INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY IN WARSAW

LET'S CELEBRATE! 20 YEARS OF IIMCB

ANNUAL REPORT

January 2017 - April 2018

Director
Jacek Kuźnicki

Deputy Director for Science
Marcin Nowotny

Deputy Director for Development
Urszula Białek-Wyrzykowska

Deputy Director for Operations
Anna Zolnik

Deputy Director for Finance
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Chair of the International Advisory Board
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Bartosz Wierzbicki (pages 1, 19, 27, 31, 35, 43, 83),
Marcin Zięba/Polish-Swiss Research Programme (page 56-top)

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Directors of the International Institute Molecular and Cell Biology in Warsaw

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for Finance

Director's note

This is my last report as Director. After 20 years of being in charge of the Institute, it is time to transfer the responsibility to the next generation. It is also time to summarize our achievements, failures, and lost opportunities and recall how it all began.

First of all, I feel privileged that I had the chance to put life into the Institute, which in the middle of the 1990s was an empty building and the Parliamentary bill. It was an idea of a few of us, who formed its organizing team. The team consisted of Maciej Nałęcz, supported by Angelo Azzi (both were driving forces in this initiative from the very beginning), Leszek Kaczmarek, Ryszard Przewłocki, Michał Witt, and myself. The idea of creating the Institute was based on our belief that research in Poland can be organized similarly to the West, and we could recruit very good scientists as group leaders, including successful Polish postdocs who were working abroad. We defined the main aims of the Institute: carry out high-quality research in molecular biomedicine and create the best possible working conditions for ambitious, motivated group leaders and their staff.

Since the law about generation of the Institute passed Parliament in 1997, we met monthly in the empty building. Only one room was equipped with a table and chairs. We discussed how to start our research activities. We had no funds for it; we only had what the government gave us for administration and maintenance of the building. Therefore, we hired our first full-time employee, Małgorzata Mossakowska, and offered part-time jobs to administrative staff, including Zbigniew Przygoda, Barbara Wiąckiewicz, and Hanna Michalska from Nencki Institute. However, we could not employ any scientists. Time was passing, and rumors were reaching us that the idea of forming the Institute was wrong and we would fail.

After many unproductive discussions, at one of the monthly meetings I warned that if we do not take fast, radical, and even risky actions to initiate the Institute's activities, then we will lose it. I heard from my colleagues, "If you are so smart, then you do it, but it will be your responsibility." So I did, accepting their challenge. I felt honored that my friends and colleagues were trusting and brave enough to decide that at this difficult stage I could handle the task of being in charge of the new Institute.

Since January 1999, as Deputy to the Institute's first Director, Prof. Angelo Azzi (an honorary director), I became the Acting Director. This was based on a clear statement from the President of the Polish Academy of Science, Prof. Mirosław Mossakowski, who expected to have in Poland a person who was responsible for the Institute's daily activities. Notably, however, major decisions were still made after in-depth discussions with members of the organizing team. This team spirit, despite changes in its composition, endures to this day, and I consider it as one of major reasons for the Institute's success.

Despite the initial challenges, I found ways to employ our first group leaders, support the growth of their groups, and obtain funding for them and subsequent groups. Each was quickly able to obtain grants from both foreign and Polish sources, and all extra funds were invested in equipment and the establishment of new groups. Seventeen research groups have been established to date, seven of which have been dissolved for a variety of reasons.

