIENTIFIC INTERESTS

Scientific interests of the Department are mostly related to:

1. Recognising neurobiological predictors and parameters in brain imagining for the effectiveness and the safety of psychoactive drugs.
2. Participation in the development of the genome therapy in depression, schizophrenia and progressive dementia. From 2004 to 2008, The Department of Psychopharmacology and Neurobiology of Behaviour participated, as the only clinical centre outside of the European Union, as a full member in the European Commission with the scientific project "Genomic-based therapies for depression /GENDEP/", FP6 financed, which included 12 clinical centres in 9 European countries. Complying with all ethical principles, scientific research in psychiatric genetics is further strengthened in collaboration with Croatian Institute for Public Health which holds one of the oldest registers of psychiatric patients in Europe.

COLLABORATION WITH THE INDUSTRY

The researchers from the Department have performed more than 70 multicentre, international clinical trials studying new methods of treatments which will subsequently be approved in clinical application in child, adolescent, adult and the geriatric population with the diagnoses of different mental disorders. The Department of Psychopharmacology and Neurobiology of Behaviour offers its partners a variety of services related to regulatory application of clinical trials, clinical trial conduction, as well as:

- Development of reports and other necessary documentation for regulatory bodies
- The development of the protocol in clinical trials
- Feasibility studies
- Educational possibilities for investigators and coordinators in clinical trials
- Coordination and performance of complete studies
- Complete clinical, laboratory and technical support, including the preparation, analysis and delivery of samples
- Computer management and conduction of the trial
- Data analysis and development of reports and meta-analysis of clinical trials
- Pharmaco-economic analysis
- Education of patients
- The Department guarantees quality assurance aiming to strengthen and comply with Good Clinical Practice and the legislative demands in conduction of clinical trials

FUTURE DEVELOPMENT

The integration of clinical psychopharmacology with the preclinical psychopharmacology research presents one of the main interests within the Department. The researchers have vast experience in

u ranim fazama razvoja lijekova. Opseg kliničkih istraživanja na HIIM-u širi se na rane faze kliničkih ispitivanja i razvoj lijekova. Cilj je daljnje jačanje već postojećih farmakogenetičkih istraživanja pri HIIM-u s drugim skupinama u Hrvatskoj, koje uključuju vodeće istraživače u psihijatriju, molekularnoj genetici, slikovnom prikazu mozga, anatomiji i molekularnoj biologiji.

early phases of drug development. The span of clinical research in CIBR is expanding to early phases of clinical trials and drug development. The aim is to further strengthen the already existing pharmacogenetic research in CIBR with the other groups in Croatia which include the leading researchers in psychiatry, molecular genetics, brain imaging, anatomy and molecular biology.

Izabrane publikacije / Selected publications:

1. Sarac H, Henigsberg N, Markeljević J, Pavlisa G, Hof PR, Simić G. Fragile X-premutation tremor/ataxia syndrome (FXTAS) in a young woman: clinical, genetics, MRI and 1H-MR spectroscopy correlates. *Coll Antropol.* 2011 Jan;35 Suppl 1:327-32. PubMed PMID: 21648356.
2. Radonić E, Rados M, Kalember P, Bajs-Janović M, Folnegović-Smalc V, Henigsberg N. Comparison of hippocampal volumes in schizophrenia, schizoaffective and bipolar disorder. *Coll Antropol.* 2011 Jan;35 Suppl 1:249-52. PubMed PMID: 21648342.
3. Loncar M, Plasć ID, Bunjevac T, Henigsberg N, Hrabac P, Groznica I, Marcinko V, Jevtović S. Self-assessment of well-being as an indicator of quality of life of former war prisoners - A Croatian study. *Coll Antropol.* 2011 Jan;35 Suppl 1:199-204. PubMed PMID: 21648334.
4. Henigsberg N, Kalember P, Hrabac P, Rados M, Bajs M, Rados M, Kovavić Z, Loncar M, Madzar T. 1-H MRS changes in dorsolateral prefrontal cortex after donepezil treatment in patients with mild to moderate Alzheimer's disease. *Coll Antropol.* 2011 Jan;35 Suppl 1:159-62. PubMed PMID: 21648328.
5. Henigsberg N, Bajs M, Hrabac P, Kalember P, Rados M, Rados M, Radonić E. Changes in brain metabolites measured with magnetic resonance spectroscopy in antidepressant responders with comorbid major depression and posttraumatic stress disorder. *Coll Antropol.* 2011 Jan;35 Suppl 1:145-8. PubMed PMID: 21648325.
6. Plasć ID, Poljarević S, Loncar M, Henigsberg N. Age-developmental stage and severity of trauma related symptoms, anxiety and depressive symptoms in participants who lost their fathers during the war in Croatia. *Coll Antropol.* 2011 Jan;35 Suppl 1:139-44. PubMed PMID: 21648324.
7. Uher R, Dernovsek MZ, Mors O, Hauser J, Souery D, Zobel A, Maier W, Henigsberg N, Kalember P, Rietschel M, Placentino A, Mendlewicz J, Aitchison KJ, McGuffin P, Farmer A. Melancholic, atypical and anxious depression subtypes and outcome of treatment with escitalopram and nortriptyline. *J Affect Disord.* 2011 Jul;132(1-2):112-20. Epub 2011 Mar 15. PubMed PMID: 21411156.
8. Strohmaier J, Wüst S, Uher R, Henigsberg N, Mors O, Hauser J, Souery D, Zobel A, Dernovsek MZ, Streit F, Schmä C, Kozel D, Placentino A, Farmer A, McGuffin P, Aitchison KJ, Rietschel M. Sexual dysfunction during treatment with serotonergic and noradrenergic antidepressants: Clinical description and the role of the 5-HTTLPR. *World J Biol Psychiatry.* 2011 Mar 9. [Epub ahead of print] PubMed PMID: 21388237.
9. Malki K, Uher R, Paya-Cano J, Binder E, Rietschel M, Zobel A, Mors O, Hauser J, Henigsberg N, Jerman B, Souery D, Placentino A, Ng MY, Cohen-Woods S, Sluyter F, Farmer A, Aitchison KJ, Craig IW, Lewis CM, McGuffin P, Schalkwyk LC. Convergent animal and human evidence suggests a role of PPM1A gene in response to antidepressants. *Biol Psychiatry.* 2011 Feb 15;69(4):360-5. Epub 2010 Oct 20. PubMed PMID: 20970119.
10. Perroud N, Uher R, Ng MY, Guipponi M, Hauser J, Henigsberg N, Maier W, Mors O, Gennarelli M, Rietschel M, Souery D, Dernovsek MZ, Stamp AS, Lathrop M, Farmer A, Breen G, Aitchison KJ, Lewis CM, Craig IW, McGuffin P. Genome-wide association study of increasing suicidal ideation during antidepressant treatment in the GENDEP project. *Pharmacogenomics J.* 2011; 11(2): 138-4. PubMed PMID: 20877300.

Odsjek za laboratorijske životinje
(Nataša Jovanov Milošević)

Voditelj:

Prof. Nataša Jovanov Milošević,
njovanov@hiim.hr

Osoblje

Nataša Kuretić, vet. tehničar
Valentina Ban Lugarić, vet. tehničar

Imenovani veterinar

Dr.sc. Jadranka Bubić Špoljar, dr.med.vet.
jadranka.bubic@mef.hr; vivarij@hiim.hr

Odsjek za laboratorijske životinje HIIM u suradnji sa nastavnim i istraživačkim timovima HIIM-a i MF-a, doprinositi izvrsnosti istraživanja koja se provode, osiguravajući kvalitetan uzgoj, držanje i njegu laboratorijskih životinja. Primarni cilj odsjeka je da uz osiguravanje najviših standarda držanja i korištenja laboratorijskih životinja zaštititi zdravlje ljudi koji rade sa ili oko životinja. Vjerujemo da su najviši standardi u korištenju i dobrobit životinja, preduvjet za izvrsnost u znanosti i edukaciji koja koristi animalne modele. Životinje koje koristimo u edukaciji i istraživanjima na HIIM-a su u programu zaštite dobrobiti životinja koji je osmišljen tako da se zadovolje svi kriteriji definirani hrvatskom zakonskom regulativom (Zakon o zaštiti životinja NN 135/06 i 37/13, Pravilnik o zaštiti životinja koje se koriste u znanstvene svrhe NN55/13, te pravni akti javnog zdravstva). Odsjek za laboratorijske životinje HIIM-a je registriran i odobren za uzgoj držanje i korištenje laboratorijskih glodavaca za edukativne i istraživačke svrhe od strane Uprave za veterinarstvo i sigurnost hrane pri Ministarstva poljoprivrede RH od 2013. godine (HR- POK006).

Division for animal care and use
(Nataša Jovanov-Milošević)

The LAS works cooperatively and collaboratively with research and educational teams enhancing research excellence providing highest quality animal care. Our overarching goals are to assure laboratory animal's quality care while protect the health of people who work with and around animals. We believe that excellence in research and teaching requires excellence in animal care and use program. Animals that are used in research and teaching at LAS CIBR are covered by our Animal Care and Use Program. The LAS CIBR program is designed to assure that it is in compliance with the EU Directive 63/10 and Croatian Animal Welfare Regulation Acts (NN135/06; NN 37/13; NN55/13) and Public Health Policy. The LAS CIBR maintains accreditation for laboratory animals care and use for educational and research purposes by Croatian Ministry of Agriculture, Veterinary and Food Safety Directorate (HR-POK006).

In general, Guide to the Care and Use of Laboratory Animals (NIH, Ed. 8th, 2011) serves as the primary source for standards in procedures used in the LAS CIBR. Additional detailed information regarding policies and guidance may be found through links from the Animal Welfare Committee of the UZMF website.

LAS CIBR covers animal housing and care, veterinary medical care, facilities management, training, occupational health, and assurance of compliance with EU and Croatian laws and policies that govern use of animals in research and teaching.

Services provided include: animal procurement, animal housing space assignment, maintenance of genetically altered colonies, animal health surveillance, day-to-day care and oversight, procurement of appropriate feed, bedding, cages, other supplies and equipment, animal cage sanitation, monitoring of animal room environment, sanitation of animal facilities, maintenance of facility and equipment, waste and carcass disposal, maintenance of facility security system, human termination of animals. The veterinary microbiological monitoring and pathology services are performed by the outsourced accredited laboratories. Researchers also may have training, consultation on animal model selection and assistance in animal use protocol development.

Animal Housing Availability

Any investigator who wishes to conduct research with animals should contact the Attending Veterinarian by email: vivarij@hiim.hr, as soon as possible to determine the availability of space required to perform your animal subject-based research.

Personnel

Nataša Kuretić, vet. technician
Valentina Ban Lugarić, vet. technician

Attending Veterinarian

Dr.sc. Jadranka Bubić Špoljar, dr.med.vet.

Assoc. prof. Natasa Jovanov Milosevic, Head

**Laboratorij za razvojnu neurolingvistiku
(Maja Cepanec)**

Voditelj:

Doc. dr. sc. Maja Cepanec (logoped),

Suradnici:

Prof. dr. sc. Draženka Blaži (logoped)

Dr.sc. Blaženka Brozović (logoped)

Doc. dr. sc. Jasmina Ivšac Pavliša (logoped)

Prof. dr. sc. Marta Ljubešić (psiholog)

Dr.sc. Sanja Šimleša (psiholog)

Laboratorij za istraživanje dječje komunikacije (LIDEK) osnovan je 2001. godine pod imenom Laboratorij za razvojnu neurolingvistiku i vodstvom prof.dr.sc. Marte Ljubešić. Laboratorij je nastao temeljem ugovora Edukacijsko-rehabilitacijskog fakulteta Sveučilišta u Zagrebu i Hrvatskog instituta za istraživanje mozga, a utemeljen je na dugogodišnjoj suradnji stručnjaka iz biomedicinskih i bihevioralnih znanosti uključenih u istraživanje ranog razvoja.

Ciljevi:

Istraživanje razvoja komunikacije, jezika i govora, te razvojnih odstupanja u navedenim područjima

Istraživanje uloge i međuodnosa viših kognitivnih funkcija u razvoju komunikacije, jezika i govora u različitim kliničkim populacijama

Istraživanje povezanosti neurobiološke osnove i bihevioralnih razvojnih pokazatelja u djece urednog i narušenog razvoja

Istraživanje utjecaja okolinskih čimbenika (roditeljski stilovi, različiti terapijski pristupi i sl.) na razvojne ishode

Razvoj dijagnostičkog instrumentarija za procjenu ranog dječjeg razvoja

Projekti:

- Analiza ključnih bihevioralnih obilježja djece s autizmom u predškolskoj dobi kao pretpostavka kvantifikacije razvojnih profila (UNIZG)
- Autism Diagnostic Observation with Robot Evaluator (ADORE) (HZZ)
- Od rane komunikacije do pismenosti u djece s poremećajem iz autističnog spektra: uloga izvršnih funkcija (UNIZG)
- Uvođenje sustava znanstveno utemeljene (rane) dijagnostike autizma u Republiku Hrvatsku (Zaklada Adris, HEP, HT)
- Kognitivni i jezični razvoj u djece s neurorazvojnim rizikom (MZOŠ)
- Rani komunikacijski i jezični razvoj u djece s ranim mozgovnim oštećenjima (MZOŠ)

Laboratory for developmental neurolinguistics (Maja Cepanec)

Head:

Assistant Professor Maja Cepanec, PhD, SLP

Associates:

Professor Draženka Blaži, PhD, SLP

Blaženka Brozović, PhD, SLP

Assistant Professor Jasmina Ivšac Pavliša, PhD, SLP

Professor Marta Ljubešić, PhD, Psychologist

Sanja Šimleša, PhD, Psychologist

Child Communication Research Laboratory was founded in 2001 by professor Marta Ljubešić as Developmental Neurolinguistics Lab, based on the agreement between the Faculty of Education and Rehabilitation Sciences (University of Zagreb) and Croatian Institute for Brain Research. It was grounded on long-lasting cooperation between biomedical and behavioral scientists.

Goals:

To study development and developmental disabilities of communication, language and speech

To study the roles and interrelations of higher cognitive functions in the development of communication, language and speech in various clinical populations

To study interrelations between neurobiological and behavioral developmental indicators

To study the role of environmental factors (e.g. parenting styles, intervention programmes etc. on developmental outcomes

To develop various measuring instruments for the assesment of early child development

Projects:

Analysis of key developmental features in preschool children with autism as prerequisite of quantification (UNIZG)

Autism Diagnostic Observation with Robot Evaluator (ADORE) (HZZ)

From early communication to literacy in children with autism spectrum disorder: the role of executive functions (UNIZG) Implementation of science-based (early) assessment of autism in Croatia (Zaklada Adris, HEP, HT)

Cognitive and language development in children at neurodevelopmental risk (MZOŠ)

Early communication and language development in children with early brain injury (MZOŠ)

Radovi / Papers:

1. Šimleša, S., Ceganec, M. (2015). Development of executive functions during childhood. U: International Encyclopedia of Social and Behavioral Sciences, 2nd Edition. New York: Elsevier.
2. Kuvač-Kraljević, J., Ceganec, M., Šimleša, S. (2014). Gestural development and its relation to a child's early vocabulary. *Infant Behav Dev*, 37, 192-202.
3. Ceganec, M., Lice, K., Šimleša, S. (2012). Mother-father differences in screening for developmental delay in infants and toddlers. *J Commun Disord*, 45(4), 255-262.
4. Polšek, D., Jagatić, M., Ceganec, M., Hof, P.R., Šimić, G. (2011). Recent developments in neuropathology of autism spectrum disorders. *Transl Neurosci*, 2(3), 256-264.
5. Ivšac Pavliša, J., Šimleša, S., Ljubešić, M. (2011). Cognitive abilities and language comprehension in preschool children with perinatal brain lesion. *Collegium Antropol*, 35, 31-38.
6. Ceganec, M., Gmajnić, I., Ljubešić, M. (2010). Early communication development in socially deprived children - similar to autism? *Transl Neurosci*, 1(3), 244-254.
7. Ivšac Pavliša, J. (2010). Atypical communicative development and socioadaptive functioning in the early age. *Drus Istraz*, 19 (1-2), 279-303.

Laboratorij za razvojnu kognitivnu psihologiju (Mirna Kostović-Srzentić)

Voditelj laboratorija: dr.sc. Mirna Kostović Srzentić, psiholog

Suradnik: Branka Bartolić, prof. psihologije

Kontakt: mirna.kostovic-srzentic@zvu.hr

O laboratoriju:

- Neuropsihološko praćenje djece s ranim (peri/prenatalnim) oštećenjem mozga od rane dobi do adolescencije primjenom standardiziranih mjernih instrumenata u prilagođenoj prostoriji s jednosmjernim staklom uz digitalno snimanje
- Povezivanje strukturnih promjena mozga oslikavanjem MR (naročito periventrikularnih križanja puteva) s intelektualnim i specifičnim kognitivnim sposobnostima: pažnja, izvršne funkcije, vidno-prostorna obrada, senzo-motorika i pamćenje
- Interes za vrijeme nastanka oštećenja mozga i mehanizme plastičnosti
- Utjecaj (ne)povoljnih socio-okolinskih čimbenika na kognitivni razvoj nakon ranog oštećenja
- Prijedlog intervjenskih programa i savjetovanje roditelja

Suradnja:

- Zavod za neonatologiju i intenzivno liječenje, KBC Zagreb
- Akademija za razvojnu rehabilitaciju, Zagreb
- Poliklinika Neuron, Zagreb

Znanost:

Suradnja na projektima (suradnik)

- 2002. - 2005. MZOŠ „Perinatalno oštećenje mozga u djece s patološkim fetoplacentarnim dopplerom“ (voditelj projekta prof. dr. sc. Vlatka Mejaški Bošnjak).
- 2007. – 2013. MZOŠ „Kognitivni i jezični razvoj u djece s neurorazvojnim rizikom“ (voditelj projekta prof. dr.sc. Marta Ljubešić).
- 2013. Sveučilišni projekt „Perinatalna reorganizacija medijalnog (limbičkog) korteksa kod čovjeka“ (voditelj prof.dr.sc. Mario Vukšić).
- 2014. „Microcircuitry of higher cognitive functions“, HRZZ (voditelj projekta prof.dr.sc. Zdravko Petanjek).

Laboratory for developmental cognitive psychology (Mirna Kostović-Srzentić)

Head: dr.sc. Mirna Kostović Srzentić, psychologist

Collaborator: Branka Bartolić, prof., psychologist

About laboratory:

- Neuropsychological follow up of children with early brain damage (peri/prenatal) from early age to adolescence with standardized measuring instruments in specially adapted room with one-way mirror system and digital recording
- Relationship between structural brain changes on MR (especially periventricular crossroads) and general intellectual and specific cognitive functions: attention and executive functioning, visuospatial processing, sensorimotor and memory
- Special focus on time of the lesion onset and plasticity
- Socio-environmental influences on cognitive development after early brain lesion
- Early intervention and parental counseling

Collaboration:

- Department for neonatology and intensive care, KBC Zagreb
- Academy for developmental rehabilitation, Zagreb
- Neuron Polyclinic, Zagreb

Science:

Collaboration on projects (collaborator)

- 2002. - 2005. MZOŠ “Perinatal brain damage in children with pathological fetoplacental doppler” („Perinatalno oštećenje mozga u djece s patološkim fetoplacentarnim dopplerom“; project leader prof. dr. sc. Vlatka Mejaški Bošnjak).
- 2007. – 2013. MZOŠ “Cognitive and language development in children with neurodevelopmental risk” („Kognitivni i jezični razvoj u djece s neurorazvojnim rizikom“, project leader prof. dr.sc. Marta Ljubešić).
- 2013. Sveučilišni projekt „Perinatal reorganization of medial limbic cortex in human” („Perinatalna reorganizacija medijalnog (limbičkog) korteksa kod čovjeka“; project leader prof.dr.sc. Mario Vukšić).
- 2014. „Microcircuitry of higher cognitive functions“, HRZZ (project leader prof.dr.sc. Zdravko Petanjek).

Publikacije / Publications:

1. Kostović, I., Jovanov-Milošević, N. Radoš, M., Sedmak, G., Benjak, V., Kostović-Srzentić, M., Vasung, L., Čuljat, M., Radoš, M., Hüppi, P., Judaš, M. (2014). Perinatal and early postnatal reorganization of the subplate and related cellular compartments in the human cerebral wall as revealed by histological and MRI approaches., *Brain Structure and Function*, 219, 231-253.
2. Kostovic I., Kostović Srzentić, M., Benjak V., Nataša Jovanov-Milošević & Rados, M. (2014). Developmental dynamics of radial vulnerability in the cerebral compartments in preterm infants and neonates". *Frontiers in Neurology*, 5, 139.
3. Kostović Srzentić, M., Pukljak Iričanin, Z. & Rukavina, M. (2013). Children cured in neonatal intensive care unit: Outcome in preschool age. *EHPs Abstracts, Psychology & Health*, 28: sup 1, p. 241.
4. Benjak, V., Čuljat, M., Pavlović, M. & Kostović Srzentić, M. (2008). Changes of corpus callosum in children who suffered perinatal injury of the periventricular crossroads of pathways. *Collegium Antropologicum*, 32 (82), 25-29.
5. Kostović Srzentić, M.; Brozović, B.; Radoš, M.; Gojmerac, T. (2005). Corpus callosum thinning and specific neurocognitive deficits: a case study of perinatal brain lesion. *Cognitive Creier Comportament (Special issue: Developmental Cognitive Neuroscience)*, IX, 2; 403-422.
6. Kostović Srzentić, M. (2010). Priopćavanje roditeljima da je dijete rođeno s teškoćama u razvoju. U: Lučanin D. i Despot Lučanin J. (ur.), *Komunikacijske vještine u zdravstvu (185-192)*. Zagreb: Zdravstveno veleučilište i Naklada Slap.
7. Kostović Srzentić M. (2009). Rana plastičnost mozga i kognitivni razvoj. *Plavi fokus – časopis hrvatske komore medicinskih sestara*, 1, V.