Over the next 20 years, the Institute became one of the best bioscience institutes in Poland. Last year, the Ministry of Science and Higher Education announced that we were again ranked as an A+ institution. These successes were possible thanks to the people who were involved in the Institute's organization: the organizing team, support staff from Nencki Institute, and members of the first International Advisory Board (chairman: Maciej J. Nałęcz; vice chairmen: Nathan Nelson and Ryszard Przewłocki; members: Ken-ichi Arai, Angelo Azzi, Frank Gannon, Willem H. Gispen, Maurizio Iaccarino, Sergei G. Inge-Vechtomov, Andrzej Jerzmanowski, Leszek Kaczmarek, Platon G. Kostyuk, Andrzej B. Legocki, Sir Marc Richmond, Wojciech Stec, and Jerzy Vetulani; https://www.iimcb.gov.pl/en/institute/annual-reports/17-annual-report-2000). They helped us select good group leaders during an open international competition and pointed out how to proceed with the Institute's organization. We considered ourselves lucky that the group leaders in turn recruited many talented coworkers, built strong groups, and produced excellent research, reflected by publications in the best journals. We were very successful in attracting funding from highly competitive sources in the West, especially from European Framework Programs, which allowed us to grow and support new groups. We are also well funded from Polish sources. Between 2013 and 2016, our success rate for grants from the National Science Center in Poland was ~60%, compared with 40% for other A+ institutes, 30% for A institutes, and 20% for B institutes. We recruited excellent administrative staff, including specialists in the Accounting Office and the Grants Office. Overall, when we sensed opportunities, we worked diligently to take chances, and this worked in many instances. Interestingly, many of the ideas we had with regard to scientific organization have been followed by other institutes, and it is gratifying to see that their experiences have also been positive. Were we successful in all attempts? No, of course not, but this is a part of our unique endeavor. Nevertheless, I feel that I met the expectations of my colleagues and coworkers over the past 20 years. However, the Institute is too small to have enough groups. Without such a critical mass, we are too vulnerable to normal funding fluctuations, research outcomes, and other unexpected problems. For the last 10 years, I was looking for funding for a new building to allow us to increase the number of laboratories to reach a critical mass. I wrote hundreds of letters, had many meetings with people in power, including in the Polish Academy of Sciences, Ministry of Science and Higher Education, Ministry of Development, Foundation for Polish Science, the President's Office, and the City of Warsaw. I trusted the words that were spoken at these meetings, which indicated an understanding of our problem and interest in supporting the Institute, which was so successful in research, obtaining funds from foreign sources, and demonstrating that a reversal of "brain drain" is possible. I heard many promises, but none came to fruition yet. I am optimistic that in the future we will move to a larger building.

However, I am leaving the Director's chair with a sense of fulfillment and without hesitation. Looking ahead, I have several years of continuing research as a group leader at the Institute with my coworkers and assistant Dominika Dubicka-Boroch. I believe that by focusing only on scientific projects, I can achieve even more in research than before being both the Director and a group leader. Some people were asking why I would not stay for one more term as Director which, in theory, was possible. My decision was based on the conviction that it is better to leave such a job a few years earlier than one day too late. I strongly feel that it is now time for me to step down and allow the younger generation to step up. The next Directors, Marcin Nowotny and beginning in January 2019 Marta Miączyńska, are the right people for this post, and I am positive that together with Deputies Hanna Iwaniukowicz, Urszula Wyrzykowska, and Anna Zolnik the Institute will be in very good hands. I would like to thank them for sharing with me a sense of team leadership. I would also like to thank all of the people who are currently at the Institute and those who already left us for building its strength and reputation and fostering team spirit, hard work, and dedication.