Laboratorij za razvojnu neurologiju
(Vlatka Mejaški Bošnjak – u mirovini od
2015.)

Voditeljica laboratorija:

Prof. dr. sc. Vlatka Mejaški Bošnjak, dr.med

ISTRAŽIVAČI I SURADNICI:

Prim. dr. sc. Vlasta Đuranović, dr. med., Klinika za dječje bolesti Zagreb

mr.sc. Tomislav Gojmerac, dr. med. Klinika za dječje bolesti Zagreb

dr. sc. Goran Krakar, dr. med., Klinika za dječje bolesti Zagreb

doc. dr. sc. Andrea Šimić Klarić, dr. med. OB Požega

doc. dr.sc. Sonja Alimović, profesor defektolog,

Dnevni centra za rehabilitaciju Mali dom

dr. sc. Ana Katušić, profesor defektolog, Dnevni centar za rehabilitaciju Mali dom

Ivana Đaković, dr. med., specijalizant pedijatrije,

doktorand, Klinika za dječje bolesti Zagreb

OBRANJENE DOKTORSKE DISERTACIJE
Medicinski fakultet Sveučilišta u Zagrebu,
Doktorski studij, smjer Biomedicina i Neuroznanost
_mentor prof. dr. sc. Vlatka Mejaški Bošnjak, dr.
med.

- Andrea Šimić Klarić: "Povezanost dinamike rasta opsega glave i neurorazvojnih poremećaja u predškolske djece rođene nakon intrauterinog zastoja rasta. (2012)
- Ana Katušić: "Učinak zvučnih vibracija frekvencije 40Hz na spastičnost motoričke funkcije djece s cerebralnom paralizom."(2012)
- Sonja Alimović: "Razvoj funkcionalnog vida u djece s perinatalnim oštećenjem mozga"(2013)
- Goran Krakar : " Ultrasonografski biljezi u dijagnozi kongenitalne citomegalovirus infekcije". (2014), Sveučilište u Zagrebu Prirodoslovno- matematički fakultet Biološki odsjek, Doktorski studij;
- Andrea Polovina : " Korelacija abnormalnih položajnih reakcija po Voiti i ultrazvučnog nalaza mozga. "

Laboratorij za razvojnu neurologiju bavi se neurorazvojnim praćenjem perinatalno rizične djece. Provođi se kliničko neurološko praćenje, metodama ovisno o dobi djece, strukturne promjene perinatalnog oštećenja procjenjuju se intrakranijskim ultrazvukom. Neurofiziološkim pretragama (evocirani potencijali EEG) funkcionalno se procjenjuje SZS.

Odstupanja se klasificiraju kao neurološki sindromi u dojenačkoj dobi, blaža ili teža

(cerebralna paraliza), neuromotorna odstupanja, Primjenjuje se funkcionalna klasifikacija cerebralne paralize prema SCPE (Surveillance cerebral palsy Europe).

Laboratorijske rotacije u Laboratoriju za razvojnu neurologiju prošlo je 20 studenata, kolegija Razvojna neurologija doktorskog studija Neuroznanosti . Troje studenata koji su pohađali Kolegij razvojne neurologije, izradilo je doktorsku disertaciju.

Laboratory for developmental neurology
(Vlatka Mejaški Bošnjak – retired since
2015.)

Head:

Vlatka Mejaški Bošnjak, MD, PhD, Professor of Child Neurology

RESEARCHERS AND COLLABORATORS:

Vlasta Đuranović, MD, PhD, Children's Hospital Zagreb

Tomislav Gojmerac, MD, MA. Children's Hospital Zagreb

Goran Krakar, MD, PhD, Children's Hospital Zagreb

Andrea Šimić Klarić, MD, PhD, Assistant Professor of Pediatrics, General Hospital Požega

Sonja Alimović, special pedagogist, Assistant Professor, Centre for Rehabilitation " Mali dom"

Ana Katušić, MD, special pedagogist , Centre for Rehabilitation," Mali dom"

Ivana Đaković, MD, resident in Pediatrics, PhD student, Children's Hospital Zagreb

Laboratory for developmental neurology comprises neurodevelopmental follow-up of children at perinatal neurorisk. Neurodevelopmental follow-up includes clinical assessment using clinical instruments appropriate for age of children examined, examinations of perinatal brain structural changes by intracranial ultrasonography, as well as neurophysiological (evoked potential, EEG) CNS functional assessment.

Deviant neurodevelopmental signs are classified as neurological syndroms of infancy (spastic, dystonic, haemisindrom) minor neurological dysfunction, or cerebral palsy. Cerebral palsy is classified according to criteria of Surveillance of Cerebral Palsy in Europe.

Practical work in Laboratory for developmental neurology attended 20 PhD students of PhD study Neuroscience. They also completed lectures and seminars on topics of neurological development, general movements, deviant neurological signs, minimal neurological dysfunction, cerebral palsy.

Three PhD students, attendees of PhD study Neurosciences and collegum Developmental neurology defended their Phd thesis. Activity of Laboratory for developmental neurology is also part of research project of Ministry of Science of Republic Croatia dealing with "Neurodevelopmental outcome of children with intrauterine growth retardation and/ or hypoxia (072-1081870-0025), principal investigator Vlatka Mejaški Bošnjak, MD, PhD, Professor of Child Neurology. This research project is part of research program of Croatian Institute for Brain Research

Defended PhD theses at Medical School, University of Zagreb, PhD Study Biomedicine and Neuroscience.

Mentorship: Vlatka Mejaški Bošnjak, dr. med., MD, PhD, Professor of Child Neurology

Aktivnost laboratorija sadržana je i u znanstvenom istraživanju u okviru:

projekta Ministarstva znanosti: "Neurorazvojni ishod djece s intrauterinim zastojem rasta ilili hipoksijom" (072-1081870-0025), voditeljica projekta: Prof. dr.sc. V. Mejaški-Bošnjak, dr.med., uže područje istraživanja: dugoročni neurorazvojni ishod nakon perinatalnog oštećenja mozga, neurofiziološka dijagnostika, intrakranijska ultrasonografija. Projekt je dio istraživačkog programa Hrvatskog instituta za istraživanje mozga

Znanstveni radovi (CC)

1. Ivana Đaković, Maria Garcia Andrada, Teres Folha, David Neubauer, Katalin Hollody, Michaela Honold, Veronika Horber, Vlasta Duranovic, Vlatka Mejaski Bosnjak. Clinical features of cerebral palsy in children with symptomatic congenital cytomegalovirus infection. *Eur J Ped Neurol*. 18: 2014, 618-628.
2. Krakar G, Đaković I, Delin S, Bošnjak VM. Evolutive leukoencephalopathy in congenital cytomegalovirus infection. *J Child Neurol* 2015, 30; 93-95
3. Katušić, Ana; Alimović, Sonja; Mejaški-Bošnjak, Vlatka.
4. The effect of vibration therapy on spasticity and motor function in children with cerebral palsy: A randomized controlled trial. *Neurorehabilitation*. 31 (2013) , 1; 1-8 .
5. Šimić Klarić, Andrea; Galić, Slavka; Kolundžić, Zdravko; Mejaški Bošnjak, Vlatka.
6. Neuropsychological Development in Preschool Children Born With Asymmetrical Intrauterine Growth Retardation and Impact of Postnatal Head Growth. *Journal of Child Neurology*. 28 (2013) , 7; 867-873
7. Šimić Klarić, Andrea; Kolundžić, Zdravko; Galić, Slavka; Mejaški Bošnjak, Vlatka.
8. Language development in preschool children born after asymmetrical intrauterine growth retardation. // *European Journal of Paediatric Neurology*. 16 (2012) , 2; 132-137
9. Alimović, Sonja; Mejaški Bošnjak, Vlatka.
10. Stimulation of Functional Vision in Children with Perinatal Brain Damage. *Collegium antropologicum*. 35 (2011) , S1; 3-9
11. Mejaški-Bošnjak, Vlatka; Đaković, Ivana; Đuranović, Vlasta; Lujčić, Lucija; Krakar, Goran; Marn, Borut.
12. Malformations of Cortical Development in Children with Congenital Cytomegalovirus Infection - A Study of Nine Children with Proven Congenital Cytomegalovirus Infection. *Collegium antropologicum*. 35 (2011) , S1; 229-235
13. Đuranović, Vlasta; Krakar, Goran; Mejaški-Bošnjak, Vlatka; Lujčić, Lucija; Gojmerac, Tomislav; Marn, Borut.
14. Lenticulostriatal Vasculopathy – a Marker for Congenital Cytomegalovirus Infection?. *Collegium antropologicum*. 35 (2011) , S1; 149-155

- Andrea Šimić Klarić: "The relationship of post-natal head growth dynamics and neurodevelopmental impairment in preschool children born with intrauterine growth retardation" (2012)
- Ana Katušić: "The effect of 40 Hz sound wave vibration on spasticity and motor functions in children with cerebral palsy" (2012)
- Sonja Alimović: "Development of functional vision in children with perinatal brain damage". (2013)
- Goran Krakar: "Brain ultrasonographic markers in the diagnosis of congenital cytomegalovirus infection" (2014)

Laboratorij za EEG i evocirane potencijale (Goran Ivkić)

Voditelj:

Goran Ivkić, dr.med.

SURADNJA

Prof.dr.sc. Silvio Bašić, KB Dubrava, Klinika za Neurologiju
Prof.dr.sc. Davor Sporiš, KB Dubrava, Klinika za Neurologiju
Prof.dr.sc. Darko Chudy, KB Dubrava, Klinika za Neurokirurgiju
Prof. Branka Bartolić, psiholog, Poliklinika NEURON

Laboratorij za EEG i evocirane potencijale dio je Hrvatskog instituta za istraživanje mozga i posjeduje sustav za višekanalnu video-EEG poligrafiju (128-kanalni EEG-uređaj – Neurofax 1000 - Nihon Kohden), jedini uređaj tog kapaciteta u Hrvatskoj.

KLINIČKI RAD

EEG uređaj se koristi u svakodnevnom kliničkom radu Jedinice za neurologiju i neuropedijatriju Poliklinike NEURON, primarno u problematici epilepsija, glavobolja i nejasnih stanja svijesti. Posebno je važno istaknuti suradnju s Klinikom za neurologiju i Klinikom za neurokirurgiju KB Dubrava u problematici farmakorezistentnih oblika epilepsije, kada je operativna opcija jedina preostala opcija liječenja. Radi se o sofisticiranoj invazivnoj stereo EEG (SEEG) preoperativnoj obradi bolesnika s epilepsijom.

NASTAVA

Osim kliničkog dijela, Laboratorij za EEG i evocirane potencijale služi i kao nastavna baza u dodiplomskoj nastavi u predmetu «Temelji neuroznanosti», u nekoliko izbornih predmeta dodiplomske nastave studija medicine («EEG i stres», «Živčana stanica u zdravlju i bolesti» i «Vrti mi se»), kao i u poslijediplomskoj nastavi «Klinička neurologija».

INTERESI

- Epilepsije i neurokirurgija epilepsija
- Glavobolje, psihosomatika
- EEG, SEEG, QEEG

ZNANOST

Projekti:

- nositelj prof.dr.sc. Zdravko Petanjek “Microcircuitry of higher cognitive functions” Croatian Science Foundation - HRZZ project (HRZZ-5943) – 2013-2017 (konzultant)
- “Migration routes of hippocampal GABA-ergic neurons in monkey and man.” Ministry of Science Education and Sport (MZOS-108-1081870-1932), 2006-2013 (suradnik)

Laboratory for EEG and evoked potentials (Goran Ivkić)

Head

Goran Ivkić, MD

COLLABORATION

Prof. Silvio Bašić, MD, DSc, Dubrava CH, Clinic for Neurology
Prof. Davor Sporiš, MD, DSc, Dubrava CH, Clinic for Neurology
Prof. Darko Chudy, MD, Dsc, Dubrava CH, Clinic for Neurosurgery
Prof. Branka Bartolić, Psychologist, Diagnostic Center NEURON

Laboratory for EEG and Evoked potentials is a part of Croatian Institute for Brain Research and contains a System for multichannel video-EEG poligraphy (128-channel EEG - Neurofax 1000-Nihon Kohden), which is the unique equipment of that capacity in Croatia. Multichannel recording improves the spatial resolution of cortical potential distribution and the signal quality of deep brain sources.

CLINIC

The EEG is most commonly used in routine clinical work of Department of Neurology and Neuropediatrics of Diagnostic Center Neuron, in the evaluation of brain disorders (especially seizures, headache and different types of disorders of consciousness). We have also very important collaboration with Clinical Hospital Dubrava (Clinic for Neurology and Neurosurgery) in Problematic of pharmacoresistant epilepsy, when the operative option remains the last option of treatment. We use a sophisticated invasive Stereo-EEG (SEEG) electrodes for recording focal epileptic activity in patients with epilepsy.

TEACHING

Besides of clinical part, Laboratory for EEG and Evoked potentials serves as a teaching basis in graduate teaching: for subject «Fundamentals of Neuroscience», in several elective subjects of graduate teaching of Medical studies («EEG and Stress», «Neural Cell in Health and Illness» and «Vetrigo»), as well as in postgraduate teaching.

INTERESTS

- Epilepsy, Neurosurgery Epilepsy
- Headache, Psychosomatic Medicine
- EEG, SEEG, QEEG

SCIENCE

Projects:

- Head Prof. Zdravko Petanjek, MD, DSc “Microcircuitry of higher cognitive functions” Croatian Science Foundation - HRZZ project (HRZZ-5943) – (2013-2017) - Consultant).
- “Migration routes of hippocampal GABA-ergic neurons in monkey and man.” Ministry of Science Education and Sport (MZOS-108-1081870-1932), 2006-2013 - Assistant).

Publikacije / Publications:

- I K Lukić, V Glunčić, G Ivkić, M Hubenstorf, A Marušić. Virtual dissection: A lesson from the XVIII century. *The Lancet* 2003; 362: 2110-2112
- G Ivkić, M Nekić. Developmental changes of the vascular network within the human fetal telencephalic wall. *Neuroembryology* 2003; 2: 184-185
- Bašić S, Sporiš D, Chudy D, Ivkić G, Vavro H. Invasive SEEG imaging in preoperative care of patients with drug resistant epilepsy. *Lijec Vjesn.* 2010 Sep-Oct;132(9-10):323-4.

Pridruženi laboratoriji na HIIM-u (Melita Šalković-Petrišić – status voditelja Odsjeka)

Laboratorij za molekularnu imunologiju

Članovi istraživačke grupe:

prof. dr.sc. Danka Grčević, prof.dr.sc. Vedran Katavić, doc.dr.sc. Nataša Kovačić, doc.dr.sc. Tomislav Kelava, dr.sc. Elvira Lazić Mosler, dr.sc. Marina Ikić, Alan Šućur, dr.med., Darja Flegar, dr.med., Antonio Markotić, dr.med., Sanja Ivčević bcca. med. lab. dg., Katerina Zrinski Petrović, lab. tehničar.

Aktivni znanstveni projekti:

Projekt HRZZ-a: Characterization of osteoclast progenitor responses to arthritis (COPERA, šifra projekta: I-2393-2014) voditelj projekta: Danka Grčević, European Commission 7th Framework Programme, Health-2013-Innovation 1 Collaborative project: "Development of Stem Cell-Based Therapy for Thymic Regeneration" (koordinatorka prof. CC Blackburn, University of Edinburgh).

Znanstveni projekti u postupku natječajne recenzije:

projekt HRZZ-a: Molecular mediators of Fas-driven osteoresorption (MEFRA), voditelj projekta: Nataša Kovačić.

Područje znanstvenog istraživanja:

izučavanje imunoregulacijskih mehanizama u patogenezi reumatoidnog artritisa i osteoporoze, djelovanje imunskih medijatora na apoptotske mehanizme u stanicama.

Odabrane publikacije / Selected publications:

1. Kuzmac S, Grcevic D, Sucur A, Ivcevic S, Katavic V. Acute hematopoietic stress in mice is followed by enhanced osteoclast maturation in the bone marrow microenvironment. *Exp Hematol.* 2014 Nov;42(11):966-75.
2. Kovacic N, Grcevic D, Katavic V, Lukic IK, Grubisic V, Mihovilovic K, Cvija H, Croucher PI, Marusic A. Fas receptor is required for estrogen deficiency-induced bone loss in mice. *Lab Invest.* 2010 Mar;90(3):402-13.
3. Grcevic D, Lukic IK, Kovacic N, Ivcevic S, Katavic V, Marusic A. Activated T lymphocytes suppress osteoclastogenesis by diverting early monocyte/macrophage progenitor lineage commitment towards dendritic cell differentiation through down-regulation of receptor activator of nuclear factor-kappaB and c-Fos. *Clin Exp Immunol.* 2006 Oct;146(1):146-58.

Associated laboratories at the CIBR (Melita Šalković Petrišić – same status as a Head of Division)

Laboratory for Molecular Immunology

Research Group Members: Prof Danka Grčević, MD, PhD, Prof Vedran Katavić, Prof Nataša Kovačić, MD, PhD, Prof Tomislav Kelava, MD, PhD, Elvira Lazić Mosler, MD, PhD, Marina Ikić, MD, PhD, Alan Šućur, MD, Darja Flegar, MD, Antonio Markotić, MD, Sanja Ivčević, bachelor of laboratory medicine, Katerina Zrinski Petrović, Lab Technician.

Ongoing research projects:

Project of Croatian Science Foundation: Characterization of osteoclast progenitor responses to arthritis (COPERA, Grant Number: I-2393-2014) principal investigator: Danka Grčević, European Commission 7th Framework Programme, Health-2013-Innovation 1 Collaborative project: "Development of Stem Cell-Based Therapy for Thymic Regeneration" (coordinator prof. CC Blackburn, University of Edinburgh).

Projects under review:

Project of Croatian Science Foundation: Molecular mediators of Fas-driven osteoresorption (MEFRA), principal investigator: Nataša Kovačić.

Area of scientific research:

Interactions between bone and immune system in pathogenesis of rheumatoid arthritis and osteoporosis; Effects of immune mediators on cell apoptotic processes.

Laboratorij za molekularnu neurofarmakologiju

ISTRAŽIVAČKI TIM

- prof. dr. sc. Šalković-Petrišić Melita, dr. med., redoviti profesor farmakologije u trajnom zvanju (su-voditelj) (melitas@mef.hr)
- prof. dr. sc. Zdravko Lacković, dr. med., redoviti profesor farmakologije u trajnom zvanju (su-voditelj) (lac@mef.hr)
- prof. dr. sc. Lidija Bach.-Rojecky, mg. pharm. (izvanredni profesor farmakologije Farmaceutsko-biokemijskog fakulteta)
- dr. sc. Osmanović Barilar Jelena, dr. med. (viši asistent)
- dr. sc. Ivica Matak, dipl. ing. biol. (znanstveni novak, doktorirao na poslijediplomskom Doktorskom studiju Biomedicine i zdravstvo)
- Knezović Ana, dipl. ing. biol. (znanstveni novak, student poslijediplomskog Doktorskog studija Biomedicine i zdravstvo)
- Andrija Lončar, dr. med. (student poslijediplomskog Doktorskog studija Biomedicine i zdravstvo)
- Višnja Drinovac, mg. pharm. (student poslijediplomskog Doktorskog studija Farmaceutsko-biokemijskog fakulteta)
- Boris Filipović, dr. med. (student poslijediplomskog Doktorskog studija Biomedicine i zdravstvo Medicinskog fakulteta)
- Una Smailović, (studentica 6. godine Medicinskog studija)

Laboratorij je smješten na dvije lokacije (Zavod za farmakologiju i Hrvatski Institut za mozak /HIIM/), a u sastavu HIIM-a nalazi se od osnutka Instituta. Su-voditelji laboratorija su prof. dr. sc. Zdravko Lacković i prof. dr. sc. Melita Šalković-Petrišić čija su istraživanja usmjerena na dva područja, učinka botulinum toksina na bol i eksperimentalnu Alzheimerovu bolest. Istraživanja eksperimentalne Alzheimerove bolesti koja predvodi prof. dr. Šalković-Petrišić bave se razvojem i karakterizacijom netransgeničnog štakorskog modela sporadične Alzheimerove bolesti (sAB). Model se temelji na nastajanju inzulinske rezistencije u mozgu izazvane intracerebroventrikularnom primjenom streptozotocina (STZ-icv model), a pokazuje kognitivne i brojne neurokemijske te pojedine strukturne/ultrastrukturne promjene koje oponašaju one nađene u sAB bolesnika. Istraživanja antinocicpetivne aktivnosti botulinum toksina koja predvodi prod. dr. Lacković dovela su do otkrića aksonalnog transporta ovog toksina kroz senzorne živce do senzornih jezgara u središnjem živčanom sustavu te da neuobičajena upućna reakcija dure prati različite vrste boli u trigeminalnom području.

PROJEKTI (posljednjih 5 godina)

Voditelj / su-voditelj (međunarodni kolaborativni projekti)

- Cytopathological characterization of the brain in a rat model of sporadic Alzheimer's disease:

Laboratory for molecular neuropharmacology

LABORATORY RESEARCH TEAM

- Šalković-Petrišić Melita, MD, PhD, Tenured Professor of Pharmacology (Co-Chair) (melitas@mef.hr)
- Zdravko Lacković, MD, PhD, Tenured Professor of Pharmacology (Co-Chair) (lac@mef.hr)
- Lidija Bach.-Rojecky, MrPh, PhD, Associate Professor, School of Pharmacy and Biochemistry
- Osmanović Barilar Jelena, MD, PhD (senior research assistant)
- Ivica Matak, MSc, PhD, (graduated PhD student, Doctoral studies Biomedicine and Health)
- Knezović Ana, MA, mol. biol. ing (PhD student, Doctoral studies Biomedicine and Health)
- Andrija Lončar, MD (PhD student, Doctoral studies Biomedicine and Health)
- Višnja Drinovac, MrPh (PhD student, Doctoral studies School of Pharmacy and Biochemistry)
- Boris Filipović, MD (PhD student, Doctoral studies Biomedicine and Health)
- Una Smailović, (undergraduate student of medicine, 6th year)

The Laboratory is placed on two locations (Department of Pharmacology and Croatian Institute for Brain Research /HIIM/) and has been a part of Croatian Institute for Brain Research since its establishment. It is co-chaired by Professor Zdravko Lacković and Professor Melita Šalković-Petrišić whose research goes in two directions, botulinum toxin effects on pain and experimental Alzheimer's disease. The research on experimental Alzheimer's disease (headed by Professor Salkovic-Petrisic) has been focused on development and characterization of a non-transgenic rat model of sporadic Alzheimer's disease (sAD). The model is based on generation of insulin resistant brain state following the intracerebroventricular administration of streptozotocin (STZ-icv rat model) and demonstrates cognitive and a number of neurochemical and certain structural/ultrastructural changes that mimic those found in sAD patients. The research on pain (headed by professor Zdravko Lackovic) was focused on antinociceptive action of botulinum toxin, where we discovered axonal transport through sensory nerves to sensory nuclei in the CNS. In parallel we discovered unusual inflammatory pain reaction of dura that accompanies different form of pain in trigeminal region.

PROJECTS (last 5 years)

Principal investigator/co-PI (international collaborative projects)

- Cytopathological characterization of the brain in a rat model of sporadic Alzheimer's disease: Unity through Knowledge Fund collaborative project 2010-2012 (Croatia-USA)
- Combined experimental model of genetic and sporadic dementia: Deutscher Akademischer

Unity through Knowledge Fund collaborative project **2010-2012** (Croatia-USA)

- Combined experimental model of genetic and sporadic dementia: Deutscher Akademischer Austauschdienst (DAAD) collaborative project **2012** (Croatia-Bosnia and Herzegovina-Germany)
- Botulinum toxin and pain: DAAD collaborative project **2011** (Croatia-Bosnia and Herzegovina-Germany)
- Early (≤ 1 month) and late (9 months) changes in brain insulin system of STZ-icv rat model: DAAD collaborative project **2010** (Croatia-Bosnia and Herzegovina-Germany)
- IGF-I receptor and chronic intensive physical activity in STZ-icv rat model: DAAD collaborative project **2009** (Croatia-Bosnia and Herzegovina-Germany)

Voditelj (domaći projekti)

- Rane promjene u mozgu štakorskog modela sporadične Alzheimerove bolesti izazvane središnjom primjenom streptozotocina: Sveučilište u Zagrebu, **2014**
- Botulinum toksin, mozak i bol: Sveučilište u Zagrebu, **2014**
- Etiopatogenetski mehanizmi eksperimentalne sporadične Alzheimerove bolesti izazvane središnjom primjenom streptozotocina: Sveučilište u Zagrebu, **2013-2014**
- Botulinum toksin, mozak i bol: Sveučilište u Zagrebu, **2013-2014**
- Mozak, eksperimentalni i cerebralni dijabetes, kognitivni i drugi poremećaji: Ministarstvo znanosti, obrazovanja i športa (MZOS) **2007-2013**
- Neurotransmitori i novi mehanizmi djelovanja lijekova i otrova, Ministarstvo znanosti, obrazovanja i športa (MZOS) **2007-2013**

Austauschdienst (DAAD) collaborative project **2012** (Croatia-Bosnia and Herzegovina-Germany)

- Botulinum toxin and pain: DAAD collaborative project **2011** (Croatia-Bosnia and Herzegovina-Germany)
- Early (≤ 1 month) and late (9 months) changes in brain insulin system of STZ-icv rat model: DAAD collaborative project **2010** (Croatia-Bosnia and Herzegovina-Germany)
- IGF-I receptor and chronic intensive physical activity in STZ-icv rat model: DAAD collaborative project **2009** (Croatia-Bosnia and Herzegovina-Germany)

Principal investigator (national projects)

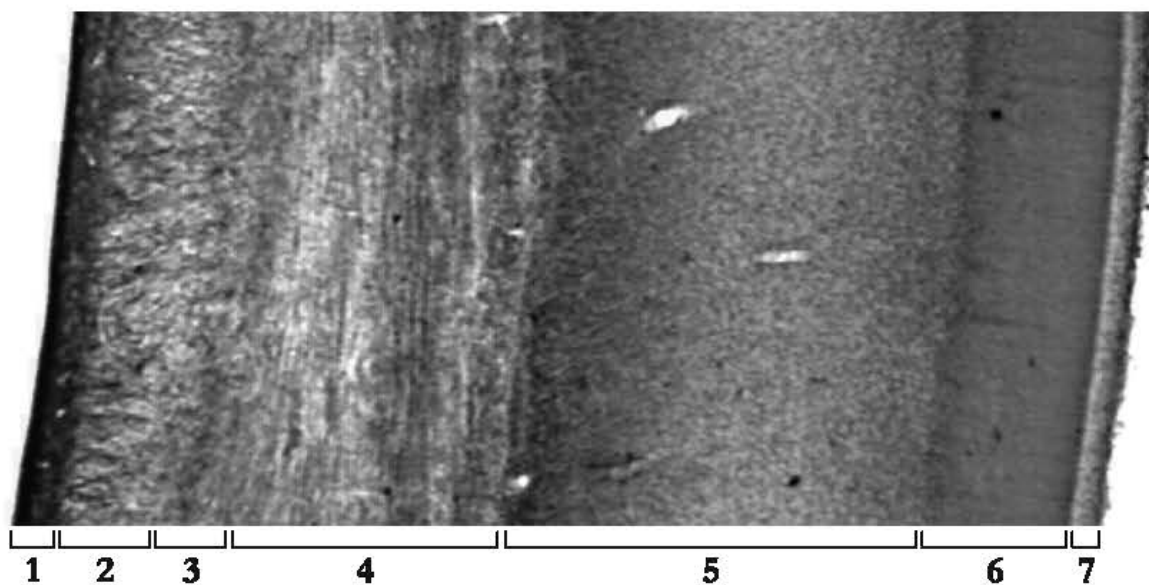
- Early changes in the brain of a rat model of sporadic Alzheimer's disease induced by intracerebroventricular administration of streptozotocin: University of Zagreb, **2014**
- Botulinum toxin A, brain and pain. University of Zagreb, **2014**
- Etiopatogenetic mechanisms of experimental sporadic Alzheimer's disease induced by central administration of streptozotocin: University of Zagreb, **2013-2014**
- Botulinum toxin A, brain and pain. University of Zagreb, **2013-2014**
- Neurotransmitters and new mechanisms of action of drugs and toxins, Croatian Ministry of Science, Education and Sport (MZOS) **2007-2013**
- Brain, experimental and cerebral diabetes, cognitive and other related disorders: Croatian Ministry of Science, Education and Sport (MZOS) **2007-2013**

ODABRANE PUBLIKACIJE (posljednjih 5 godina) / SELECTED PUBLICATIONS (in the last 5 years):

1. Osmanovic Barilar J, Knezovic A, Grünblatt E, Riederer P, Salkovic-Petrisic M. Nine-month follow-up of the insulin receptor signalling cascade in the brain of streptozotocin rat model of sporadic Alzheimer's disease. *J Neural Transm* 2014 Dec 12. [Epub ahead of print]
2. Salkovic-Petrisic M, Osmanovic-Barilar J, Knezovic A, Hoyer S, Mosetter K, Reutter W. Long-term oral galactose treatment prevents cognitive deficits in male wistar rats treated intracerebroventricularly with streptozotocin. *Neuropharmacology* 2014;77:68-80.
3. Filipović B, Matak I, Lacković Z. Dural neurogenic inflammation induced by neuropathic pain is specific to cranial region. *J Neural Transm.* 2014;121:555-63.
4. Matak I, Rossetto O, Lacković Z. Botulinum toxin type A selectivity for certain types of pain is associated with capsaicin-sensitive neurons. *Pain.* 2014; 155: 1516-1526.
5. Matak I, Lacković Z. Botulinum toxin A, brain and pain. *Prog Neurobiol.* 2014; 119-120, 39-59.
6. Drinovac V, Bach-Rojecky L, Babić A, Lacković Z. Antinociceptive effect of botulinum toxin type A on experimental abdominal pain. *Eur J Pharmacol.* 2014;745:190-5.
7. Drinovac V, Bach-Rojecky L, Matak I, Lacković Z. Involvement of μ -opioid receptors in antinociceptive action of botulinum toxin type A. *Neuropharmacology* 2013; 70: 331-337.
8. Matak I, Riederer P, Lacković Z. Botulinum toxin's axonal transport from periphery to the spinal cord. *Neurochem Int* 2012; 61: 236-239.
9. Filipović B, Matak I, Bach-Rojecky L, Lacković Z. Central action of peripherally applied botulinum toxin type A on pain and dural extravasation in rat model of trigeminal neuropathy. *PLoS ONE* 2012;7: e29803.
10. Salkovic-Petrisic M, Osmanovic-Barilar J, Brückner MK, Hoyer S, Arendt T, Riederer P. Cerebral amyloid angiopathy in streptozotocin rat model of sporadic Alzheimer's disease: a long-term follow up study. *J Neural Transm* 2011;118:765-772.

11. Bach-Rojecky L, Šalković-Petrišić M, Lacković Z. Botulinum toxin type A reduces pain supersensitivity in experimental diabetic neuropathy: bilateral effects after unilateral injection. *Eur J Pharmacol* 2011; 633: 10-14.
12. Matak I, Bach-Rojecky L, Filipović B, Lacković Z. Behavioral and immunohistochemical evidence for central antinociceptive activity of botulinum toxin A. *Neuroscience* 2011;186:201-207.
13. Plaschke K, Kopitz J, Siegelin M, Schliebs R, Salkovic-Petrisic M, Riederer P, Hoyer S. Insulin-resistant brain state after intracerebroventricular streptozotocin injection exacerbates Alzheimer-like changes in Tg2576 AbetaPP-overexpressing mice. *J Alzheimers Dis* 2010;19:691-704.
14. Filipović B, Bach-Rojecky L, Lacković Z. Lasting reduction of postsurgical hyperalgesia after single injection of botulinum toxin type A in rat. *Fundamen Clin Pharmacol* 2010; 24: 43-45.
15. Salkovic-Petrisic M, Osmanovic J, Grünblatt E, Riederer P, Hoyer S. Modeling sporadic Alzheimer's disease: the insulin resistant brain state generates multiple long-term morphobiological abnormalities including hyperphosphorylated tau protein and amyloid-beta. *J Alzheimers Dis* 2009;18:729-750.
16. Bach-Rojecky L, Lacković Z. Central origin of the antinociceptive action of botulinum toxin type A. *Pharmacol Biochem Behav* 2009;94:234-238.

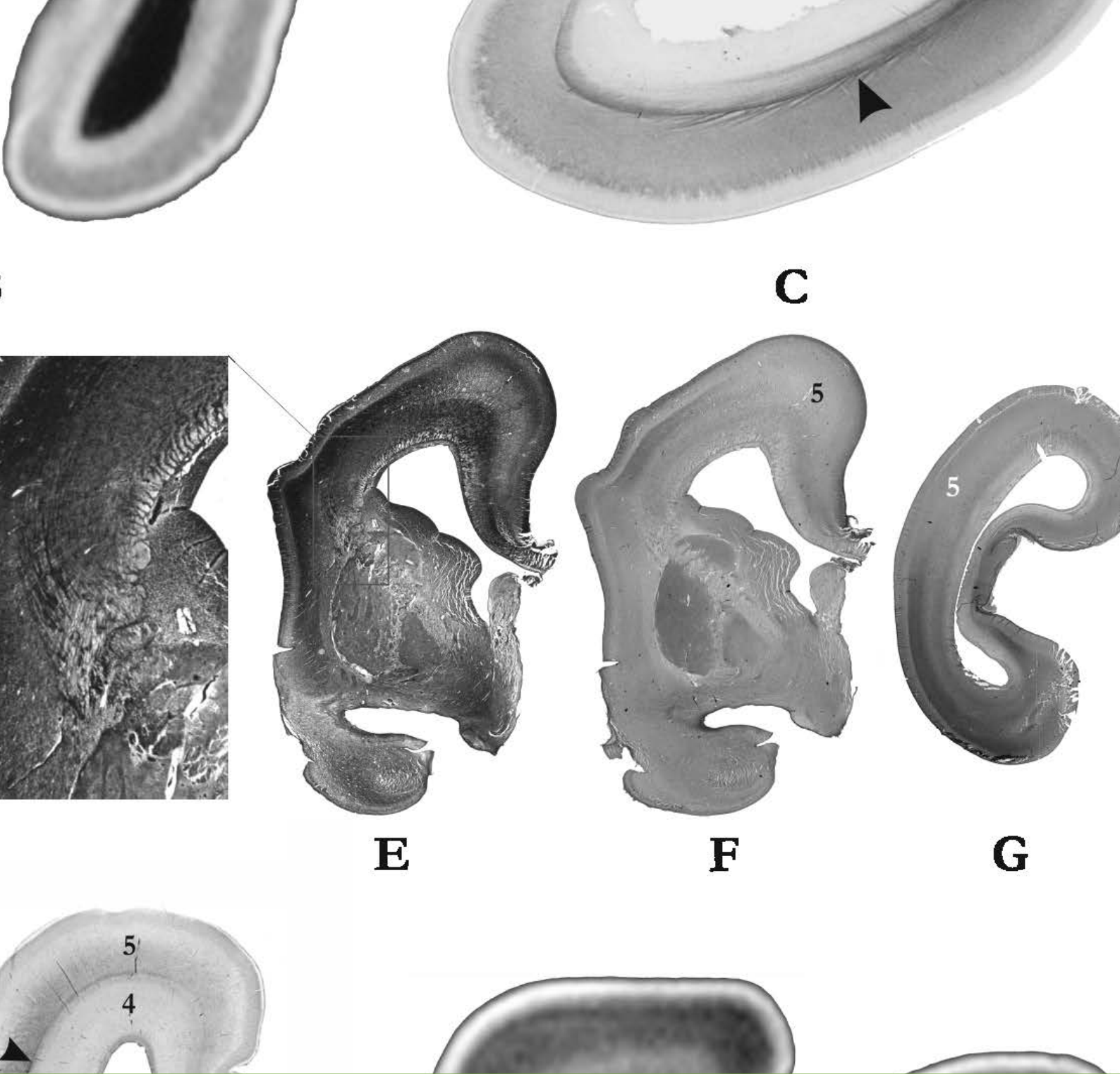
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D

POPIS RADOVA, OBRANJENIH DIPLOMSKIH, MAGISTARSKIH I DOKTORSKIH RADOVA, POZVANIH PREDAVANJA I USAVRŠAVANJA U INOZEMSTVU

Na sljedećim stranicama nalaze se prilozi, počevši s popisom publikacija. Navedeni su samo radovi istraživača koji su u znanstvenim programima HIIM-a sudjelovali od osnutka do danas (abecednim, a ne kronološkim slijedom), kao i oni radovi ostalih istraživača koji su objavljeni dok su ti istraživači bili dio našeg znanstvenog programa. Za neke, koji su s nama bili cijelo vrijeme (ili veći dio vremena), ali kao tzv. ektramuralni laboratoriji (smješteni izvan samog HIIM-a), smatrali smo primjerenim dati izdvojene popise publikacija (vidi i poglavlje 4).



LIST OF SCIENTIFIC PAPERS, GRADUATION, MASTER'S AND PHD THESES, INVITED LECTURES AND RESIDENCES ABROAD

Annexes, beginning with the list of publications, can be found on the following pages. Mentioned are only papers from researchers who participated in the scientific programs of the CIBR from its founding until today (in alphabetical, not chronological order), as well as papers from researchers who participated in our scientific programs at the time of publication. For some of them, who were with us the whole time (or most of the time), but in the role of the so-called "extramural" laboratories (located outside the CIBR), we thought it was appropriate to supply separate publications lists (see also Chapter 4).

PRILOG 1: Popis odabranih publikacija objavljenih u sklopu glavnih znanstvenih programa Hrvatskog instituta za istraživanje mozga

ANNEX 1: List of selected papers published within main scientific programs of the Croatian Institute for Brain Research

1. Andjus, P. R., Bataveljic, D., Vanhoutte, G., **Mitrečić, D.**, Pizzolante, F., Djogo, N., Nicaise, C., Kengne, F. G., Gangitano, C., Michetti, F., Van Der Linden, A., Pochet, R. and Bacic, G.; (2009); "In vivo morphological changes in animal models of amyotrophic lateral sclerosis and alzheimer's-like disease: Mri approach." Anatomical Record-Advances in Integrative Anatomy and Evolutionary Biology **292**(12): 1882-1892; Times Cited: 26; ANATOMY & MORPHOLOGY-Q3; IF-1,530; 5-year IF-1,595.
2. Aurer, I., Lauc, G., Dunic, J., Rendic, D., Maticic, D., Milos, M., **Heffer-Lauc, M.**, Flogel, M. and Labar, B.; (2007); "Aberrant glycosylation of igg heavy chain in multiple myeloma." Collegium Antropologicum **31**(1): 247-251; Times Cited: 4; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
3. Ayoub, A. E. and **Kostović, I.**; (2009); "New horizons for the subplate zone and its pioneering neurons." Cerebral Cortex **19**(8): 1705-1707; Times Cited: 21; NEUROSCIENCES-Q1; IF-8,305; 5-year IF-8,372.
4. Babić, M., Strac, D. S., Mück-Seler, D., Pivac, N., Stanic, G., Hof, P. R. and **Šimić, G.**; (2014); "Update on the core and developing cerebrospinal fluid biomarkers for alzheimer disease." Croatian Medical Journal **55**(4): 347-365; Times Cited: 0; MEDICINE, GENERAL & INTERNAL-Q2; IF-1,373; 5-year IF-1,603.
5. Babić, M., Vogrinc, Z., Diana, A., Klepac, N., Borovečki, F., Hof, P. R. and **Šimić, G.**; (2013); "Comparison of two commercial enzyme-linked immunosorbent assays for cerebrospinal fluid measurement of amyloid beta(1-42) and total tau." Translational Neuroscience **4**(2): 234-240; Times Cited: 1; NEUROSCIENCES-Q4; IF-0,716;
6. Babić, T., **Folnegović-Šmalc, V.** and **Henigsberg, N.**; (1999); "Rational diagnosis and treatment of alzheimer's dementia." Neurologia Croatica **48**(1): 29-34; Times Cited: 0; CLINICAL NEUROLOGY-Q4; IF-0,000; 5-year IF-0,024.
7. Bačić Baronica, K., **Ivkić, G.**, **Ozretić, D.** and Milicevic, G.; (2011); "Differential diagnostic relevance of high resolution magnetic resonance in patients with possible multiple system atrophy (msa) - a case report." Collegium Antropologicum **35**: 287-292; Times Cited: 0; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
8. Bačić Baronica, K., Mlinac, K., **Ozretić, D.**, Vladić, A. and **Kalanj Bogнар, S.**; (2011); "Arylsulfatase a gene polymorphisms in relapsing remitting multiple sclerosis genotype-phenotype correlation and estimation of disease progression." Collegium Antropologicum **35**: 11-16; Times Cited: 5; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
9. Bačić Baronica, K., Mlinac, K., Petlevski, R., **Ozretić, D.**, Vladić, A., **Kalanj Bogнар, S.** and Zuntar, I.; (2014); "Progression of multiple sclerosis is associated with gender differences in glutathione s-transferase detoxification pathway." Acta Neurobiologiae Experimentalis **74**(3): 257-265; Times Cited: 0; NEUROSCIENCES-Q3; IF-2,244; 5-year IF-2,111.
10. Bajs, M., Janovic, S., Bajs, M., Dordevic, V., Jevtovic, S., **Radonić, E.** and **Kalember, P.**; (2011); "Correlation of cognitive functions with some aspects of illness, treatment and social functioning in recurrently hospitalized schizophrenic patients." Collegium Antropologicum **35**: 39-44; Times Cited: 1; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
11. Bajs-Janović, M., Kalember, P., Janovic, S., Hrabač, P., Grošić, P. F., Grošić, V., **Radoš, M.** and **Henigsberg, N.**; (2014); "No change in n-acetyl aspartate in first episode of moderate depression after antidepressant treatment: H-1 magnetic spectroscopy study of left amygdala and left dorsolateral prefrontal cortex." Neuropsychiatric Disease and Treatment **10**: 1753-1762; Times Cited: 0; CLINICAL NEUROLOGY-Q3, PSYCHIATRY-Q3; IF-2,154;
12. **Banfić, H.**, Bedalov, A., York, J. D. and **Višnjić, D.**; (2013); "Inositol pyrophosphates modulate s phase progression after pheromone-induced arrest in saccharomyces cerevisiae." Journal of Biological Chemistry **288**(3): 1717-1725; Times Cited: 1; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,600; 5-year IF-4,863.