Warsaw, March 11, 2018

Jacek Kuźnicki

International Advisory Board

2014-2017 term

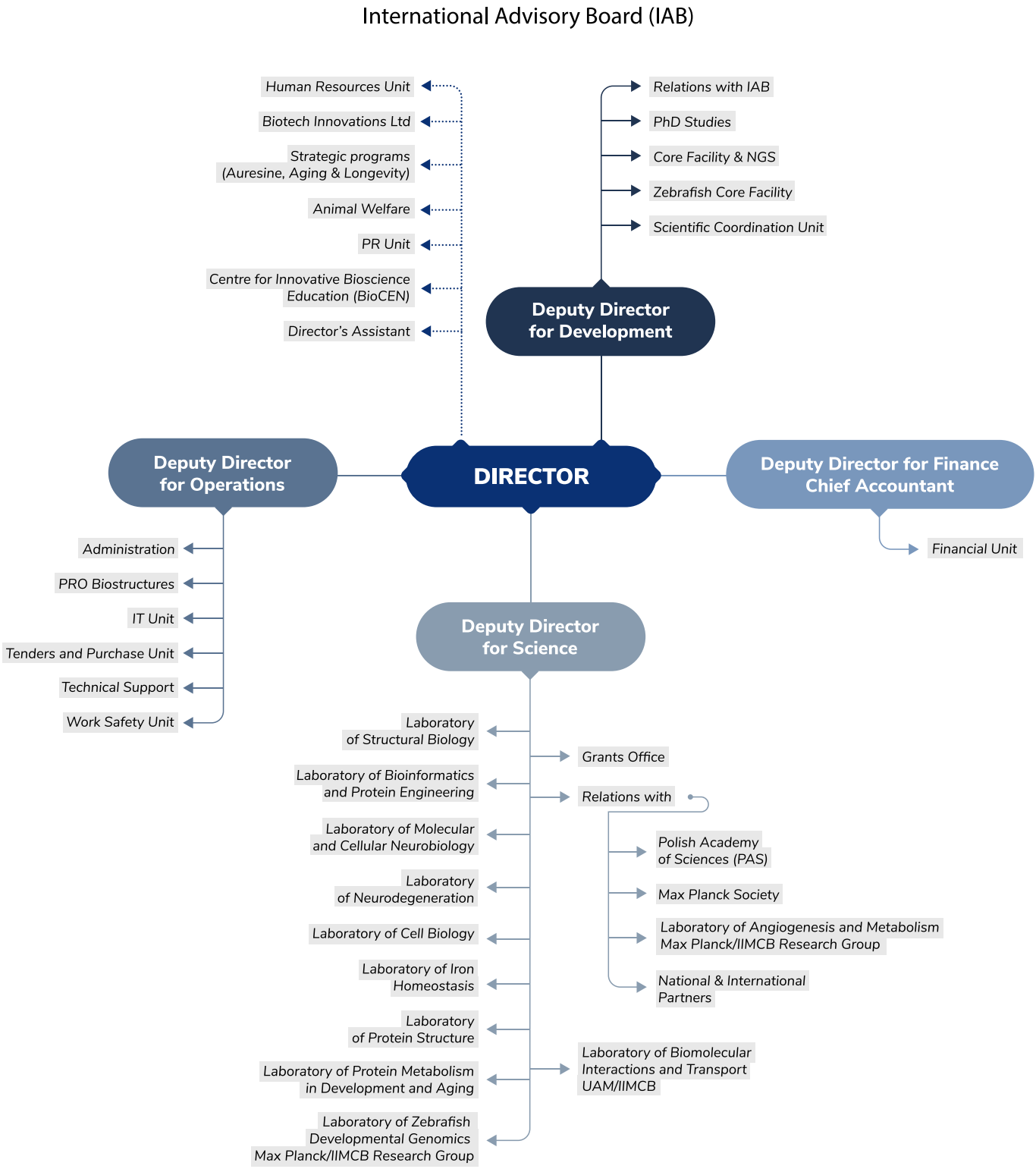
Walter Chazin *(Chair)*	Vanderbilt University, USA
Artur Jarmołowski *(Secretary)*	Adam Mickiewicz University, Poland
Angelo Azzi *(Permanent Advisor)*	Tufts University, USA
Nicolaus Blin	University of Tuebingen, Germany
Ineke Braakman	Utrecht University, The Netherlands (until May 2015)
Thomas Braun	Max Planck Institute for Heart and Lung Research, Germany
Bernd Bukau	University of Heidelberg, Germany
Ivan Dikič	Goethe University Medical School, Germany (until May 2015)
Witold Filipowicz	Friedrich Miescher Institute for Biomedical Research, Switzerland
Klaus Hahlbrock	Max Planck Institute for Plant Breeding Research, Germany
Urszula Hibner	Institut de Génétique Moléculaire de Montpellier, France
Fred van Leuven	Katholieke Universiteit Leuven, Belgium
Maciej Nałęcz	UNESCO Representative/Nencki Institute of Experimental Biology PAS, Poland
Didier Picard	University of Geneva, Switzerland
Helen Saibil	Institute for Structural and Molecular Biology, United Kingdom (until May 2014)
Piotr Sicinski	Harvard Medical School, USA
Adam Szewczyk	Nencki Institute of Experimental Biology PAS, Poland
Anna Tramontano	University of Rome “La Sapienza”, Italy (until March 2017)
Alexander Wlodawer	National Cancer Institute at Frederic, USA