13. **Banfić, H.**, Downes, C. P. and Rittenhouse, S. E.; (1998); "Biphasic activation of pkb alpha/akt in platelets - evidence for stimulation both by phosphatidylinositol 3,4-bisphosphate, produced via a novel pathway, and by phosphatidylinositol 3,4,5-trisphosphate." Journal of Biological Chemistry **273**(19): 11630-11637; Times Cited: 75; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,600; 5-year IF-4,863.
14. **Banfić, H.**, Tang, X. W., Batty, I. H., Downes, C. P., Chen, C. S. and Rittenhouse, S. E.; (1998); "A novel integrin-activated pathway forms pkb/akt-stimulatory phosphatidylinositol 3,4-bisphosphate via phosphatidylinositol 3-phosphate in platelets." Journal of Biological Chemistry **273**(1): 13-16; Times Cited: 105; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,600; 5-year IF-4,863.
15. **Banfić, H.**, **Višnjić, D.**, Miše, N., Balakrishnan, S., Deplano, S., Korchev, Y. E. and Domin, J.; (2009); "Epidermal growth factor stimulates translocation of the class ii phosphoinositide 3-kinase pi3k-c2 beta to the nucleus." Biochemical Journal **422**: 53-60; Times Cited: 6; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,779; 5-year IF-4,950.
16. **Banfić, H.**, Vuica, M., Knotek, M., Moslavac, S. and Divecha, N.; (1993); "Inositol lipid signaling occurs in brush-border membranes during initiation of compensatory renal growth in the rat." Biochemical Journal **295**: 599-605; Times Cited: 8; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,779; 5-year IF-4,950.
17. **Banfić, H.**, Žižak, M., Divecha, N. and Irvine, R. F.; (1993); "Nuclear diacylglycerol is increased during cell-proliferation invivo." Biochemical Journal **290**: 633-636; Times Cited: 107; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,779; 5-year IF-4,950.
18. Banovic, V., Skrablin, S., Banovic, M., **Radoš, M.**, Gveric-Ahmetasevic, S. and Babić, I.; (2014); "Fetal brain magnetic resonance imaging and long-term neurodevelopmental impairment." International Journal of Gynecology & Obstetrics **125**(3): 237-240; Times Cited: 0; OBSTETRICS & GYNECOLOGY-Q3; IF-1,562; 5-year IF-1,946.
19. Barić, H., Polšek, D., Andrijasevic, L. and **Gajović, S.**; (2013); "Open access - is this the future of medical publishing?"; Croatian Medical Journal **54**(4): 315-318; Times Cited: 1; MEDICINE, GENERAL & INTERNAL-Q2; IF-1,373; 5-year IF-1,603.
20. **Barić, I.**, Cuk, M., Fumic, K., Vugrek, O., Allen, R. H., Glenn, B., Maradin, M., Pažanin, L., Pogribny, I., **Radoš, M.**, Sarnavka, V., Schulze, A., Stabler, S., Wagner, C., Zeisel, S. H. and Mudd, S. H.; (2005); "S-adenosylhomocysteine hydrolase deficiency: A second patient, the younger brother of the index patient, and outcomes during therapy." Journal of Inherited Metabolic Disease **28**(6): 885-902; Times Cited: 36; GENETICS & HEREDITY-Q1, ENDOCRINOLOGY & METABOLISM-Q2; IF-4,138; 5-year IF-3,614.
21. **Barić, I.**, Fumic, K., Glenn, B., Cuk, M., Schulze, A., Finkelstein, J. D., James, S. J., **Mejaški-Bošnjak, V.**, Pažanin, L., Pogribny, I. P., **Radoš, M.**, Sarnavka, V., Scukanec-Spoljar, M., Allen, R. H., Stabler, S., Uzelac, L., Vugrek, O., Wagner, C., Zeisel, S. and Mudd, S. H.; (2004); "S-adenosylhomocysteine hydrolase deficiency in a human: A genetic disorder of methionine metabolism." Proceedings of the National Academy of Sciences of the United States of America **101**(12): 4234-4239; Times Cited: 92; MULTIDISCIPLINARY SCIENCES-Q1; IF-9,809; 5-year IF-10,727.
22. Barišić, I., Balenovic, D., Klicek, R., Radić, B., Nikitovic, B., Drmic, D., Udovicic, M., Strinic, D., Bardak, D., Berkopic, L., Djuzel, V., Sever, M., Cvjetko, I., Romic, Z., **Sindić, A.**, Bencic, M. L., Seiwerth, S. and Sikiric, P.; (2013); "Mortal hyperkalemia disturbances in rats are no-system related. The life saving effect of pentadecapeptide bpc 157." Regulatory Peptides **181**: 50-66; Times Cited: 1; ENDOCRINOLOGY & METABOLISM-Q3, PHYSIOLOGY-Q3; IF-2,014; 5-year IF-2,155.
23. **Barišić, N.**, Sertić, J., Billi, C., **Barić, I.**, Sarnavka, V., Babić, T., Hrabač, P., Begovic, D., Florentin, L. and Stavljenic-Rukavina, A.; (1998); "Molecular analysis and electromyoneurographic abnormalities in croatian children with proximal spinal muscular atrophies." Clinical Chemistry and Laboratory Medicine **36**(8): 667-669; Times Cited: 3; MEDICAL LABORATORY TECHNOLOGY-Q1; IF-2,955; 5-year IF-2,527.
24. Beara-Lasic, L., Knotek, M., Cejvan, K., Jakšić, O., Lasic, Z., Skoric, B., Brkljačić, V. and **Banfić, H.**; (1997); "The effect of big endothelin-1 in the proximal tubule of the rat kidney." British Journal of Pharmacology **120**(4): 625-630; Times Cited: 3; PHARMACOLOGY & PHARMACY-Q1; IF-4,990; 5-year IF-4,994.
25. Belovari, T., Stevic, N., **Gajović, S.** and **Kostović-Knežević, L.**; (2004); "Differentiation and developmental potential of rat post-implantation embryo without extra-embryonic membranes cultured in vitro or grafted in vivo." Anatomia Histologia Embryologia-Journal of Veterinary Medicine Series C **33**(2): 90-95; Times Cited: 1; VETERINARY SCIENCES-Q3, ANATOMY & MORPHOLOGY-Q4; IF-0,742; 5-year IF-0,745.

26. Benjak, V., Čuljat, M., Pavlovic, M. and Kostović-Srzić, M.; (2008); "Changes of the corpus callosum in children who suffered perinatal injury of the periventricular crossroads of pathways." *Collegium Antropologicum* **32**: 25-29; Times Cited: 6; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
27. Biermann, J., Lang, D., Gorboulev, V., Koepsell, H., Sindić, A., Schroter, R., Zvirbliene, A., Pavenstadt, H., Schlatter, E. and Ciarimboli, G.; (2006); "Characterization of regulatory mechanisms and states of human organic cation transporter." *American Journal of Physiology-Cell Physiology* **290**(6): C1521-C1531; Times Cited: 29; PHYSIOLOGY-Q1, CELL BIOLOGY-Q2; IF-3,674; 5-year IF-3,952.
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29. Boban, M., Brinar, V. V., Habek, M. and Radoš, M.; (2007); "Isolated hypoglossal nerve palsy: A diagnostic challenge." *European Neurology* **58**(3): 177-181; Times Cited: 7; CLINICAL NEUROLOGY-Q4, NEUROSCIENCES-Q4; IF-1,362; 5-year IF-1,685.
30. Boban, M., Grbić, K., Mladinov, M., Hof, P. R., Sussmair, C., Ackl, N., Stanic, G., Bader, B., Danek, A. and Šimić, G.; (2008); "Cerebrospinal fluid markers in differential diagnosis of alzheimer's disease and vascular dementia." *Collegium Antropologicum* **32**: 31-36; Times Cited: 11; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
31. Boban, M., Kostović, I. and Šimić, G.; (2006); "Nucleus subputaminalis: Neglected part of the basal nucleus of meynert." *Brain* **129**: 2005-2006; Times Cited: 1; CLINICAL NEUROLOGY-Q1, NEUROSCIENCES-Q1; IF-10,226; 5-year IF-10,846.
32. Boban, M., Malojcic, B., Mimica, N., Vukovic, S., Zrilic, I., Hof, P. R. and Šimić, G.; (2012); "The reliability and validity of the mini-mental state examination in the elderly croatian population." *Dementia and Geriatric Cognitive Disorders* **33**(6): 385-392; Times Cited: 7; CLINICAL NEUROLOGY-Q2, GERIATRICS & GERONTOLOGY-Q2, PSYCHIATRY-Q2; IF-2,812; 5-year IF-2,960.
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34. Bohaček, I., Cordeau, P., Lalancette-Hebert, M., Gorup, D., Weng, Y. C., Gajović, S. and Križ, J.; (2012); "Toll-like receptor 2 deficiency leads to delayed exacerbation of ischemic injury." *Journal of Neuroinflammation* **9**: 17; Times Cited: 17; IMMUNOLOGY-Q1, NEUROSCIENCES-Q1; IF-4,902; 5-year IF-5,473.
35. Bosnar, M. H., De Gunzburg, J., Bago, R., Brečević, L., Weber, I. and Pavelić, J.; (2004); "Subcellular localization of a and b nm23/ndpk subunits." *Experimental Cell Research* **298**(1): 275-284; Times Cited: 30; ONCOLOGY-Q2, CELL BIOLOGY-Q3; IF-3,246; 5-year IF-3,377.
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38. Brečević, L., Basaran, S., Dutly, F., Rothlisberger, B. and Schinzel, A.; (2000); "Tandem triplication of chromosome 13q14 with inverted interstitial segment in a 4 year old girl." *Journal of Medical Genetics* **37**(12): 964-967; Times Cited: 7; GENETICS & HEREDITY-Q1; IF-6,335; 5-year IF-5,855.
39. Brečević, L., Michel, S., Starke, H., Muller, K., Kosyakova, N., Mrasek, K., Weise, A. and Liehr, T.; (2006); "Multicolor fish used for the characterization of small supernumerary marker chromosomes (ssmq) in commercially available immortalized cell lines." *Cytogenetic and Genome Research* **114**(3-4): 319-324; Times Cited: 9; CELL BIOLOGY-Q4, GENETICS & HEREDITY-Q4; IF-1,561; 5-year IF-1,764.
40. Brečević, L., Rincic, M., Krsnik, Z., Sedmak, G., Hamid, A. B., Kosyakova, N., Galic, I., Liehr, T. and Borovečki, F.; (2015); "Association of new deletion/duplication region at chromosome 1p21 with intellectual disability, severe speech deficit and autism spectrum disorder-like behavior: An all-in approach to solving the dpyd enigma." *Translational Neuroscience* **6**(1): 59-86; Times Cited: 0; NEUROSCIENCES-Q4; IF-0,716;

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42. Bregant, T., Radoš, M., Derganc, M., Neubauer, D. and Kostović, I.; (2011); "Pineal cysts - a benign consequence of mild hypoxia in a near-term brain?"; Neuroendocrinology Letters **32**(5): 663-666; Times Cited: 1; ENDOCRINOLOGY & METABOLISM-Q4, NEUROSCIENCES-Q4; IF-0,935; 5-year IF-1,131.
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550. Uzun, S., Mimica, N., **Folnegović-Šmalc, V.**, Markan-Sosic, V. and Ljubin, T.; (2003); "Ziprasidone: An overview of clinical trials of a novel antipsychotic conducted in croatia." Periodicum Biologorum **105**(1): 71-80; Times Cited: 0; BIOLOGY-Q3; IF-0,180;
551. Van Eden, C. G., Mrzljak, L., Voorn, P. and Uylings, H. B. M.; (1989); "Prenatal development of gaba-ergic neurons in the neocortex of the rat." Journal of Comparative Neurology **289**(2): 213-227; Times Cited: 194; ZOOLOGY-Q1, NEUROSCIENCES-Q2; IF-3,508; 5-year IF-3,841.
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556. Vidovic, V., **Henigsberg, N.** and Juresa, V.; (2003); "Anxiety and defense styles in eating disorders." Collegium Antropologicum **27**: 125-134; Times Cited: 2; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
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578. **Vukšić, M.**, Del Turco, D., Vlachos, A., Schuldt, G., Muller, C. M., Schneider, G. and Deller, T.; (2011); "Unilateral entorhinal denervation leads to long-lasting dendritic alterations of mouse hippocampal granule cells." Experimental Neurology **230**(2): 176-185; Times Cited: 9; NEUROSCIENCES-Q1; IF-4,617; 5-year IF-4,478.
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581. **Vukšić, M.**, **Radoš, M.** and **Kostović, I.**; (2008); "Structural basis of developmental plasticity in the corticostriatal system." Collegium Antropologicum **32**: 155-159; Times Cited: 5; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
582. Vyas, A. A., Patel, H. V., Fromholt, S. E., **Heffer-Lauc, M.**, Vyas, K. A., Dang, J. Y., Schachner, M. and Schnaar, R. L.; (2002); "Gangliosides are functional nerve cell ligands for myelin-associated glycoprotein (mag), an inhibitor of nerve regeneration." Proceedings of the National Academy of Sciences of the United States of America **99**(12): 8412-8417; Times Cited: 176; MULTIDISCIPLINARY SCIENCES-Q1; IF-9,809; 5-year IF-10,727.
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586. Zeba, M., **Jovanov-Milošević, N.** and **Petanjek, Z.**; (2008); "Quantitative analysis of basal dendritic tree of layer iiic pyramidal neurons in different areas of adult human frontal cortex." Collegium Antropologicum **32**: 161-169; Times Cited: 7; ANTHROPOLOGY-Q3; IF-0,609; 5-year IF-0,586.
587. Zhang, J., **Banfić, H.**, Straforini, F., Tosi, L., Volinia, S. and Rittenhouse, S. E.; (1998); "A type ii phosphoinositide 3-kinase is stimulated via activated integrin in platelets - a source of phosphatidylinositol 3-phosphate." Journal of Biological Chemistry **273**(23): 14081-14084; Times Cited: 81; BIOCHEMISTRY & MOLECULAR BIOLOGY-Q1; IF-4,600; 5-year IF-4,863.
588. Zmajević, M., **Klarica, M.**, Varda, R., Kudelic, N. and **Bulat, M.**; (2002); "Elimination of phenolsulfonphthalein from the cerebrospinal fluid via capillaries in central nervous system in cats by active transport." Neuroscience Letters **321**(1-2): 123-125; Times Cited: 19; NEUROSCIENCES-Q3; IF-2,055; 5-year IF-2,201.
589. Zuntar, I., **Kalanj-Bognar, S.**, Topic, E., Petlevski, R., Stefanovic, M. and Demarin, V.; (2004); "The glutathione s-transferase polymorphisms in a control population and in alzheimer's disease patients." Clinical Chemistry and Laboratory Medicine **42**(3): 334-339; Times Cited: 11; MEDICAL LABORATORY TECHNOLOGY-Q1; IF-2,955; 5-year IF-2,527.

PRILOG 2. Popis obranjenih diplomskih radova te Rektorovih i Dekanovih nagrada

ANNEX 2: List of graduates, Rector's and Dean's awards

Diplomirali do 1990. / Graduated to 1990

1. Judaš Miloš (1984) Morfološke i funkcionalne asimetrije čovječjeg mozga. Diplomski rad. (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
2. Kalanj Bognar Svjetlana (1989) Gangliozidi mozga u Alzheimerovoj bolesti. Diplomski rad. (mentor: Ivan Kračun). Medicinski fakultet Sveučilišta u Zagrebu
3. Heffer Marija (1989) Promjene gangliozida u mozgu pilećeg embrija in vitro. Diplomski rad. (mentor: Ivan Kračun). Medicinski fakultet Sveučilišta u Zagrebu.

Diplomirali od 1991. do 1999. / Graduated from 1991 to 1999

1. Šimić Goran (1992) Računalska obrada mozgovih Zagrebačke neuroembriološke zbirke. Diplomski rad. (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
2. Milas Ivan (1992) Regulacija intrakranijskog tlaka. Diplomski rad. (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu.
3. Jovanov Nataša (1995) Svojstva hemaglutinacije, elucije i termorezistencije sojeva virusa Newcastle-ske bolesti izoliranih u Hrvatskoj. Diplomski rad. Veterinarski fakultet Sveučilišta u Zagrebu
4. Šestan Nenad (1995) Stanični razmještaj imunoreaktivnosti na sintetazu I dušikova monoksida i NADPH dijaforazne aktivnosti u moždanoj kori čovjeka. Diplomski rad. (mentor: Miloš Judaš) Medicinski fakultet Sveučilišta u Zagrebu.
5. Vučković Ante (1995) Ispitivanje nastajanja likvora u izoliranim moždanim komorama. Diplomski rad. (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu.
6. Ilčić Marija (1997) Vrste privremenih fetalnih neurona u ljudskoj moždanoj kori. Diplomski rad. (mentor: Miloš Judaš). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, Biološki odsjek.
7. Darmopil Sanja (1999) Pojavljivanje i raspodjela nitrinergičkih neurona u marginalnoj zoni moždane kore tijekom razvoja ljudskog fetusa. Diplomski rad. (mentor: Miloš Judaš) Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, Biološki odsjek.
8. Ozretić David (1999) Ekspresija NADPH-d reaktivnosti u subpopulaciji migrirajućih i njima sličnih neurona u stijenci telencefalona ljudskih fetusa. Diplomski rad. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Diplomirali od 2000. do 2015. / Graduated from 2000 to 2015:

2001.:

1. Puljić Ružica (2001) Farmakologija intrakranijskog tlaka. Diplomski rad. (mentor: Marijan Klarica). Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu.
2. Runjić Marina (2001) Atipični komunikacijski razvoj. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Talapko Bojana (2001) Mehanizam djelovanja manitola pri povišenom intrakranijskom tlaku. Diplomski rad. (mentor: Marijan Klarica). Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu.

2002.:

1. Bagarić Ana-Marija (2002) Model poticanja neverbalne komunikacije. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
2. Piacun Martina (2002) Predlingvistički razvoj i pojava verbalne komunikacije. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.

2003.:

1. Grizelj Martino (2003) Perinatalni razvitak NADPHd-reaktivnih neurona bazalnog telencefalona u mozgu čovjeka. Diplomski rad. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.
2. Krstulović Marina (2003) Pragmatički poremećaj kod djece. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Sporiš Biljana (2003) Komunikacijski i jezični razvoj u djece s perinatalnim oštećenjem mozga. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.

2004.:

1. Golubić Anita (2004) Neurobiologija posttraumatskog stresnog poremećaja. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
2. Matković Katarina (2004) Mehanizam djelovanja inzulina na stanice leukemijske linije HL-60. Diplomski rad. (mentor: Dora Višnjić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu - Biološki odsjek.
3. Zeba Martina (2004) Usporedba morfologije asocijativnih neurona različitih područja čeonog režnja kore velikog mozga u čovjeka. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.

2005.:

1. Gavranović Ivana (2005) Komunikacija djeteta s Downovim sindromom. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
2. Lulić Sonja (2005) Analiza interakcije majak-dijete u spontanoj igri kod djece s perinatalnim oštećenjima mozga. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Perić Jelena (2005) Izolacija DNA iz tumorskog tkiva te umnažanje gena CDH1 i APC. Diplomski rad. (mentor: Nives Pećina-Šlaus). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.

2006.:

1. Mihoković Ana (2006) Mehanizam djelovanja manitola u liječenju intrakranijske hipertenzije. Diplomski rad. (mentor: Marijan Klarica). Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu.

2007.:

2. Brzić Tina (2007) Neurobiologija kognitivnog stresa. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
3. Knežević Ana (2007) Protein kinaza C u jezgrama stanica HL-60. Diplomski rad. (mentor: Dora Višnjić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu - Biološki odsjek.
4. Lončar Vera (2007) Poremećaj pažnje i hiperaktivnost. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
5. Markanjević Ivana (2007) Neurobiološka osnova disleksije. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
6. Petrovečki Kristina (2007) Neurobiologija Alzheimerove bolesti i ostalih demencija u usporedbi s normalnim starenjem. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
7. Ranilović Aleksandra (2007) Razlike između muškog i ženskog mozga. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
8. Lehner Ulrike (2007, Münster) Ligands and signaling of the G-protein-coupled receptor, GPR14, expressed in human kidney cells (mentor: Aleksandra Sinđić) (Med Klinik und Poliklinik D, Exp Nephrologie, Universitätsklinikum Münster) – kasnije rad: Lehner U, Velic A, Schlatter E, Sinđić A (2007) Ligands and signaling of the G-protein-coupled receptor, GPR14, expressed in human kidney cells. *Cell Physiol Biochem* 20:181-192.

2008.:

1. Crnković Maja (2008) Električna aktivnost moždane kore i kreativnost. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije
2. Mušinović Hana (2008) Analiza izraženosti proteina beta-*katenina* u neuroepitalnim tumorima mozga. Diplomski rad. (mentor: Nives Pećina Šlaus). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
3. Vasung Martina (2008) Polimorfizam gena glutation S-transferaze P1 i multiple skleroza. Diplomski rad. (mentori: Irena Žuntar i Svjetlana Kalanj Bognar). Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu.

2009.:

1. Cvitković Marion (2009) Praćenje ranog komunikacijskog razvoja pomoću ljestvice ranoga dječjega razvoja. Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
2. Gmajnić Iva (2009) Rani komunikacijski razvoj u djece u domskom smještaju. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Gudeljević Ivana (2009) Zdržena pažnja: kako je odrasli razumiju i potiču? Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
4. Kiš Ivona (2009) Obaviještenost roditelja o ranom jezično-govornom razvoju. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
5. Kulenović Lana (2009) Prozopagnozija. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
6. Majić Željka (2009) Analize promjena gena CTNNA1 i APC u metastazama mozga. Diplomski rad. (mentor: Nives Pećina Šlaus). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
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8. Sesar Ivana (2009) Neurobiologija psihopatije. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.

2010.:

1. Bačić Niko (2010) Promjena gena NF2 u neurinomima. Diplomski rad. (mentor: Nives Pećina Šlaus). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
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3. Kologranić Lana (2010) Primjena komunikacijske ljestvice u roditelja djece s teškoćama socijalne komunikacije. Diplomski rad. (mentori: Marta Ljubešić i Sanja Šimleša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
4. Meštrović Klara (2010) Neurobiologija kognitivnog razvoja u adolescenciji. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.

2011.:

1. Baćani Suzana (2011) Prevencija suicida kod bolesnika s psihijatrijskim poremećajima. Diplomski rad. (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
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4. Domazet Ivan (2011) Prikaz lezija spinalnog kanala na MR. Diplomski rad. (mentor: Marko Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
5. Feješ Andrea (2011) Poticanje komunikacije i jezika u djeteta s teškoćama socijalne komunikacije. Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.

6. Jagatić Tomislav (2011) A novel therapeutic approach to autism: review. Diplomski rad. (mentor: Goran Šimić). Medicinski fakultet Sveučilišta u Zagrebu.
7. Jerečić Ivana (2011) Uporaba potpomognute komunikacije u logopedskoj praksi. Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
8. Marčelja Vlatka (2011) Uloga socijalnog pedagoga u konzilijarnoj terapiji osoba s PTSP-om. Diplomski rad. (mentor: Neven Henigsberg). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
9. Melada Anja (2011) Istraživanja psihijatrijskih poremećaja spektroskopijom putem magnetske rezonancije. Diplomski rad. (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
10. Paladin Ivan (2011) Kvalitativna i kvantitativna obilježja morfologije dendrita u subpopulaciji projekcijskih neurona infragranularnih slojeva prefrontalnog korteksa u čovjeka. Diplomski rad. (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.
11. Perković Franjić Jelena (2011) Logopedska intervencija u obitelji kod djeteta s poremećajem iz autističnog spektra (prikaz slučaja). Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
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13. Ropac Morana (2011) Selektivni mutizam: intervencija u vrtiću. Diplomski rad. (mentori: Marta Ljubešić i Sanja Šimleša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
14. Sabo Tamara (2011) Farmakoterapija depresije. Diplomski rad. (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
15. Sitaš Barbara (2011) Ekstracelularni matriks u razvitku ljudskog telencefalona. Diplomski rad. (mentor: Nataša Jovanov Milošević). Medicinski fakultet Sveučilišta u Zagrebu.
16. Strmečki Marija (2011) Rani komunikacijski razvoj u prijevremeno rođene djece. Diplomski rad. (mentori: Marta Ljubešić i Maja Capanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
17. Šimović Sanja (2011) Praćenje jezično-govornog razvoja tijekom druge godine života djeteta (prikaz slučaja). Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
18. Težak Dijana (2011) Rodne razlike u ranom komunikacijskom razvoju. Diplomski rad. (mentori: Marta Ljubešić i Maja Capanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
19. Veir Hrvoje (2011) Neurobiologija motoričkih poremećaja bazalnih ganglija. Diplomski rad. (mentor: Sanja Darmopil). Medicinski fakultet Sveučilišta u Zagrebu.
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21. Žaja Mate (2011) Dopaminergički putevi i receptori. Diplomski rad. (mentor: Goran Šimić). Medicinski fakultet Sveučilišta u Zagrebu.

2012.:

1. Dembitz Vilma (2012) Rapamicin i sve-trans-retinska kiselina pospješuju učinke arsenova trioksida na proliferaciju leukemijskih stanica. Diplomski rad. (mentor: Dora Višnjić). Medicinski fakultet Sveučilišta u Zagrebu.
2. Galkowski Valentina (2012) Morfološki parametri talamokortikalnih odnosa u čovjeka na magnetnoj rezonanciji. Diplomski rad. (mentor: Milan Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
3. Gašpar Maja (2012) Magnetska rezonancija u dijagnostici degenerativnih promjena vratne kralježnice. Diplomski rad. (mentor: Marko Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
4. Grizelj Mateja (2012) Varijabilnost veličine odraslog ljudskog mozga. Diplomski rad. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.
5. Kokotović Tomislav (2012) Ubikvitin i sinaptička plastičnost. Diplomski rad. (mentor: Svjetlana Kallan Bognar). Medicinski fakultet Sveučilišta u Zagrebu.

6. Kucijan Zdravka (2012) Analiza diferencijacijskog potencijala živčanih matičnih stanica stereotaksijski transplantiranih u mozak miša. Diplomski rad. (mentor: Dinko Mitrečić). Medicinski fakultet Sveučilišta u Zagrebu.
7. Nenadić Jelena (2012) Neurobiologija poremećaja jedenja. Diplomski rad. (mentor: Zdravko Petanjek). Hrvatski studiji – studij psihologije.
8. Pap Mislav (2012) Mozak čovjekolikih majmuna. Diplomski rad. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.
9. Paulić Mateja (2012) Povezanost rezultata na ljestvici CSBS i procjene ekspresivne komunikativnosti u predškolske djece s poremećajima socijalne komunikacije. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
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11. Raguz Marina (2012) Morfologija premotoričkog korteksa u čovjeka na magnetnoj rezonanciji. Diplomski rad. (mentor: Milan Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
12. Tantegl Vedran (2012) Rasvjetljavanje uloga moždanih gangliozida primjenom genetički preinačenih mišjih modela. Diplomski rad. (mentor: Svjetlana Kalanj Bognar). Medicinski fakultet Sveučilišta u Zagrebu.
13. Židov Maja (2012) Analiza gena Axin-1 u meningeomima. Diplomski rad. (mentor: Tamara Nikuševa-Martić). Medicinski fakultet Sveučilišta u Zagrebu.
14. Županić Sven (2012) Regionalne razlike podslojeva subventrikularne zone u stijenci telencefalona čovjeka. Diplomski rad. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

2013.:

1. Caren Tamara (2013) Percepcija kliničkih ispitivanja u javnosti. Diplomski rad. (mentor: Neven Henningsberg). Zdravstveno veleučilište Zagreb
2. Čalić Ana (2013) Potpomognuta komunikacija kod djeteta s Downovim sindromom. Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Gačić Martina (2013) Molekule stanične adhezije kao biljezi plastičnosti u hipokampalnom tkivu u neurodegeneraciji. Diplomski rad. (mentor: Svjetlana Kalanj Bognar). Medicinski fakultet Sveučilišta u Zagrebu.
4. Grgurić Maja (2013) Primjena ljestvice KORALJE kod djece s poremećajima socijalne komunikacije. Diplomski rad. (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
5. Habek Nikola (2013) Čimbenik prepisivanja KLF8 nalazi se u mozgu miša samo u živčanim stanicama. Diplomski rad. (mentor: Srećko Gajović). Medicinski fakultet Sveučilišta u Zagrebu
6. Ilić Katarina (2013) Izražaj neuroplastina u ljudskom hipokampusu tijekom fetalnog razvoja. Diplomski rad. (mentor: Svjetlana Kalanj Bognar). Medicinski fakultet Sveučilišta u Zagrebu.
7. Kuktin Aleksandar (2013) Generiranje respiratornog ritma. Diplomski rad. (mentor: Mario Vukšić). Medicinski fakultet Sveučilišta u Zagrebu.
8. Kuštek Ivana (2013) Ukupni i fosforilirani tau proteini pT231 u likvoru kao biološki biljezi Alzheimerove bolesti. Diplomski rad. (mentor: Goran Šimić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
9. Miše Joško (2013) Učinci inhibitora signalnih puteva Ras/Raf/MEK/ERK i PI3K/Akt/mTOR na diferencijaciju leukemijskih stanica potaknutu s PMA. Diplomski rad. (mentor: Dora Višnjic). Medicinski fakultet Sveučilišta u Zagrebu.
10. Pleskalt Matea (2013) Rana logopedska procjena: analiza podataka iz Kabineta za ranu komunikaciju. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
11. Rubik Karolina (2013) Učinak guanilinskih peptida na signalni sustav bradikinina u kulturi HEK293 stanica. Diplomski rad. (mentor: Aleksandra Sinđić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
12. Sukser Viktorija (2013) Razina izraženosti transkripcijskog faktora LEF-1 u glioblastomima. Diplomski rad. (mentor: Nives Pećina Šlaus). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.

13. Veljača Jelena (2013) Poticanje komunikacijskog razvoja kod djeteta s poremećajem iz autističnog spektra. Diplomski rad. (mentori: Marta Ljubešić i Jasmina Ivšac Pavliša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.

2014.:

1. Brdarić Blanka (2014) Uloga humanoidnih robota u dijagnostici autizma djece predškolske dobi. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
2. Ćurić Marija (2014) Razlikovanje djece s poremećajem iz autističnog spektra i djece urednog razvoja na ADOS-u. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Jurin Anamarija (2014) Prepoznavanje emocija kod djece predškolske dobi. Diplomski rad. (mentori: Marta Ljubešić i Maja Cepanec). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
4. Lukić Ljiljana (2014) Izražaj tenascina C u sloju pod pločom čeonog režnja mozga čovjeka tijekom prenatalnog razvoja. Diplomski rad. (mentor: Nataša Jovanov Milošević). Medicinski fakultet Sveučilišta u Zagrebu.
5. Mandić Dora (2014) Volumetrijska analiza razvoja kortikalne i subkortikalne sive tvari kod čovjeka. Diplomski rad. (mentor: Milan Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
6. Mastelić Tea (2014) Sociodemografski prediktori prepoznavanja emocija u djece predškolske dobi. Diplomski rad. (mentori: Marta Ljubešić i Sanja Šimleša). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
7. Rak Benedict (2014) Javnozdravstveno značenje depresivnog poremećaja. Diplomski rad. (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.

2015.:

1. Kopčok Ivana (2015) Utjecaj epigalokatehin-3-galata na staničnu smrt izazvanu okadaičnom kiselinom. Diplomski rad. (mentor: Goran Šimić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
2. Langer Lea (2015) Utjecaj inhibitora monoamino oksidaze A i B na fosforilaciju tau proteina – terapijski učinak u Alzheimerovoj bolesti. Diplomski rad. (mentor: Goran Šimić). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.

DOBITNICI REKTOROVE NAGRADE / RECIPIENTS OF THE RECTOR'S AWARD:

Akademski godina 1997./1998.:

Mladen-Roko Rašin i Martino Grizelj: Morfologija kortikalnih neurona impregniranih Golgijevom metodom u semilobarnoj holoprosencefaliji. (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.

Akademski godina 1998./1999.

Dinko Mitrečić: Razvoj kaudalnog dijela zametka u splotch i truncate miševa. (mentor: Srećko Gajović). Medicinski fakultet Sveučilišta u Zagrebu.

David Ozretić: Ekspresija NADPH-d reaktivnosti u subpopulaciji migrirajućih i njima sličnih neurona u stijenci telencefalona ljudskih fetusa. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Akademski godina 2000./2001.:

Tina Tomić i Romana Ptičar: Učinak obogaćene sredine na morfologiju piramidnih neurona okcipitalnog korteksa u starenju kod štakora. (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.

Akademski godina 2001./2002.

Pero Hrbač: Različite metode bojanja prolaznih struktura u fetalnom korteksu. (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.

Jelena Bošnjak i Alma-Martina Cepika: Prekomjerna produkcija elemenata kortikalnih krugova u asocijativnom prefrontalnom korteksu čovjeka prisutna je tijekom adolescencije i korelira s produženim kognitivnim razvojem. (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.

Martina Zeba, Marija Krmek, Marija Šakić: Usporedba strukture dendritičkog stabla piramidnih živčanih stanica u funkcionalno različitim područjima kore velikog mozga u čovjeka. (mentor: Zdravko Petanjek) Hrvatski studiji – studij psihologije

Akademska godina 2004./2005.

Lana Đonlagić: Aktivacija fosfolipaze C u jezgrama stanica HL 60 tijekom G₂/M i kasne G₁ faze staničnog ciklusa. (mentor: Hrvoje Banfić). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2005./2006.

Raphael Béné: Razvoj morfoloških tipova i dendritičkog razgranjenja nitrinergičkih neurona u neostrijatumu čovjeka. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Ivana Pogledić: Pilocitični astrocitomi dna treće mozgovne komore. Medicinski fakultet Sveučilišta u Zagrebu.

Perić Jelena: Usporedba dviju metoda izolacije genomske DNA iz tumora središnjeg živčanog sustava čovjeka. (mentor: Nives Pećina-Šlaus).

Radić Krešimir: Genske nestabilnosti gena prigušivača tumora E-kadherin i APC kod karcinoma bubrega. (mentor: Nives Pećina-Šlaus)

Akademska godina 2006./2007.

Goran Sedmak: Razvoj dendrita neokortikalnih neurona u lisencefaliji tipa II (syndroma Walker-Warburg) (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Domagoj Dlaka i Lana Vasung: Prognostički čimbenici i čimbenici ishoda liječenja radiokirurgijom gama nožem bolesnika oboljelih od refraktorne idiopatske neuralgije trigeminusa. (mentor: Darko Chudy). Medicinski fakultet Sveučilišta u Zagrebu.

Martina Zeljko: Promjene gena E-kadherina u metastazama u mozgu. (mentor: Nives Pećina-Šlaus). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2007./2008.

Tomislav Kokotović: Istraživanje ekspresije aksina u neuroepitelnim tumorima mozga. (mentor: Nives Pećina-Šlaus). Medicinski fakultet Sveučilišta u Zagrebu.

Mihovil Pletikos i Siniša Roginić: Razvoj nitrinergičkih neurona fetalne subplate zone u moždanoj kori čovjeka. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2008./2009.

Ivan Paladin: Kvalitativna i kvantitativna obilježja morfologije dendrita u subpopulaciji projekcijskih neurona infragranularnih slojeva prefrontalnog korteksa u čovjeka (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.

Joško Miše: Učinci inhibitora signalnih puteva RAS/RAF/MEK/ERK i PI3K/AKTmTOR na diferencijaciju leukemijskih stanica potaknutu s PMA. (mentor: Dora Višnjić). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2009./2010.

Vilma Dembitz: Rapamicin i sve-trans-retinska kiselina pojačavaju učinak arsenovog trioksida na proliferaciju leukemijskih stanica (mentor: Dora Višnjić). Medicinski fakultet Sveučilišta u Zagrebu.

Zdravka Kucijan i Vedran Tantegl: Genski izražaj neuroplastina u moždanom tkivu miševa s nedostatnom sintezom gangliozida (mentor: Svjetlana Kalanj Bogнар). Medicinski fakultet Sveučilišta u Zagrebu.

Janko Orešković i Radovan Prijčić: Fizikalne karakteristike novog modela cerebrospinalnog likvora. (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2010./2011.

Martina Gačić i Katarina Ilić: Izražaj neuroplastina u tkivu hipokampusu u Alzheimerovoj bolesti (mentor: Svjetlana Kalanj Bogнар). Medicinski fakultet Sveučilišta u Zagrebu.

Nikola Habek: Čimbenik prepisivanja KLF8 nalazi se u mozgu miša samo u živčanim stanicama (mentor: Srećko Gajović). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2011./2012.

Ljiljana Lukić: Izražaj tenascina C u sloju pod pločom čeonog režnja mozga čovjeka tijekom prenatalnog razvitka (mentor: Nataša Jovanov-Milošević). Medicinski fakultet Sveučilišta u Zagrebu.

Akademska godina 2012./2013.

Ivan Prepolec: 5-aminoimidazol-4-karboksiamid-1-β-D-ribofuranozid potiče nakupljanje leukemijskih stanica u S-fazi (mentor: Dora Višnjić). Medicinski fakultet Sveučilišta u Zagrebu.

DEKANOVA NAGRADA ZA NAJBOLJI STUDENTSKI ZNANSTVENI RAD / DEAN'S AWARD FOR THE BEST STUDENT SCIENTIFIC WORK:

Akadska godina 2006./2007.

Ivana Zobić i Boris Bene: Volumen temporalnog roga lateralnih moždanih komora u poremećajima s psihotičnim obilježjima. (Mentor: Elizabeta Radonić). Medicinski fakultet Sveučilišta u Zagrebu.

Akadska godina 2010./2011.

Mislav Pap i Sven Županić: Regionalne razlike podslojeva subventrikularne zone u stijenci telencefalona čovjeka. (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.

Akadska godina 2011./2012.

Marina Raguz i Valentina Galkowski: Postnatalne promjene u odnosu volumena moždanog tkiva i endokranijalnog volumena. (mentor: Milan Radoš). Medicinski fakultet Sveučilišta u Zagrebu.

Akadska godina 2012./2013.

Leon Marković i Petar-Krešimir Okštajner: Čimbenici transkripcije TCF-1 i LEF-1 uključeni u signalni put WNT izraženi su u tumorima mozga astrocitomima. (mentor: Nives Pećina-Šlaus). Medicinski fakultet Sveučilišta u Zagrebu.

PRILOG 3. Popis obranjenih magistarskih radova.

ANNEX 3: Master's theses

Magistrirali do 1990.

1. Kostović Ivica (1970) Akcesorni vidni putovi nekih sisavaca. **Magistarski rad.** (mentor: Jelena Krm-potić) Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.
2. Kelović Zlatko (1979) Vanjski aferentni sustavi hipokampusa u fetusa čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
3. Miklić Pavle (1980) Rani prenatalni razvitak dubokih slojeva slušnog korteksa u fetusa čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
4. Štampalija Ante (1980) Prenatalni razvoj gornjih kolikula u čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
5. Kračun Ivan (1983) Citoarhitektonska građa bazalnog telencefalona u mozgu fetusa čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
6. Mrzljak Ladislav (1983) Razvitak prepiriformnog korteksa u fetusa čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
7. Bexheti Sadi (1985) Odnos između endoplastike i modularne organizacije entorinalne areje čovjeka. **Magistarski rad.** (mentor: Zlatko Kelović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
8. Fučić Aleksandra (1985) Razvitak intersticijskih neurona u prednjoj komisuri čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
9. Kukolja Sunčana (1986) Utjecaj plazme uninefektomiranih štakora na ugradnju 32P u fosfolipide bubrenih ploški. **Magistarski rad.** (mentor: Hrvoje Banfić). Medicinski fakultet Sveučilišta u Zagrebu.
10. Mijić August (1986) Morfologija i laminarna distribucija neurona u ranoj osnovi frontalnog korteksa fetusa čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
11. Judaš Miloš (1987) Perinatalni razvoj citoarhitektonike prospektivnih motoričkih područja za govor u čeonom režnju čovjeka. **Magistarski rad.** (mentor: Ivica Kostović) Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
12. Klarica Marijan (1988) Uloga osmotski aktivnih tvari u regulaciji intrakranijalnog tlaka. **Magistarski rad.** (mentor: Marin Bulat). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
13. Krušlin Božo (1988) Čimbenici rasta u malignim tumorima ljudi. **Magistarski rad.** (mentor: Krešimir Pavelić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
14. Vlačić Anton (1988) Utjecaj aktivnog transporta na distribuciju tvari u cerebrospinalnom likvoru. **Magistarski rad.** (mentor: Marin Bulat). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
15. Delalle Ivana (1990) Ontogeneza peptidgergičke inervacije perfrontalnog korteksa: laminarna distribucija neurona prepoznatih NPY-protutijelom. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.

Magistralni od 1991. do 1999.