International Advisory Board Meeting, 03.06.2017, Warsaw, Poland

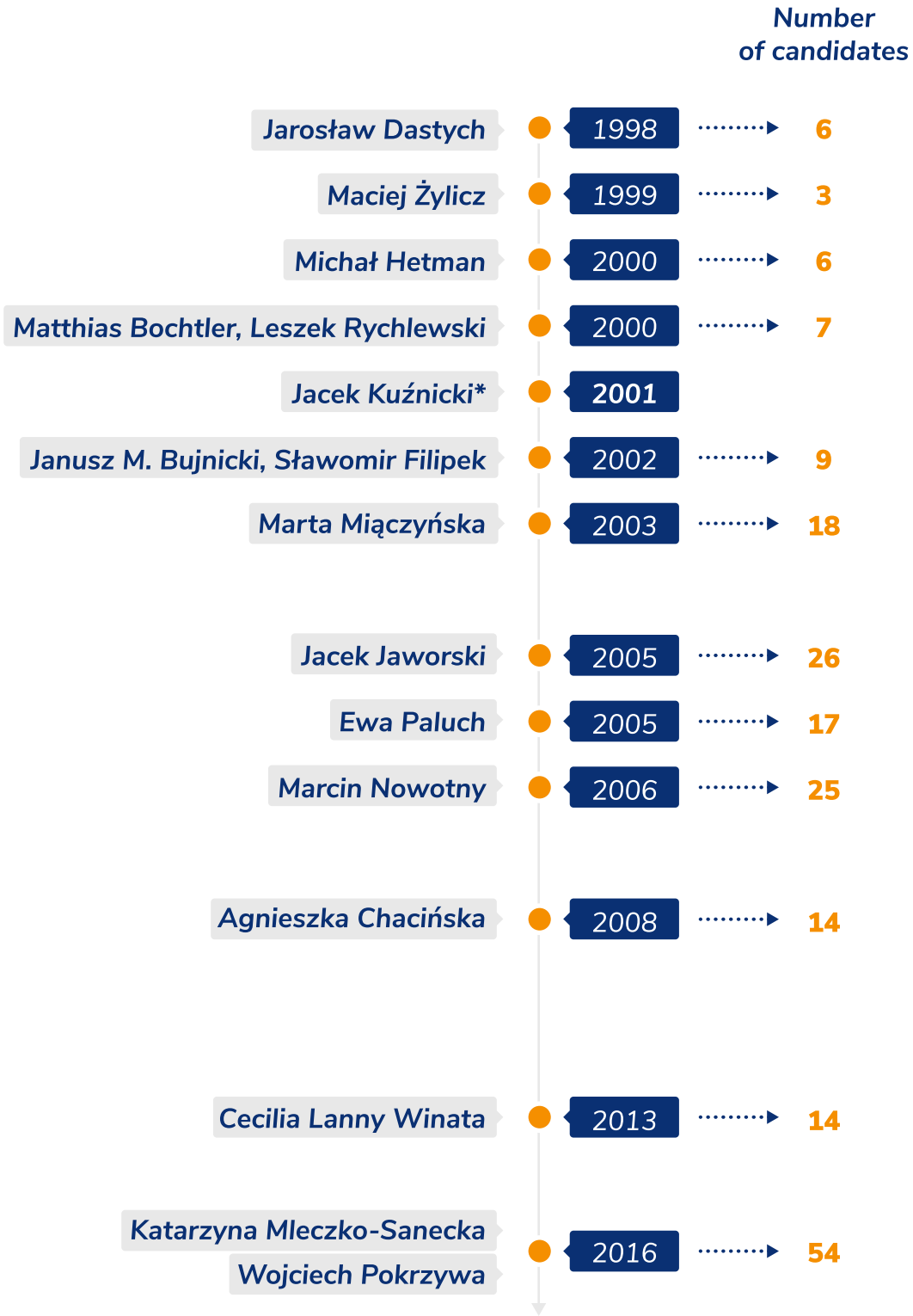
2018-2021 term

Thomas Braun	Max Planck Institute for Heart and Lung Research, Germany
Bernd Bukau	University of Heidelberg, Germany
Jo Bury	Vlaams Instituut voor Biotechnologie, Belgium
Walter Chazin	Vanderbilt University, USA
Aaron Ciechanover	Israel Institute of Technology, Israel
Urszula Hibner	Institut de Génétique Moléculaire de Montpellier, France
Artur Jarmołowski	Adam Mickiewicz University, Poland
Piotr Sicinski	Harvard Medical School, USA
Lillianna Solnica-Krezel	Washington University School of Medicine, USA
Anne Spang	University of Basel, Switzerland
Angelo Azzi *(Permanent Advisor)*	Tufts University, USA
Martiale G. Zebaze Kana *(UNESCO Representative)*	Division of Science Policy and Capacity Building, Natural Sciences Sector, UNESCO

Structure of the International Institute of Molecular and Cell Biology in Warsaw



Successful competitions for the Lab Leader position



* Jacek Kuźnicki became a director of the Institute and a group leader

HR Excellence in Research Award*
IIMCB activities in 2017

In 2017 the **HR Excellence in Research award** strengthened our open attitude towards researchers and made us more responsive to their needs. It was a motivator to set important rules and procedures in the right directions. It also created fantastic occasions to connect us with the outside world.

1 Career Development events

19/01/2017

Career Path Day for researchers from IIMCB and neighboring institutes with invited professionals from academia, clinical trials, pharma & start-up companies, consulting services and patent attorney offices.

01/02/2017

Workshop with professionals from Merck Sharp & Dohme corporation on pros and cons of work at clinical trials.

2 Good Scientific Practices

We emphasised the importance of good standards in research conduct and updated policy on the Principles of Good Practices in Scientific Research and Data management plan; Internal Policy No. 10/2017.

3 Open, Transparent and Merit-based recruitment at IIMCB

We created a guide on recruitment rules, a set of helpful recruitment forms, and colorful posters promoting IIMCB as a fair recruiter. We organized information campaign on the recruitment processes scientists should follow while engaging new team members.

4 Sharing the knowledge

Agnieszka Kolano, HR Group Leader at the Institute, was an expert evaluator of applications from institutions applying for HR Excellence in Research Award; January-July 2017.

Dorota Libiszowska, HR Group Member, presented IIMCB's experience from HR Award related activities at the Information Day, Brussels, October, 2017.

** 'HR Excellence in Research' award is acknowledged by the European Commission which identifies the institutions as providers and supporters of a stimulating and favorable working environment for researchers.*

Description of IIMCB's Activities

The International Institute of Molecular and Cell Biology in Warsaw (IIMCB) was founded as an innovative research center, with rules of operation that are similar to leading scientific institutions throughout the world.