1. Crljen-Manestar Vladiana (1991) Djelovanje inzulinu sličnog nadzornika rasta i na metabolizam fosfolipida u kortikalnim bubrežnim ploškama. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
2. Žižak Mirza (1992) Promjene metabolizma inozitol lipidnog kruga u staničnim jezgrama tijekom kompenzacijskog rasta jetre i bubrega. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
3. Ajhler Tatjana (1994) Učinak antidepressiva na kinetiku unosa i razinu serotonina u štakorskim trombocitima. **Magistarski rad.** (mentor: Branimir Jernej). Medicinski fakultet Sveučilišta u Zagrebu.
4. Fröbe Ana (1994) Eksperimentalna metoda praćenja kinetike aktivnog unosa serotonina u trombocite štakora. **Magistarski rad.** (mentor: Branimir Jernej). Medicinski fakultet Sveučilišta u Zagrebu.
5. Henigsberg Neven (1994) **Magistarski rad.** Medicinski fakultet Sveučilišta u Zagrebu.
6. Petanjek Zdravko (1994) Postnatalni razvitak dendritičnih trnova piramidnih neurona u prefrontalnom korteksu čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
7. Knotek Mladen (1995) Istraživanje uloge endotelina-1 kao stimulatora fosfolipaze C u četkastim membranama proksimalnih kanalića štakorskog bubrega. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
8. Renić Marija (1995). Histološke i funkcionalne promjene u jetri miševa s eksperimentalno izazvanim oštećenjem jetre. **Magistarski rad.** (mentor: Filip Čulo). Medicinski fakultet Sveučilišta u Zagrebu.
9. Šimić Goran (1995) Procjena broja neurona hipokampalne formacije pomoću optičkog disektora u normalnih i osoba oboljelih od Alzheimerove bolesti. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
10. Beara-Lasić Lada (1996) Učinak proendotelina-1 na stanice proksimalnog kanalića štakorskog bubrega. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
11. Hranilović Dubravka (1996) Serotoninski prijenosnik: veza između kontrolirane selekcije i ekspresije gena na modelu štakora. **Magistarski rad.** (mentor: Branimir Jernej). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
12. Vukelić Željka (1997) Metabolizam sfingolipida u bolesti chondrodysplasia rhizomelica punctata. **Magistarski rad.** (mentor: Ivan Kračun). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
13. Vukić Miroslav (1997) Učinak akutne opstrukcije Sylvijevog akvedukta na intrakranijski tlak i razvoj hidrocefalusa. **Magistarski rad.** (mentor: Marijan Klarica). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
14. Čizmić Ante (1999) Vrijednost određivanja ekspresije proliferacijskih obilježivača PCNA, Ki-67 te bcl-2 i p53 u kongenitalnim tumorima. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
15. Čupić Hrvoje (1999) Vrijednost određivanja izraženosti proliferacijskih obilježivača (PCNA, Ki-67) te bcl-2 i p53 u diferenciranim tumorima štitne žlijezde. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
16. Jakšić Ozren (1999) Odnos kliničkih obilježja i tumorskih biljega u serumu i limfocitima periferne krvi u kroničnoj limfocitnoj leukemiji. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
17. Jukić Tomislav (1999) Učinak stenozne spinalnog subarahnoidnog prostora na intrakranijski tlak i razvoj hidrocefalusa. **Magistarski rad.** (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski studij iz Pretkliničke i eksperimentalne farmakologije.

Magistralni od 2000. do 2015.

2000.

1. Ilčić Marija (2000) Istraživanje mišjeg gena *Lobel* pronađenog postupkom genske zamke. **Magistarski rad.** (mentor: Srećko Gajović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
2. Varda Robert (2000) Učinak manitola na intrakranijski tlak u stenozi spinalnog subarahnoidnog prostora. **Magistarski rad.** (mentor: Marijan Klarica) Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.

2001.

1. Glunčić Vicko (2001) Stereološka usporedba broja neurona u jediničnom volumenu primarnog motoričkog, osjetnog i vidnog polja moždane kore čovjeka. **Magistarski rad.** (mentor: Miloš Judaš). Medicinski fakultet Sveučilišta u Zagrebu.
2. Jovanov Nataša (2001) Utjecaj semaforina 5a na rast neokortikalnih aksona miša in vitro. **Magistarski rad.** (mentori: Jürgen Bolz (Jena), Draško Šerman i Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
3. Krsnik Željka (2001) Postnatalni razvitak Cajal-Retziusovih stanica u primarnoj vidnoj i asocijativnoj čeonj kori velikog mozga čovjeka. **Magistarski rad.** (mentor: Ivica Kostović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
4. Radoš Milan (2001) Utjecaj položaja tijela na tlak cerebrospinalnog likvora. **Magistarski rad.** (mentor: Marijan Klarica). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
5. Vuica Milena (2001) Promjene metabolizma inozitol lipidnog kruga u četkastim membranama bubrega štakora tijekom započinjanja kompenzacijskog rasta. **Magistarski rad.** (mentor: Hrvoje Banfić).

2002.

1. Aleksandrova Oberstar Aleksandra (2002) In vitro učinak proendotelina-1 na razinu 1,2 diacilglicerola u izoliranim proksimalnim kanalicima štakorskog bubrega. **Magistarski rad.** (mentor: Hrvoje Banfić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
2. Darmopil Sanja (2002) Utjecaj stimulativne okoline na morfologiju zrnatih neurona u vijuzi gyrus dentatus starih štakora. **Magistarski rad.** (mentor Zdravko Petanjek). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
3. Lukinović-Škudar Vesna (2002) Obuzdavanje eksperimentalnog alergijskog encefalomijelitisa primjenom mijelinske bazične bjelančevine. **Magistarski rad.** (mentor: Milan Taradi). Medicinski fakultet Sveučilišta u Zagrebu.
4. Muller Danko (2002) Izražajnost hormona rasta, receptora hormona rasta i c-erb-2 onkoproteina na stanicama displastičnih nevusa i malignog melanoma kože. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
5. Vukšić Mario (2002) Perinatalni razvitak piramidnih neurona sloja IIIc u prefrontalnoj moždanoj kori djece s Downovim sindromom. **Magistarski rad.** (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu.

2003.

1. Bordukalo Nikšić Tatjana (2003) Ekspresija gena za elemente serotoninergične sinapse u mozgu štakora s promijenjenom serotoninском homeostazom. **Magistarski rad.** (mentor: Branimir Jernej). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
2. Filipović Čugura Jakša (2003) Usporedba biokemijskih i imuno-histokemijskih metoda u analizi estrogenskih receptora tkiva karcinoma dojke. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

3. Tomasović Lončarić Čedna (2003) Vrijednost nalaza apoptoze u tumorima štitne žlijezde. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
4. Vučić Majda (2003) Određivanje mitotičkog i apoptotičkog indeksa u primarnim melanomima kože. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

2004.

1. Filić Vedrana (2004) Molekularno-genetička i biokemijska istraživanja monoaminoksidaza A i B u zdravih ispitanika i osoba koje boluju od migrene. **Magistarski rad.** (mentor: Branimir Jernej). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
2. Tomas Davor (2004) Odnos stupnja solarne elastoze i promjena epidermisa u aktiničkoj keratozi. **Magistarski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

2005.

1. Majdančić Željko (2005) Genetska anticipacija u dijagnostičkim kategorijama shizofrenije. **Magistarski rad.** (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
2. Žigmund Martina (2005) Analiza ekspresije proteinskih produkata gena E-kadherina i beta-katenina u stanicama malignog melanoma. **Magistarski rad.** (mentor: Nives Pećina-Šlaus). Medicinski fakultet Sveučilišta u Zagrebu.

2006.

1. Erceg Goran (2006) Utjecaj položaja tijela i kranijektomije na tlak cerebrospinalnog likvora. **Magistarski rad.** (mentor: Marijan Klarica). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.
2. Kljaić-Dujić Milka (2006) Promjene tumor supresorskih gena APC i CDH1 u stanicama tumora grkljana. **Magistarski rad.** (mentor: Nives Pećina-Šlaus). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
3. Nikuševa-Martić Tamara (2006) Analiza gena CDH1 i CTNNB1 u tumorima središnjeg živčanog sustava. **Magistarski rad.** (mentor: Nives Pećina-Šlaus). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.

2007.

1. Mojsović Ana (2007) Raspodjela gangliozida u mozgu kralježnjaka. (mentor: Marija Heffer)

2009.

1. Bačić Baronica Koraljka (2009) Genski polimorfizam arilsulfataze A u bolesnika s multiplom sklerozom. **Magistarski rad.** (mentor: Svjetlana Kalanj Bogнар). Prirodoslovno-matematički fakultet Sveučilišta u Zagrebu.

PRILOG 4. Popis obranjenih doktorskih radova i nagrada Medicinskog fakulteta za najbolje doktorande.

ANNEX 4: List of PhD theses and School of Medicine's awards for best PhD students

Doktorirali do 1990.

1. Kostović Ivica (1972) Terminalna degeneracija u limbičnom sustavu štakora nakon lezije tegmentuma srednjeg mozga. **Doktorski rad.** (mentor: Jelena Krmpotić) Medicinski fakultet Sveučilišta u Zagrebu.
2. Kostović-Knežević Ljiljana (1976) Elektronska i svjetlosnomikroskopska zapažanja o odnosu između mezenhimskih i neuroepitelnih tvorbi tijekom embrionalnog razvitka telencefalona štakora. **Doktorski rad.** (mentor: Anton Švajger). Medicinski fakultet Sveučilišta u Zagrebu.
3. Šoša Tomislav (1981) Prenatalni razvitak aferentnih sustava optičkog područja metatalamusa čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
4. Kelović Zlatko (1981) Razvitak neuronskih veza entorinalnog korteksa u čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
5. Ciglar Srećko (1982) Razvitak hipotalamusa i njegovih aferentnih sustava u fetusa čovjeka – prilog tumačenju integrativne uloge središnjeg živčanog sustava u regulaciji reprodukcije. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
6. Banfić Hrvoje (1984) Ugradnja 32P u fosfolipide bubrega miša in vivo u toku procesa kompenzacijskog rasta bubrega. **Doktorski rad.** (mentor: Nikša Pokrajac). Medicinski fakultet Sveučilišta u Zagrebu.
7. Kračun Ivan (1985) Biokemijski pokazatelji regionalnog razvitka i građe mozga čovjeka – ganglioziidi. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
8. Bexheti Sadi (1987) Citoarhitektonska organizacija staničnih kolumni u entorinalnom korteksu čovjeka. **Doktorski rad.** (mentor: Zlatko Kelović). Medicinski fakultet Sveučilišta u Zagrebu.
9. Jernej Branimir (1987) Eksperimentalni model za istraživanje trombocitnog serotonina u štakora i mogućnosti njegove primjene. **Doktorski rad.** (mentor: ?). Medicinski fakultet Sveučilišta u Zagrebu.
10. Miklić Pavle (1988) Citoarhitektonika i kemoarhitektonika piramidnih neurona u asocijativnom korteksu čeonog režnja čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
11. Mrzljak Ladislav (1988) Kvalitativni i kvantitativni pokazatelji autogeneze neurona u asocijativnom frontalnom korteksu čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
12. Hadžić Amela (1990) Stimulacija aktivnosti Ca²⁺-ATPaze u bazolateralnim membranama kore bubrega štakora tokom kompenzacijskog rasta bubrega. **Doktorski rad.** (mentor: Hrvoje Banfić). Medicinski fakultet Sveučilišta u Zagrebu.

Doktorirali od 1991. do 1999.

1. Delalle Ivana (1992) Distribucija i morfologija NPY-imunoreaktivnih neurona u prefrontalnom korteksu čovjeka tijekom razvoja: komparacija lateralnog i koronalnog dijela srednjeg frontalnog girusa. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
2. Klarica Marijan (1992) Uloga osmolalnosti likvora u patofiziologiji intrakranijalnog tlaka. **Doktorski rad.** (mentor: Marin Bulat). Medicinski fakultet Sveučilišta u Zagrebu.
3. Gajović Srećko (1993) Morfološka analiza ventralnog grebena zametka štakora. **Doktorski rad.** (Mentor: Ljiljana Kostović-Knežević). Medicinski fakultet Sveučilišta u Zagrebu.
4. Somogyi Lehel (1994) Učinak kolagena na mobilizaciju kalcija u egzokrinim stanicama gušterače. **Doktorski rad.** (mentor: Hrvoje Banfić). Medicinski fakultet Sveučilišta u Zagrebu.
5. Črljen Vladijana (1995) Utjecaj hepatoidnog čimbenika rasta na mehanizam inozitol lipidnog kruga u četkastim i bazolateralnim membranama štakora. **Doktorski rad.** (mentor: Hrvoje Banfić). Medicinski fakultet Sveučilišta u Zagrebu.
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11. Judaš Miloš (1996) Razvojno pojavljivanje i regionalni razmještaj neurona „subplate“ zone reaktivnih na sintetazu dušičnog monoksida u moždanoj kori čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu.
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Doktorirali od 2000. do 2015.

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2. Henigsberg Neven (2000) Sezonstvo rođenja i osobitosti razvijene slike shizofrenije. **Doktorski rad.** (mentor: Vera Folnegović-Šmalc). Medicinski fakultet Sveučilišta u Zagrebu.
3. Hranilović Dubravka (2000) Struktura gena za serotoninški prijenosnik u uvjetima promijenjene homeostaze serotonina. **Doktorski rad.** (mentor: Branimir Jernej). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
4. Stepan Giljević Jasminka (2000) Vrijednost određivanja ekspresije proliferacijskih obilježivača PCNA i Ki-67, te bcl-2, bax i p53 u neuroblastomima. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

2002.

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2. Vukić Miroslav (2002) Ispitivanje fiziologije cerebrospinalnog likvora ventrikulo-akveduktalnom perfuzijom. **Doktorski rad.** (mentor: Marijan Klarica). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija – Biomedicina.

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1. Balija Melita (2003) Serotoninški sustav u trombocitima zdravih ljudi. **Doktorski rad.** (mentor: Branimir Jernej) Medicinski fakultet Sveučilišta u Zagrebu.

2. Čizmić Ante (2003) Vrijednost određivanja sadržaja DNK i stanične proliferacije u kongenitalnim tumorima. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
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4. Tomas Davor (2005) Miofibroblastična reakcija strome i izraženost tenascina-C i laminina u adenokarcinomu prostate. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

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3. Martinac Dorčić Tamara (2007) Prilagodba roditelja djece oboljele od cerebralne paralize. **Doktorski rad.** (Mentor: Marta Ljubešić). Filozofski fakultet Sveučilišta u Zagrebu.
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4. Tomić Karla (2008) Patološke promjene bubrežnih arterija u bolesnika s karcinomom bubrežnih stanica. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.

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1. Boban Marina (2009) Vrijednost određivanja ukupnog i fosforiliranog tau proteina iz likvora u diferencijalnoj dijagnozi sindroma demencije. **Doktorski rad.** (mentor: Goran Šimić). Medicinski fakultet Sveučilišta u Zagrebu.
2. Cepanec Maja (2009) Kvantitativna analiza citoarhitektonike fronto-operkularnog područja ljudskog mozga u prenatalnom, predjezičnom i ranom jezičnom razdoblju. **Doktorski rad.** (mentori: Miloš Judaš i Marta Ljubešić). Sveučilište u Zagrebu - Sveučilišni interdisciplinarni poslijediplomski znanstveni studij „Jezična komunikacija i kognitivna neuroznanost“.
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4. Ivšac Pavliša Jasmina (2009) Predvještine čitanja u djece s rizikom za teškoće učenja. **Doktorski rad.** (mentori: Marta Ljubešić i Mirjana Lenček). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
5. Lončar Mladen (2009) Dugoročne psihofizičke posljedice zatočeništva na mortalitet bivših logoraša. **Doktorski rad.** (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
6. Skelin Ivan (2009) Promjene iskorištenja glukoze u mozgu bulbektomiranih štakora izazvane farmakološkim djelovanjem na serotoninški sustav. **Doktorski rad.** (ko-mentor: Dubravka Hranilović). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
7. Živković Saša (2009) Neurološke komplikacije u bolesnika nakon transplantacije pluća. **Doktorski rad.** (mentor: Nina Barišić). Medicinski fakultet Sveučilišta u Zagrebu.

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2. Matković Katarina (2010) Uloga proteinske kinaze B/Akt u leukemijskim stanicama koje se diferenciraju s pomoću retinoične kiseline. **Doktorski rad.** (mentor: Dora Višnjić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu.
3. Šakić Marija (2010) Izrazi za mentalna stanja i teorija uma predškolske djece u odnosu na dob i socijalnu okolinu. **Doktorski rad.** (mentori: Marta Ljubešić i Dunja Pavličević-Franić). Sveučilište u Zagrebu - Interdisciplinarni poslijediplomski studij „Jezična komunikacija i kognitivna neuroznanost“.

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3. Demirović Alma (2011) Povezanost izraženosti VEGF-a i HIF-1alfa s promjenama bubrežne arterije u bolesnika s karcinomom bubrežnih stanica. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
4. Dijanić Plašć Ivana (2011) Ljutnja u odrasle djece poginulih branitelja. **Doktorski rad.** (mentor: Neven Henigšberg). Medicinski fakultet Sveučilišta u Zagrebu.
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6. Renić Marija (2011) Uloga 20-HETE u eksperimentalno izazvanom ishemijskom oštećenju mozga štakora. **Doktorski rad.** (mentor: Marko Radoš). Medicinski fakultet Sveučilišta u Zagrebu.
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1. Bohaček Ivan (2012) Uloga receptora TLR2 u odgovoru mozga nakon ishemijskoga oštećenja. **Doktorski rad.** (mentori: Srećko Gajović i Jasna Križ). Medicinski fakultet Sveučilišta u Zagrebu.
2. Brozović Blaženka (2012) Rani komunikacijski i jezični razvoj djece s prenatalnim i perinatalnim moždanim lezijama. **Doktorski rad.** (mentor: Marta Ljubešić). Edukacijsko-rehabilitacijski fakultet Sveučilišta u Zagrebu.
3. Čuljat Marko (2012) Razvojne promjene mediosagitalnog presjeka korpusa kalozuma kao pokazatelji perinatalnog rasta interhemisferičnih veza u mozgu čovjeka. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.
4. Havelka Meštrović Ana (2012) Kognitivne funkcije u osoba s ratnim posttraumatskim stresnim poremećajem. **Doktorski rad.** (mentori: Dragica Kozarić-Kovačić i Miloš Judaš). Sveučilište u Zagrebu - Interdisciplinarni poslijediplomski doktorski studij „Jezik i kognitivna neuroznanost“
5. Kapuralin Katarina (2012) Izražaj gena *Stam2* u živčanom sustavu miša određen na razini mRNA, bjelančevine, te pomoću *lacZ* reporterskoga sustava. **Doktorski rad.** (mentor: Srećko Gajović). Medicinski fakultet Sveučilišta u Zagrebu.
6. Katušić Ana (2012) Učinak zvučnih vibracija frekvencije 40Hz na spastičnost i motoričke funkcije u djece sa cerebralnom paralizom. **Doktorski rad.** (Mentor: Vlatka Mejaški Bošnjak). Medicinski fakultet Sveučilišta u Zagrebu.
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8. Kotrla Topić Marina (2012) Razvoj teorije uma i koncepta želje kod jednojezične hrvatske djece u kontekstu dobi i temperamenta djeteta. **Doktorski rad.** (mentori: Marta Ljubešić i Ranko Matasović). Sveučilište u Zagrebu - Interdisciplinarni poslijediplomski studij „Jezična komunikacija i kognitivna neuroznanost“.
9. Mlinac Kristina (2012) Utjecaj gangliozida na izražaj membranskih proteina u mozgu miša. **Doktorski rad.** (mentor: Svjetlana Kalanj Bognar). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu.

10. Šimić Klarić Andrea (2012) Povezanost dinamike rasta opsega glave i neurorazvojnih poremećaja u predškolske djece rođene nakon intrauterinog zastoja rasta. **Doktorski rad.** (mentor: Vlatka Mejaški-Bošnjak). Medicinski fakultet Sveučilišta u Zagrebu.
11. Štajduhar Emil (2012) Ekspresija autokrinog hormona rasta, receptora hormona rasta, plakoglobina i NEDD9 u duktalnom invazivnom karcinomu dojke. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
12. Ulamec Monika (2012) Odnos pojavnosti periglandularnih pukotina i izraženost proteina ekstracelularnog matriksa tenascina, fibronektina i galektina u adenokarcinomu prostate. **Doktorski rad.** (mentor: Božo Krušlin). Medicinski fakultet Sveučilišta u Zagrebu.
13. Zeljko Martina (2012.) Analiza gena i proteina E-kadherina (CDH1) i beta-katenina (CTNNB1) u metastazama u mozgu. **Doktorski rad.** (mentor: Nives Pećina-Šlaus). Medicinski fakultet Sveučilišta u Zagrebu.
14. Žižić Mitrečić Marica (2012) Uloga gena *Noto* u razvoju kaudalnoga notokorda u zametku miša. **Doktorski rad.** (mentor: Srećko Gajović). Medicinski fakultet Sveučilišta u Zagrebu.