Short history of its establishment and management:

1991 The proposal to create the Institute was published in the UNESCO Bulletin of MCBN.

1994 The State Committee for Scientific Research (KBN) accepted activities that seek to establish the Institute, and the Presidium of the Polish Academy of Sciences (PAS) voted to support the Institute.

1995 An agreement was signed between Poland and UNESCO to establish the Institute.

1996 The Department of Molecular and Cell Biology was created by PAS with Prof. M.J. Nałęcz as Head.

1997 The Polish Parliament passed a bill to establish the Institute.

1998 The Institute's International Advisory Board met for the first time. Prof. A. Azzi was appointed Head of the Institute, with deputies Prof. J. Kuźnicki and Prof. M. Witt.

1999 The Institute commenced its independent activities (after the Department of Molecular and Cell Biology was dissolved), and Prof. J. Kuźnicki was appointed Acting Director.

2001 Prof. J. Kuźnicki was elected by the International Advisory Board as Director of the Institute and held this position for four terms.

2017 Prof. M. Miączyńska was recommended by the International Advisory Board to be the Director of IIMCB and will take the position on January 1, 2019. In 2018, Prof. J. Kuźnicki was appointed Acting Director until June 30, 2018.

IIMCB is one of Poland's most modern research institutes in the life sciences, holding the **highest scientific category** (A+) based on a parametric evaluation of research entities in Poland by the Ministry of Science and Higher Education. In 2017, IIMCB received an A+ rating. Of the 218 institutions in the Life Sciences category that were evaluated, only 13 received an A+ rating. Achievements in the years 2013-2016 were considered in the evaluation.

IIMCB is directly subordinate to the President of the Polish Academy of Sciences, who supervises the organization and activities of the Institute. The President of PAS nominates members of the International Advisory Board and the Institute's Director. IIMCB occupies a building that was loaned to it by PAS. An important link between the Institute and the President of PAS is the Division II: Biological and Agricultural Sciences PAS, to which the Institute belongs together with 19 PAS institutes.

The main goals of IIMCB are to perform high-quality research in molecular biomedicine and to create the best possible conditions for ambitious, motivated group leaders and their staff to implement modern biotechnology and teach and popularize molecular biology and medicine. Research topics at IIMCB cover a wide range of topics, including structural biology, molecular and cell biology, neurobiology, cancer biology, bioinformatics, computer modeling, iron homeostasis, developmental genomics (zebrafish model), ageing, and neurodegeneration. Nine high-profile research groups and one partner laboratory comprise the present structure of IIMCB:

- Laboratory of Structural Biology (M. Bochtler)
- Laboratory of Bioinformatics and Protein Engineering (J.M. Bujnicki)
- Laboratory of Molecular and Cellular Neurobiology (J. Jaworski)
- Laboratory of Neurodegeneration (J. Kuźnicki)
- Laboratory of Cell Biology (M. Miączyńska)
- Laboratory of Iron Homeostasis (K. Mleczko-Sanecka)
- Laboratory of Protein Structure (M. Nowotny)
- Laboratory of Protein Metabolism in Development and Aging (W. Pokrzywa)
- Laboratory of Zebrafish Developmental Genomics Max Planck/ IIMCB Research Group (C.L. Winata)
- (External) Laboratory of Biomolecular Interactions and Transport (J. Brezovsky), located in AMU, Poznań, Poland

The international character of IIMCB is strongly reflected by all aspects of its functioning. All positions of laboratory leaders are filled through open international competitions, and successful candidates are selected by the International Advisory Board (IAB), a body that is unique to Polish research institutions that consists of renowned scientists and science managers. The IAB ensures that the Group Leaders' selection process maintains full objectivity. International Advisory Board members also consult on the steering and functioning of the Institute. The open and highly competitive character of the Group Leader selection process and IIMCB's achievements attract outstanding researchers from all over the world. This leads to "brain gain." Seven of the ten current Group Leaders are Poles who returned to Poland after postdoctoral training at leading European and American centers. The other three Group Leaders are from Czech Republic (J. Brezovsky), Germany (M. Bochtler), and Singapore (C.L. Winata). In total, 13% of IIMCB researchers are foreigners, representing eight nationalities. This creates a multinational and multicultural character of the Institute. English is the official language of communication and is used for correspondence, seminars, and meetings.