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1. Alimović Sonja (2013) Razvoj funkcionalnog vida kod djece s perinatalnim oštećenjem mozga. **Doktorski rad.** (mentor: Vlatka Mejaški-Bošnjak). Medicinski fakultet Sveučilišta u Zagrebu.
2. Arbanas Goran (2013) Metabolički sindrom u osoba s posttraumatskim stresnim poremećajem. **Doktorski rad.** (Mentor: Vera Folnegović-Šmalc). Medicinski fakultet Sveučilišta u Zagrebu.
3. Blažević Sofia (2013) Utjecaj perinatalne primjene prekursora sinteze ili inhibitora razgradnje serotonina na serotoninsku homeostazu u odraslih štakora. **Doktorski rad.** (mentor: Dubravka Hranić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
4. Ćuk Mario (2013) Utjecaj nedostatne aktivnosti S-adenozilhomocistein-hidrolaze na metilaciju proteina. **Doktorski rad.** (mentor: Ivo Barić). Medicinski fakultet Sveučilišta u Zagrebu.
5. Dobrivojević Marina (2013) Učinak natriuretskih peptida na signalni put bradikinina nakon ishemijskog oštećenja mišjeg mozga. **Doktorski rad.** (mentor: Aleksandra Sindić). Medicinski fakultet Sveučilišta u Zagrebu.
6. Fabris Dragana (2013) Sastav i strukturna karakterizacija gangliozida u moždanim tumorima čovjeka. **Doktorski rad.** (mentor: Željka Vukelić). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu.
7. Kuzman Tomislav (2013) Novi eksperimentalni pristup u istraživanju povezanosti intrakranijskog i intraokularnog tlaka. **Doktorski rad.** (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu.
8. Lež Cvjetko (2013) Odnos ekspresije matriks metaloproteinaze-2 i p63 s peritumorskim pukotinama u karcinomu dojke. **Doktorski rad.** (mentor: Božo Krušlin). Prirodoslovno matematički fakultet Sveučilišta u Zagrebu – Postdiplomski studij prirodnih znanosti, smjer Biologija.
9. Maraković Jurica (2013) Učinak promjene osmolarnosti krvi i cerebrospinalnog likvora na volumen i tlak cerebrospinalnog likvora. **Doktorski rad.** (mentor: Darko Orešković). Medicinski fakultet Sveučilišta u Zagrebu.
10. Pogledić Ivana (2013) Distribution and phenotypic features of glial cells in developmental layers of the frontal lobe in injured premature brain. **Doktorski rad.** (mentori: Ivica Kostović i Catherine Verney, Paris). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.
11. Sedmak Goran (2013) Razvojno porijeklo intersticijskih neurona i regionalne razlike u njihovoj raspodjeli, brojnosti i fenotipovima u mozgu čovjeka. **Doktorski rad.** (mentori: Miloš Judaš i Nenad Šestan, Yale University). Medicinski fakultet Sveučilišta u Zagrebu.
12. Šarac Helena (2013) Koncentracija serotonina u trombocitima i polimorfizam serotoninskog transportera u bolesnika sa Sjögrenovim sindromom. **Doktorski rad.** (mentor: Jasenka Markeljević). Medicinski fakultet Sveučilišta u Zagrebu.
13. Šimleša Sanja (2013) Međuodnos izvršnih funkcija, teorije uma i jezičnog razumijevanja u djece predškolske dobi. **Doktorski rad.** (mentor: Marta Ljubešić). Filozofski fakultet Sveučilišta u Zagrebu.

14. Vasung Lana (2013) Analiza kvantitativnih i kvalitativnih promjena fetalnih zona, prikazanih magnetskom rezonancijom, kao pokazatelja glavnih histogenetskih događaja u normalnom razvoju ljudskog mozga. **Doktorski rad.** (mentor: Ivica Kostović). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.

2014.

1. Bajs Janović Maja (2014): Povezanost promjene gama-aminomaslačne kiseline mjerene spektroskopijom putem magnetske rezonancije s obilježjima kliničke slike i terapijskog odgovora u depresivnom poremećaju. **Doktorski rad.** (mentor: Neven Henigsberg). Medicinski fakultet Sveučilišta u Zagrebu.
2. Grošić Vladimir (2014): Terapijski odgovor i promjena koncentracije N-acetil aspartata u liječenju shizofrenije novim antipsihoticima. **Doktorski rad.** (mentor: Neven Henigsberg) Medicinski fakultet Sveučilišta u Zagrebu.
3. Jurjević Ivana (2014) Učinak prekida komunikacije na različitim mjestima unutar likvorskog sustava na tlak i volumen likvora. **Doktorski rad.** (mentor: Marijan Klarica). Medicinski fakultet Sveučilišta u Zagrebu.
4. Krakar Goran (2014) Ultrazvučni biljezi mozga u dijagnozi kongenitalne citomegalovirusne infekcije. **Doktorski rad.** (mentor: Vlatka Mejaški-Bošnjak). Medicinski fakultet Sveučilišta u Zagrebu.
5. Špiranec Katarina (2014) Učinak natriuretskih peptida na signalni put bradikinina u primarnoj kulturi neurona. **Doktorski rad.** (mentor: Aleksandra Sindić). Veterinarski fakultet Sveučilišta u Zagrebu.

2015.

1. Drmić Ivan Domagoj (2015) Protektivni učinak pentadekapeptida BPC 157 na cijeljenje oštećenja želuca, duodenuma, jetre i mozga uzrokovanih visokom dozom celekoksiba kod štakora. **Doktorski rad.** (mentor: P. Sikirić?). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.
2. Džaja Domagoj (2015) Morfološka i kemijska obilježja kalretininskih neurona u neokorteksu primata. **Doktorski rad.** (mentor: Zdravko Petanjek). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.
3. Lalić Hrvoje (2015) Uloga signalnog puta AMPK/mTOR u diferencijaciji leukemijskih stanica. **Doktorski rad.** (mentor: Dora Višnjić). Medicinski fakultet Sveučilišta u Zagrebu.
4. Ozretić David (2015) Endovaskularno liječenje intrakranijskih aneurizmi zavojnicama uz ugradnju potpornice. **Doktorski rad.** (mentor: Marko Radoš). Medicinski fakultet Sveučilišta u Zagrebu.

NAJBOLJE DISERTACIJE (NAGRADE MEDICINSKOG FAKULTETA) / BEST PhD THESES (SCHOOL OF MEDICINE'S AWARDS):

Akademski godina 2013/2014

Pogledić Ivana (2013) Distribution and phenotypic features of glial cells in developmental layers of the frontal lobe in injured premature brain. **Doktorski rad.** (mentori: Ivica Kostović i Catherine Verney, Paris). Medicinski fakultet Sveučilišta u Zagrebu – Poslijediplomski doktorski studij Neuroznanost.

Akademski godina 2012./2013.:

Goran Sedmak: Razvojno porijeklo intersticijskih neurona i regionalne razlike u njihovoj raspodjeli, brojnosti i fenotipovima u mozgu čovjeka. (rad obranjen 13. 09. 2013.; Mentor: Prof. dr. sc. Miloš Judaš; Ko-mentor: Prof. dr. sc. Nenad Šestan, Yale University School of Medicine).

Lana Vasung: Analiza kvantitativnih i kvalitativnih promjena fetalnih zona, prikazanih magnetskom rezonancijom, kao pokazatelja glavnih histogenetskih događaja u normalnom razvoju ljudskog mozga. (rad obranjen 07. 03. 2013.; Mentor: akademik Ivica Kostović).

Akademski godina 2011./2012.:

Alma Demirović: Povezanost izraženosti VEGF-a i HIF-1-alfa s promjenama bubrežne arterije u bolesnika s karcinomom bubrežnih stanica. (rad obranjen 16. 12. 2011.; Mentor: Prof. dr. sc. Božo Krušlin)

Monika Ulamec: Odnos pojavnosti periglandularnih pukotina i izraženost proteina ekstracelularnog matriksa tenascina, fibronektina i galektina u adenokarcinomu prostate. (rad obranjen 29. 02. 2012.; Mentor: Prof. dr. sc. Božo Krušlin)

Katarina Kapuralin: Izražaj gena *Stam2* u živčanom sustavu miša određen na razini mRNA, bjelančevine, te pomoću lacZ reporterskoga sustava. (rad obranjen 207. 07. 2012.; Mentor: Prof. dr. sc. Srećko Gajović)

Martina Zeljko: Analiza gena i proteina E-kadherina (*CDH1*) i beta-kačenina (*CTNNB1*) u metastazama u mozgu. (rad obranjen 11. 05. 2012.; Mentor: Prof. dr. sc. Nives Pećina-Šlaus).

PRILOG 5. NAŠI ISTRAŽIVAČI KAO POZVANI PREDAVAČI U INOZEMSTVU.

ANNEX 5: OUR RESEARCHERS AS INVITED SPEAKERS ABROAD

Kostović Ivica

1. Kongres neuropatologa, Njemačka, Leipzig, 2000. g.
2. Symposium "The acting brain", SISSA, Trst, 21-22.09. 2000. g.
3. "1st International Symposium on Normal and Abnormal Development of the Human Fetal Brain", Sveučilište u Hong-Kongu, Hong-Kong, 18-21. 03. 2001. g.
4. International Conference " Neurobiology in Eastern and Western Europe", SISSA, Trst, 01-03. prosinca 2001.g.
5. "2nd Symposium on Normal and Abnormal Development of the Human Fetal Brain", Sveučilište u Rostocku, Rostock, 24-25.05. 2002.g.
6. «3rd International Symposium on Normal and Abnormal Development of the Human Fetal Brain, Hrvatsko društvo za neuroznanost, Zagreb, Croatia, June 13-15, 2003. g.
7. "4th Graz Symposium on Developmental Neurology", Društvo za neuroradiologiju, Graz, 22-24.05.2003. g.
8. Research Course Series in Human Neuroanatomy and Neurodegeneration, Karolinska institut, Stockholm, 12-15.04.2004. g.
9. "Fetal MRI Course", Sveučilište u Beču, Beč, 12-16.05.2004. g.
10. 1st IBRO/FENS Summer School «**Development** and Plasticity of the Human Cerebral Cortex», **Hrvatsko društvo za neuroznanost**, Dubrovnik-Zagreb, 24.09- 4.10. 2004. g.
11. " 1st International Symposium on Fetal Behaviour", World Association of Perinatal Medicine Barcelona , 18- 19.02.2005. g.
12. Research Course Series in Human Neuroanatomy and Neurodegeneration, Karolinska institute, Stockholm, 06- 10.03.2005. g.
13. May Symposium Helsinki – "Development of cerebral cortex", Sveučilište u Helsinkiju, Helsinki, 24-29.05.2005. g.
14. NATO Workshop – «NOVEL APPROACHES TO THE DIAGNOSIS OF PTSD», Dubrovnik, 13-16.06.2005
15. "7th World Congress of Perinatal Medicine", Hrvatsko društvo za perinatalnu medicinu, Zagreb, 21-24.09.2005. g.
16. 2nd IBRO/FENS Summer School «Development and Plasticity of the Human Cerebral Cortex», Hrvatsko društvo za neuroznanost, Zadar-Zagreb 24.09-1.10.2005. g.
17. Sinapsa – Neuroscience Symposium 2005, Slovensko društvo za neuroznanost, Ljubljana, 19-21.11.2005. g.
18. Int. Professional Meeting and Workshop for Diagnostic Imaging by Ultrasound – "Early Brain Lesion", Sveučilište u Mariboru, Maribor, 09- 11.12.2005. g.
19. Castang lecture, EACD's 19th Annual Meeting, Groningen, 12-13.06.2007.
20. Symposium Mark Molliver, Johns Hopkins, Baltimore, 22.06.2007.
21. 7th International Congress on Early Brain Damage, Bled, 23-26.04.2008.
22. 2. Fetal MRI kongres u Beču, 16-17.05. 2008.
23. Summer Institute in Cognitive Neuroscience, Lake Tahoe, California, 23-24.06.2008.
24. Symposium „Molecular view of a synapse and its surroundings in physiological and pathological neuronal plasticity" u Wierzbi (Poljska), 01-05.09.2009.
25. Training Course „Vascular surgery" (EANS'09) u Opatiji, 13-17.09.2009.
26. Cajal Club i kongres Talijanskog društva za neuroznanost, u Paviji i Milanu, od 29. 09. do 02. 10.2009.
27. Dva doktorska tečaja iz Kognitivne neuroznanosti i neuroanatomije na Karolinska institutu u Stockholmu od 16.-18.09.2009. i 02.-04.10. 2009.

28. Ipokrates Seminar u Ateni 23.-27. 11.2009.
29. Symposium „Development of the Human Cortex“ (Winter meeting of the Anatomical Society of Great Britain and Ireland)na Oxfordu 05.- 07.01. 2010.
30. BIOMAG simpozij „Human brain development“, u Dubrovniku, 28. - 29.03.2010.
31. 3. Fetal MRI kongres u Beču, 13. - 15. 05. 2010.
32. Ipokrates Seminar u Madridu, 03.- 04. 06.2010.
33. Mini-simpozij u okviru godišnjeg sastanka Human Brain Mapping Organization u Barceloni, 05. - 07.06.2010.
34. State-of the –art lecture na 9. kongresu European Pediatric Neurology Society u Cavtatu, 11.05.2011
35. FENS Regionalni sastanak u organizaciji SINAPSA-e u Ljubljani, 22-25-09.2011.
36. 6. kongres Hrvatskog neurokirurškog društva u Opatiji, 25-29.05.2011.
37. Simpoziju „From Ruđer Bošković to today: Contribution of Croatian Scientists to the World Scientific Heritage“ u Dubrovniku, 29.05-02.06.2011.
38. 17th Annual Meeting of the Organization for Human Brain Mapping u Quebec Cityu, 26-30.06.2011.
39. Stručni skup „Vukovar ‘91 – dvadeset godina poslije“ u Vukovaru, 14.11.2011.
40. Simpozij „Prospects in Brain Development: from Cell to Environment“ u Amsterdamu, 28.10.2011.
41. Seminar u Hôpital des Enfants des HUG u Genevi, 26.03.2012.
42. 50-godišnjica Centra za sluh in govor u Mariboru, 29.05.2012.
43. Simpozij „Aktualnost Guberinine misli u Stoljeću uma“, SUVAG,Zagreb, 22-23.05.2013
44. Congress of European Society of Magnetic Resonance in Neuropediatrics, Beč, 4-8.06.2013.
45. Hrvatski liječnički zbor, simpozij „Akademici u HLZ“, Zagreb, 22.02.2013.
46. Okrugli stol „Položaj i perspektive temeljnih medicinskih znanosti u Hrvatskoj“, Hrvatska akademija znanosti i umjetnosti, Zagreb, 18.04.2013.
47. 4. hrvatski kongres neuroznanosti, Zagreb, 20-21.09.2013.
48. SINAPSA, Neuroscience Conference, Ljubljana, 27-29.09.2013.
49. IX. znanstveno – stručni simpozij:„Ratna bolnica Vukovar 1991. – dr. Juraj Njavro,, Vukovar, 17.11.2013.
50. 17. simpozij vojne i krizne medicine, Požega, 6-7. 12.2013.
- 51.
52. 10th International Congress „New developments in the assesment of early brain damage – 30 years later“, Bled, 25.09.2014.
53. XII. AINR (Italian Association of Neuroradiology) Meeting of Pediatric Neuroradiology, Milano, 02.10.2014.
54. X. znanstveno – stručni simpozij:„Ratna bolnica Vukovar 1991. – dr. Juraj Njavro,, Vukovar, 17. 11.2014.

Judaš Miloš

1. International FENS/IBRO Summer School Development and Plasticity of the Human Cerebral Cortex (2003, 2005);
2. The 6th Neurochemistry Winter Conference: Neuronal Plasticity During Development and Adulthood, Innsbruck, Austria (2004);
3. Fetal MRI Course & Congress, Vienna (2006, 2008);
4. The 11th Meeting of the International Clinical Phonetics and Linguistics Association (ICPLA), Dubrovnik, Croatia (2006);
5. The 6th Graz Symposium on Developmental Neurology: Early Developmental Transformations – In Honour of Heinz F.R. Prechtel, Graz, Austria (2007);
6. The 4th European Course on Paediatric Neuroradiology, London, UK (2008);
7. The IPOKRATES Seminar Neurodevelopmental Follow-up of «at risk» Children, Turku, Finland (2008);
8. Symposium “Development of the Human Neocortex” (Oxford, January 6-10, 2010);

9. "4th Fetal MRI Course & Congress" (Wien, May 2010);
10. International Meeting "Reverse Engineering of the Human Brain" u organizaciji European Science Foundation, National Science Foundation USA & USA Air Force Institute (Dubrovnik, May 2010);
11. "The 6th Meeting of the International Academy of Perinatal Medicine - International Symposium on Fetal Neurology" (Osaka, Japan, October 22-24, 2010);
12. 2nd International Workshop Perinatal Biomagnetism, (Jena, Germany, 02-05 June 2011);
13. Human cerebral cortex development Course at the Faculty of Molecular Medicine (Tübingen 2013);
14. Congres of European Society of Magnetic Resonance in Neuropediatrics (Vienna 2013);
15. Cold Spring Harbor Laboratory Meeting „Wiring the Brain“ (July 18-22, 2013).

Klarica Marijan

1. Rotterdam 1991: "VIII International Symposium on ICP"
2. Milano 1995: "First European Congress of Pharmacology"
3. Williamsburg 1997: "X International Symposium on ICP"
4. Budapest 1998: "Central European Symposium on Traumatic Brain Injury"
5. Budapest 1999: "2nd European Congress of Pharmacology"
6. Kopenhagen 1999: "11th European Congress of Neurosurgery"
7. Prag 1999: "Second FEBS Congress"
8. Cambridge 2000: "11th International Symposium on Intracranial Pressure and Brain Monitoring"
9. Kos 2001: "3rd International hydrocephalus workshop"
10. Hong Kong 2004: "Twelfth International Symposium on Intracranial pressure and Brain Monitoring"
11. Goteborg 2006: "Hydrocephalus 2006"
12. Hannover 2008: "Hydrocephalus 2008"
13. Tubingen 2010: "14th International conference of intracranial pressure and brain monitoring"
14. New York 2011: "CHDI Workshop on the Blood-Brain Barrier"
15. Salzburg 2012: Annual Main Meeting Society for Experimental Biology
16. Osaka 2012: The 71st Annual Meeting of the Japan Neurosurgical Society
17. Kyoto 2012: : Hydrocephalus 4th Meeting of the International Society for Hydrocephalus and CSF Disorders
18. Singapore 2013: 15th International Conference on Intracranial pressure and Brain Monitoring
19. Athens 2013: Hydrocephalus Fifth Meeting of the International Society for Hydrocephalus and CSF Disorders
20. Gunzburg 2014: 12th Psychoimmunology Expert Meeting
21. Budapest 2014: 11th Symposium of the International Neurotrauma Society
22. Bristol 2014: Hydrocephalus 2014 6th Meeting of the International Society for Hydrocephalus and CSF Disorders

Vukšić Mario

1. The structural basis of developmental plasticity in the human brain, 33. Jahrestagung der Gesellschaft für Neuropädiatrie, Passau, Njemačka, 22.-24. ožujka 2007.
2. Development and plasticity of the hippocampal dentate gyrus, Neurogenomics and neuroimaging of developmental disorders, Dubrovnik; Hrvatska, 30. travnja-5. svibnja, 2009.
3. Plasticity following lesion: dendritic reorganization of the dentate granule cells after entorhinal denervation, Medicinski fakultet Ljubljana, Doktorski studij iz neuroznanosti; Slovenija, 14. ožujak 2011.
4. Structural plasticity in the hippocampal dentate gyrus, 9. European Pediatric Neurology Society Congress, Cavtat; Hrvatska, 11.-15. svibnja 2011.

Šimić Goran

1. 12th International Spinal Muscular Atrophy Research Group Meeting, Boston, MA, USA, 19th June 2008
2. The 53rd Annual Meeting of the German Society for Neuropathology and Neuroanatomy, Würzburg, 10th October 2008
3. COST CM1103 Meeting "Structure-based drug design for diagnosis and treatment of neurological diseases: dissecting and modulating complex function in the monoaminergic systems of the brain", Bruxelles, Belgium, 2nd February 2012
4. Dan hrvatsko-slovenske suradnje, Medicinski fakultet Ljubljana, Ljubljana, Slovenija, 14. III. 2011.
5. Intensivkurs Neuroanatomie 2006: Okzipitallappen, Hirnstamm, Marklager, Ludwig-Maximilians-Universität Munich, Munich, Germany, 28th September 2006
6. North East Wales Institute Brain Symposium, Wrexham, UK, 24th February 2004
7. OPEN University, Milton Keynes, UK, 23rd February 2004
8. Department of Cognitive Neuroscience, Bangor University, Bangor, U.K., 23rd May 2003
9. North East Wales Institute Brain Symposium, Wrexham, UK, 21st May 2003

Mitrečić Dinko

1. IBRO/NERKA workshop Neurophotonics 2014.
2. Multinational conference in microscopy, Urbino, Italy 2011.
3. Invited speaker at "One hundred years of Jean Giaja", Belgrade, Serbia 2010.
4. Joint meeting of Anatomische Gesellschaft, Nederlandse Anatomen Vereniging and COST B30: The rat model for ALS and its potential in development of stem cell therapy, Antwerpen, Belgium 2009.
5. COST B30 symposium, Cluny, France 2008.
6. 3rd Serbian congress of microscopy with international scientific board 2007.
7. Global College for Neuroprotection and Neuroregeneration and COST B30 working group meeting, Garmisch-Partenkirchen, Germany 2007.
8. IBRO Conference „Confocal microscopy in neuroscience“, Belgrade, Serbia 2005.
9. IBRO/FENS School "Development and plasticity of the human cerebral cortex" 2005.
10. Bioscience 2004, Glasgow, UK 2004.

Pećina Šlaus Nives

1. 13th World Congress on Advances in Oncology and 11th International Symposium on Molecular Medicine 9-11 October, 2008, Hersonissos, Crete, Greece.
2. Target Meeting, Genetics & Genomics Online Conference held on May 17-19, 2012

Petanjek Zdravko

1. Ian Donald 3rd International Symposium Fetal Neurology –Fetal Brain Function, May 04-06. 2012.
2. SINAPSA Neuroscience Conference '11, Central European FENS Featured Regional Meeting, Ljubljana, Slovenia, September 22-25.2011.
3. 9th European Paediatric Neurology Society (EPNS) Congress, Cavtat, 11-14.05.2011.
4. XVIII. European Federation for all Psychiatric Trainees (EPTF) Forum. Dubrovnik, Croatia, June 2-5, 2010.
5. National Congress of the SINS. Milano, 2-5. 10. 2009.