IIMCB has close **scientific collaborations** with world-renowned foreign research centers, such as the Max Planck Society (MPS). Under this strategic partnership, **four laboratories were established with double MPS and IIMCB affiliations**: two laboratories at IIMCB (Prof. Bochtler's Laboratory of Structural Biology MPS/PAS [2001] and Dr. Winata's Laboratory of Developmental Zebrafish Genomics Max Planck/IIMCB [2014]) and two laboratories at MPS Institutes (Dr. Paluch's Laboratory of Cell Cortex Mechanics MPS/PAS located at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden [2006] and Dr. Potente's Laboratory of Angiogenesis and Metabolism at the Max-Planck Institute for Heart and Lung Research in Bad Nauheim [2015]). The Institute also boasts **cooperation with national research centers**, including the Intercollegiate Faculty of Biotechnology at the University of Gdańsk/Medical University of Gdańsk, Museum and Institute of Zoology PAS in Warsaw, and Institute of Molecular Biology and Biotechnology at Adam Mickiewicz University in Poznań (AMU). Under this framework of cooperation, the Laboratory of Biomolecular Interactions and Transport AMU/IIMCB in Poznań was created (see page 46). In addition to institutional agreements, IIMCB research groups develop individual international collaborations through common grants, regular contacts, exchange visits, and open seminars that are systematically organized to include outstanding invited speakers from all over the world.

Since 2013, the Institute has been a holder of the **HR Excellence in Research logo**. This prestigious recognition acknowledges IIMCB as an attractive place for researchers to work and develop their careers. Currently, IIMCB comprises 180 staff members, including 78 researchers, 40 PhD students, and 15 technicians. The Institute **is partly financed by state budgets** (statutory subvention from the Ministry of Science and Higher Education, budgetary subvention from the Polish Academy of Sciences) **and numerous grants from both foreign and domestic sources**. From 2000 to 2017, IIMCB scientists received 284 grants from national, European, an international sources. In this period the share of external funding from competitive sources has constituted on the average 69% of IIMCB's annual budget.

IIMCB **actively collaborates with pharmaceutical and biotechnology companies**, such as OncoArendi Therapeutics, A&A Biotechnology, Adamed, Over Group, CelonPharma, UbiQ Bio, and IONIS, to develop new therapies in oncology and neurology and biotechnological products. Measures that are implemented by IIMCB to commercialize its inventions and serve as a resource for industrial partners are continually adapted to scientific output and the needs and expectations of commercial partners. The commercialization of IIMCB inventions and technologies in the life sciences, biotechnology, biomedicine, and bioinformatics was initiated by the Technology Transfer Office (BioTech-IP) in 2010. Numerous national and international grants and initiatives have resulted in several patent applications and license agreements. BioTech-IP gradually evolved, and a need arose to transfer the most advanced projects to an external entity, thus allowing further development in the economic environment. Currently, patent applications and patents are transferred to Biotech Innovations Ltd (see page 61), a special-purpose vehicle that is funded by IIMCB and is committed to turning scientific progress into marketable products and technologies and returning income to the inventors and IIMCB to support further research. IIMCB's portfolio of inventions ranges from platforms that are open to the scientific community (e.g., services offered by the Bujnicki Laboratory; http://genesilico.pl/) to inventions that are protected by worldwide patents.

The most advanced implementations of the research results to business practice:

- **Auresine** (www.auresine.com): a technology for the highly selective elimination of staphylococci bacteria using Auresine enzyme (see page 51).

- **Futurenzymes** (www.futurenzymes.com): a technology of potential importance in medical diagnostics and genetic engineering, using restriction enzymes that specifically cut double-stranded RNA molecules.