Sinđić Aleksandra

1. Department of Physiology, Emory University, School of Medicine, Atlanta; 2002
2. Department of Physiology & Biophysics, University of Alabama, Birmingham; 2002
3. Department of Cellular & Molecular Physiology, Yale Univ. School of Medicine, New Haven, 2002.
4. CCD. Aventis Frankfurt, Germany 2003
5. University of Münster, Germany, 2003
6. University of Münster, Germany, 2010

PRILOG 6. POPIS POZVANIH PREDAVANJA INOZEMNIH ZNANSTVENIKA NA HIIM-u

ANNEX 6: LIST OF INVITED LECTURES BY FOREIGN SCIENTIST AT CIBR

1998.:

1. Folker Hanefeld (Göttingen) dva pozvana predavanja 15. rujna 1998. (o primjeni MR spektroskopije u dijagnostici i terapiji bolesti mozga kod djece)

1999.:

2. Andres F. Muro (ICGEB Trieste) Spherocytic hereditary elliptocytosis and hypertension in b-adducin deficient mice (13. prosinca 1999.)
3. Asim Kurjak (studeni 1999.)
4. Folker Hanefeld (Göttingen) održao predavanje 02. rujna 1999. i cijeli dan radio MR spektroskopiju s pacijentima u Jedinici za magnetsku rezonanciju HIIM-a.
5. Jens Frahm (Göttingen): Magnetic Resonance Imaging of Human Brain Function (27. listopada 1999.)
6. Jens Frahm (Göttingen): Magnetic Resonance Spectroscopy in children with unclassified leucoencephalopathies (27. listopada 1999.)
7. Mary Scheetz (S.A.D.): Promoting Integrity in Research (18. listopada 1999.)

2000:

1. Rainer Rienmüller /Graz, Austrija): 3 pozvana predavanja 21. lipnja 2000. (uz redoviti sastanak Hrvatskog društva za radiologiju). – trodnevni tečaj za 30 sudionika s 3 pozvana predavača iz „Royal College of Radiologists / Bracco International“ (voditelj: Eugene McNally, Department of MRI, Nuffield Orthopaedic Centre Oxford, U.K.)
2. Vida Demarin (veljača 2000)

2001:

1. Antonio Bedalov (S.A.D.): Chemical genetics – how to discover new cancer treatment (21. rujna 2001.)
2. David Rowe (S.A.D.): An integrated strategy for gene therapy for osteogenesis imperfecta (10. rujna 2001.)
3. Glenn E. Morris (United Kingdom): Emery-Dreifuss muscular dystrophy (6. svibnja 2001.)
4. Milivoj Veličković-Perat (Slovenija): Team-approach to diagnostics and treatment of children with cerebral palsy and the role of parents (13. prosinac 2001.)
5. Mitja Peruš (Slovenija): Attractor theory of recognition and memory- simulations (7. prosinac 2001.)

2002.:

1. Dieter B. Wildenauer (Njemačka): Searching for molecular causes in schizophrenia: from linkage to candidate genes (13. prosinac 2002.)
2. Margit Kerestes (Mađarska): How could adhesion affect the behavior of neutrophils? – The role of major F-actin-binding membrane proteins (28. lipanj 2002.)
3. Tamas Freund (Mađarska): Functional diversity of inhibitory circuits in the hippocampus, their involvement in epileptogenesis and cannabinoid actions (13. lipanj 2002.)

2003.:

1. Božena Kaminska (Poljska): Molecular mechanisms of the neuroprotective effect of immunosuppressants in focal ischemia (17. lipanj 2003.)
2. Bushby Kate (Institute of Human Genetics, International Centre for Life, University of Newcastle upon Tyne): The impact of molecular diagnosis on management and counselling in muscle disease – lessons for the new millennium. (7. ožujka 2003.)

3. Leszek Kaczmarek (Poljska): From c-Fos to matrix metalloproteinases (17. lipanj 2003.)
4. Lucia Wittner (Mađarska): Changes in perisomatic and dendritic inhibition in the human epileptic hippocampus (27. veljače 2003.).
5. Zsafia Magloczky (Mađarska): Epileptic reorganization in hippocampal formation of human temporal lobe epilepsy patients: sclerosis and progression (27. veljače 2003.)

2004.:

1. Adrijan Danek (Klinikum der Universität München-Grosshadern): Differential diagnosis of dementia
2. Alexandre Ribeiro (Lisbon University, Portugal): Adenosine modulation of sodium uptake.
3. Gavin Clowry (Newcastle upon Tyne University, U.K.): Development and plasticity of corticospinal system.
4. Glenn E. Morris (Ujedinjeno Kraljevstvo): The molecular defect in spinal muscular atrophy and prospects for therapy (5. svibnja 2004.)
5. Jean-Pierre Julien (Laval University, Québec, Canada): The generation of a mouse model for juvenile amyotrophic lateral sclerosis
6. José M. Delgado-García (Pablo de Olavide University, Seville, Spain): Neural learning and memory processes in wild-type and genetically-manipulated mice. (u sklopu COST B10 Action Meeting „Brain Damage Repair“)
7. Mijna Hadders-Algra (Nizozemska): Development of postural control: effect of age, brain lesion and preterm birth (25. ožujak 2004.)
8. Ole Petter Ottersen (University of Oslo, Norway): Deficient glutamate homeostasis in temporal lobe epilepsy (u sklopu COST B10 Action Meeting „Brain Damage Repair“)
9. Roberto Navarrete (Imperial College, London, U.K.): Potential of human umbilical cord mesenchymal stem cells for neural repair. (u sklopu COST B10 Action Meeting „Brain Damage Repair“)
10. Thomas H. Deller (Njemačka): Lesion-induced anatomical plasticity in the hippocampus (2. ožujak 2004.)
11. Thomas Herdegen (Kiel University, Germany): c-Jun N-terminal kinases as mediators of neurodegeneration (u sklopu COST B10 Action Meeting „Brain Damage Repair“)
12. Zorka Mikloška (IRB + University of Sidney): Imunopatogeneza infekcije Herpes virusom u čovjeka: implikacije za razvoj cjepiva (9. studenog 2004.).

U 2005./2006.:

1. Eijiro Ozawa (Director General Emeritus, National Institute of Neuroscience, NCNP, Tokyo, Japan): Molecular and cellular mechanisms of Duchenne and related muscular dystrophies.
2. Jacqueline Stark (Department of Linguistics and Communication Research, Austrian Academy of Sciences, Wien): On Language Recovery from Aphasia – Data from Therapy Application.
3. Jasna Križ (Service d'endocrinologie-clinique Pavillon CHUL Université Laval, Québec, Canada): Brain response to injuries: Mouse models and novel therapeutic strategies.
4. Jean-Pierre Julien (Centre de recherche, Pavillon CHUL, Université Laval, Québec, Canada): Secretion of misfolded superoxide dismutase: A novel pathway to inflammation and motor neuron death.
5. Milan Randić (Drake University, Des Moines, Iowa, USA): Novi pristupi karakterizaciji DNA i kvantitativna analiza proteomskih mapa.
6. Mirko Dikšić (Mc Gill University, Montreal, Canada): Introduction to Neurochemistry: Serotonergic System.
7. Philippe Auby (CNS Abilify, Global Medical Science, Global Development & Commercialization, Otsuka America Pharmaceutical, Inc.): Child and Adolescent Psycho-Pharmacotherapy: Do we really know much?
8. Robert D. Van Valin, Jr. (Department of Linguistics, University at Buffalo, The State University of New York, Buffalo, USA): Neurosyntax.
9. Venu Balasubramanian (Seton Hall University, South Orange, New Jersey, USA): Dysgraphias following focal lesions: Implications for cognitive/neurological models of writing.
10. Werner Kilb (Institute of Physiology and Pathophysiology, Johannes Gutenberg-University, Mainz, Germany): Electrophysiological properties of different cell types in the developing cerebral cortex.

2007.:

1. Jean-Pierre Julien (Université Laval, Québec, Canada): Pathogenesis of amyotrophic lateral sclerosis.
2. Krešimir Krnjević (McGill University, Canada): Molecular mechanisms of synaptic signalization.

2008.:

1. Andrej Marušič (Medicinski fakultet Sveučilišta u Ljubljani): Suicidalni mozak: Geni i suicid (14. ožujka 2008. – Tjedan mozga)
2. Charles Nicaise (Université libre de Bruxelles, Belgium): Amyotrophic lateral sclerosis (ALS): what's new in transgenic animal models?
3. David Neubauer (Medicinski fakultet Sveučilišta u Ljubljani): Rijetke neurometaboličke i neurodegenerativne bolesti (15. ožujka 2008. – Tjedan mozga)
4. David Neubauer i Darja Paro-Panjan (Medicinski fakultet Sveučilišta u Ljubljani): Neonatalna neurologija i neurofiziologija (14. ožujka 2008. – Tjedan mozga)
5. David Neubauer i Metka Derganc (Medicinski fakultet Sveučilišta u Ljubljani): Neonatalna neurointenzivna dijagnostika i terapija (15. ožujka 2008. – Tjedan mozga)
6. Fajko Bajrovič i David Neubauer (Medicinski fakultet Sveučilišta u Ljubljani): Poremećaji disanja, naročito smetnje disanja u spavanju i smetnje u ranoj dobi (14. ožujka 2008. – Tjedan mozga)
7. Harry B.M. Uylings (VU University Medical Center Amsterdam, The Netherlands) Cognitive flexibility and orbital prefrontal cortex (20. studenog 2008)
8. Jean-Pierre Julien (Université Laval, Québec, Canada): Amyotrophic lateral sclerosis: Recent advances in gene discoveries and in development of immunization approaches.
9. Michel Villaz: Voltage-gated and ligand-gated ion channels: their activity-dependent contribution to neuronal development and disorders (13. ožujka 2008. – u sklopu Tjedna mozga)
10. Mirjana Randić (State University Iowa, College of Veterinary Medicine, USA): Synaptic plasticity in the spinal cord (18. rujna 2008. HIIM)
11. Mirko Dikšić (McGill University): Introduction to Neurochemistry: Serotonergic System
12. Nenad Šestan (Yale University) Molecular control of cortical projection neuron identity and connectivity (28. svibnja 2008)
13. Pasko Rakic (Yale University): Making maps of the mind.
14. Richard Emmanuel Eastes (Laboratoire de Didactique et d'Épistémologie des Sciences, Paris, France): Course „Science Communication“
15. Thomas Deller (Johann Wolfgang Goethe University, Department of Clinical Neuroanatomy, Frankfurt am Main, Germany): „The cellular basis of learning and memory“ & „Regeneration in the CNS: an introduction into current concepts“ (10. ožujka 2008. – u sklopu Tjedna mozga)
16. Thomas Liehr (Institut für Humangenetik und Anthropologie, Friedrich Schiller Universität Jena): Recent development sin molecular cytogenetics (16. srpnja 2008)
17. Zoran Grubič (Medicinski fakultet Sveučilišta u Ljubljani): Živčano-mišićni spoj i njegova sinaptogeneza (14. ožujka 2008. – Tjedan mozga)

2009./2010.:

1. Anto Bagić (University of Pittsburgh) Magnetoencefalografija – MEG: Osnovni principi, kliničke i neuroznanstvene primjene neuromagnetskog funkcionalnog oslikavanja mozga u kontekstu razvoja medicine 21. stoljeća (8. rujna 2009.)
2. Dani Slovensko-Hrvatske suradnje u neuroznanosti – pozvana predavanja održali: Zoran Grubič, Fajko Bajrovič, David Neubauer, Maja Bresjanac, Marko Živin, Darja Paro-Panjan i Metka Derganc.
3. Daniela Prayer (Department of Radiology, University of Vienna): In vivo MRI of prenatal brain development.
4. Daniela Prayer (Department of Radiology, University of Vienna): Structural and functional neuroimaging. (18. ožujka 2009.)
5. Michael Przybylski (University of Konstanz) Mass spectrometric approaches for elucidation of „misfolding“ and aggregation structures of neurodegenerative proteins (2. listopada 2009.)
6. Sigismund Huck (Institute for Brain Research, University of Vienna): Tricks and treats of patch clamping

2010./2011.:

1. Damir Janigro (The Cleveland Clinic Foundation, Lerner College of Medicine): Seizure disorders and role of the BBB-inflammation: the scientific and clinical data.
2. Monique Esclapez (INSERM, Marseille, France): Heterogeneity of GABAergic neuronal networks.
3. Monique Esclapez (INSERM, Marseille, France): Vulnerability and plasticity of GABAergic and glutamatergic hippocampal networks in temporal lobe epilepsy
4. Nenad Šestan (Yale University): Molecular control of cortical projection neuron identity and connectivity.
5. Philipp Khaitovich (CAS-MPG Partner Institute for Computational Biology, Chinese Academy of Sciences, China): Human-specific features of postnatal brain development. (6. prosinca 2011)

2012.

1. Harry B.M. Uylings (VU University Medical Center Amsterdam, The Netherlands) Cognitive flexibility and orbital prefrontal cortex (16. svibnja 2012.)
2. Hector Leonardo Aguila (University of Connecticut) Monocyte development: a crossroad between physiologic and pathological inflammation (18. rujna 2012.)
3. Vladimir Hlady (University of Utah) Engineering of biointerfaces for neuronal regeneration and CNS biocompatibility studies (28. lipnja 2012.)
4. Svante Pääbo (Department of Evolutionary Genetics, Max Planck Institute for Evolutionary Anthropology)

2013

1. Tomislav Domazet-Lošo (Laboratorij za evolucijsku genetiku Institut Ruđer Bošković) Evolucijski pogled na razvoj živčanog sustava, tumore i genetske bolesti (4. travnja 2013)

2014.

1. Ivana Delalle (Boston University) miRNA as biomarkers for bipolar disorder and schizophrenia (14. svibnja 2014)
2. Ivo Kalajzic (University of Connecticut) The Identity of Mesenchymal Progenitor Cells (9. listopada 2014)
3. Monique Esclapez (INSERM, Marseille, France) Caffeine consumption during pregnancy alters GABAergic neuronal network in offspring (15. prosinca 2014.)
4. Rodrigo Herrera-Molina (Leibniz institut za neurobiologiju, Magdeburg, Njemačka) Structure of Excitatory Synapses and GABAA Receptor Localization at Inhibitory Synapses Are Regulated by Neuroplastin-65 (17. travnja 2014.)
5. Sun-Kyeong Lee (University of Connecticut) Role of macrophage migration inhibitory factor in osteoclastogenesis (13. lipnja 2014)

PRILOG 7. USAVRŠAVANJA NAŠIH MLADIH ISTRAŽIVAČA U INOZEMSTVU

ANNEX 7: OUR YOUNG SCIENTISTS ON TRAINING ABROAD

1. Kostović Ivica

SAD (Fogarty and Fulbright Fellowship, Sveučilište The Johns Hopkins; 1972. – 1974.)
SAD (Harvard School of Medicine; 1976.)

2. Banfić Hrvoje

Ujedinjeno Kraljevstvo (Welcome Trust Fellow, Department of Biochemistry, AFRC Institute for Animal Physiology, Babraham, Cambridge; 1990 – 1992)
Njemačka (Max-Planck Institute for Biophysics, Frankfurt; 1985. – 1987)

3. Judaš Miloš

Njemačka (Anatomskom institutu u Kölnu; 1985, 1986)
SAD (Department of Neurobiology School of Medicine Yale University; 1998., 2005.)

4. Šimić Goran

Japan (RIKEN Brain Science Institute; 2002.)
SAD (Northwestern University, Chicago, 2000.)
Švedska (Karolinska institut, Stockholm; 1994. – 1997.)
Španjolska (Cajal institute, Madrid; 1991.)

5. Heffer Lauc Marija

Njemačka (Institute for Zoology at Hohenheim Universty; 1992.)
Njemačka (Institute for Cell Culture Technology, Technical Faculty, University of Bielefeld; 1994.)
SAD (The Johns Hopkins School of Medicine, Baltimore, MD; 1997-2003
SAD (Department of Neurobiology, School of Medicine Yale University; 2009.)

6. Kalanj Bogнар Svjetlana

Francuska (Centre de Génétique Moléculaire du CNRS, Gif-sur-Yvette; 2002.)
Slovenija (Medicinski centar za molekularnu biologiju Medicinskog fakulteta Sveučilišta u Ljubljani; 2000., 2001., i 2002.)
Njemačka (Tehnički fakultet u Bielefeldu; 1992.)

7. Gajović Srećko

Italija (Grupa za molekularnu patologiju, Međunarodni centar za genetski inženjering i biotehnologiju, Trst; 1995. – 1997.)
Njemačka (Odjel za molekularnu biologiju stanice, Max-Planck za biofizičku kemiju, Göttingen; 1993. – 1995.)

8. Klarica Marijan

Francuska (Synthelabo Recherche, Pariz; 1994. – 1995.)

9. Petanjek Zdravko

Francuska (Neurobiological Mediteran Institute INMED INSERM; 2001. – 2003.)
Nizozemska (Netherlands Institute for Brain Research, Amsterdam; 1994. i 1996.)

10. Pećina Šlaus Nives

SAD (Cold Spring Harbor Laboratory)
SAD (Georgetown University, Washington D.C.)

11. Jovanov Milošević Nataša

Njemačka (Institut za animalnu fiziologiju i opću zoologiju, Sveučilište Friedrich-Schiler, Jena, 1999.)

12. Krsnik Željka

SAD (Rutgers University, Robert Wood Johnson Medical School; 2014.)
SAD (Department of Neurobiology, Yale University School of Medicine; 2004 – 2011.)
Italija (Znanstveni institut „San Raffaele“, Milano; 2003.)
Njemačka (Institut za Antomiju, Sveučilište u Freiburgu; 1999./2000.)

- 13. Vukšić Mario**
Njemačka (Zavod za kliničku neuroanatomiju, Medicinski fakultet Sveučilišta u Frankfurtu; 2003. – 2005.)
Njemačka (Zavod za anatomiju, Medicinski fakultet Sveučilišta u Rostocku, Njemačka; 2001. – 2002.)
- 14. Šinđić Aleksandra**
SAD (Mayo Klinika, Zavod za fiziologiju i biomedicinski inženjering, Rochester; 2006. – 2007.)
SAD (Sveučilište Case Western Reserve, Medicinski fakultet, Zavod za fiziologiju i biofiziku, Cleveland; 2005. – 2006.)
Njemačka (Sveučilišna-klinika Múnster; 2000. – 2005.)
- 15. Darmopil Sanja**
Francuska (INSERM unit U751 "Epilepsy & Cognition", Universite de la Mediterranee, Faculte de medecine Timone, Marseille; 2011.)
Španjolska (Cajal Institute, CISC, Madrid; 2004. – 2009.)
Švedska (Karolinska Institute, 2001./2002.)
- 16. Radoš Milan**
Kanada (Department of Pharmacology and Therapeutics, McGill University; 2001. – 2003.)
Kanada (McConnell Brain Imaging Centre, Montreal Neurological Institute; 2009.)
Njemačka (Department of Physiology, School of Medicine University of Mainz; 2006.)
- 17. Kostović Srzentić Mirna**
SAD (University of California San Diego, Laboratory for developmental cognitive neuroscience; 2004.)
- 18. Renić Marija**
SAD (Zavod za fiziologiju, Medical College of Wisconsin, Milwaukee, Wisconsin; 2004. – 2011.)
- 19. Mladinov Mihovil**
Njemačka (Laboratoriju za molekularnu psihijatriju, Odjel za neuropsihijatriju, Charité-Universitätsmedizin, Berlin; 2009. – 2011.)
Italija (Laboratorij za citomorfologiju, Sveučilište u Cagliariju; 2007. – 2008.)
- 20. Mitrečić Dinko**
Belgija (Laboratoire d'histologie générale, de neuroanatomie et de neuropathologie, Université Libre de Bruxelles; 2008. – 2009.)
- 21. Pogledić Ivana**
Francuska (U676 INSERM, Laboratorij za patofiziologiju perinatalnih oštećenja mozga, Pariz; 2008. – 2010.)
- 22. Vasung Lana**
Kanada (McConnell Brain Imaging Centre, Montreal Neurological Institute; 2008. – 2009.)
Švicarska (Sveučilište u Ženevi; 2009. – 2011.)
- 23. Sedmak Goran**
SAD (Department of Neurobiology School of Medicine Yale University; 2009. – 2011.)
- 24. Boháček Ivan**
Kanada (Zavod za psihijatriju i neuroznanost Medicinskog fakulteta Sveučilišta Laval, Quebec City; 2009. – 2011.)
- 25. Pletikos Mihovil**
SAD (Department of Neurobiology School of Medicine Yale University; 2010. – 2013.)
- 26. Čuljat Marko**
SAD (University of Illinois at Urbana-Champaign; 2010. – 2011.)
- 27. Capanec Maja**
SAD (Yale University, University of California, University of Washington 2012. i 2013.)
- 28. Babić Mirjana**
Ujedinjeno Kraljevstvo, (Oswerty; 2014.)
Italija (Laboratory of Neurogenesis and Neurogenesis, Department of Biomedical Sciences, University of Cagliari, Città Universitaria di Monserrato; 2013)