- **PRO Biostructures** (probiostructures.com): service in the field of crystallography. The team has extensive experience in supporting drug discovery projects and other scientific endeavors with both biotechnology/pharmaceutical industry and academia. PRO Biostructures offers a complete range of protein crystallography services from gene to structure (see page 59).

The Institute also **actively supports social initiatives** that serve groups of patients with particular diseases. It fostered two patient support organizations:

- **Polish Association Supporting People with Inflammatory Bowel Disease "J-elita"** (since 2005), which brings together families of patients with Crohn's disease and Colitis.

- **Polish Ciliary Dyskinesia Society** (since 2011), which was initiated and further supported under two FP7 projects: HEALTH-PROT (RegPot) and BESTCILIA (a collaborative project that focused on better experimental screening and treatment for primary ciliary dyskinesia).

IIMCB is also engaged in **science popularization** initiatives to increase awareness and interest in the life sciences among the general public. The **Center for Innovative Bioscience Education** (BioCEN), an initiative that is supported by IIMCB, regularly hosts workshops with hands-on experiments and is engaged in science popularization events, such as the Warsaw Science Festival, Polish Radio Science Picnic, and Researchers' Nights, among others (see page 83). Moreover, IIMCB organizes popularization campaigns, such as ***Be Healthy as a Fish*** (see page 86), involving the education of primary and secondary school students using interactive tools. IIMCB also holds regular seminars for students and talented youth.

Awards, Honors, and Scientific Achievements

Prof. Marta Miączyńska was elected a **Member of the European Molecular Biology Organization**.

Prof. Janusz M. Bujnicki was nominated by the Polish Ministry of Science and Higher Education as a **Polish Representative to the European Science Advisors Forum (ESAF)**. He also continues working as a member of the High Level Group of science advisers to the European Commission within the Scientific Advice Mechanism (HLG SAM).

Prof. Jacek Kuźnicki was elected the **Deputy Chair of the Council of Provosts of Division II: Biological and Agricultural Sciences PAS** for the 2015-2018 term.

Auresine ("We sell license to kill Staphylococcus) won **3rd place in the Life Sciences & Healthcare category in the "Closer to people" competition** under the patronage of UNESCO, which was part of the "Bringing Tech & Science Closer to People" campaign.

2017 Best Papers Award

Structural analysis of mtEXO mitochondrial RNA degradosome reveals tight coupling of nuclease and helicase components. Razew M, Warkocki Z, Taube M, Kolondra A, **Czarnocki-Cieciura M, Nowak E,** Labedzka-Dmoch K, Kawinska A, Piatkowski J, Golik P, Kozak M, Dziembowski A, **Nowotny M.** ***Nat Commun.*** 2018; 9(1):97

RNArchitecture: a database and a classification system of RNA families, with a focus on structural information. Boccaletto P, Magnus M, Almeida C, Zyla A, Astha A, Pluta R, Baginski B, Jankowska E, Dunin-Horkawicz S, Wirecki TK, Boniecki MJ, Stefaniak F, Bujnicki JM. ***Nucleic Acids Res.*** 2018; 46(D1):D202-D205

Multiple routes of endocytic internalization of PDGFRβ contribute to PDGF-induced STAT3 signaling. Jastrzębski K, Zdżalik-Bielecka D, Mamińska A, Kalaidzidis Y, Hellberg C, **Miaczynska M.** ***J Cell Sci.*** 2017; 130(3):577-589

Adaptor Complex 2 Controls Dendrite Morphology via mTOR-Dependent Expression of GluA2. Koscielny A, Malik AR, Liszewska E, Zmorzynska J, Tempes A, Tarkowski B, Jaworski J. ***Mol Neurobiol,*** 2018; 55(2):1590-1606

New equipment and subsidies for maintenance

Cryo-EM set-up (120 kV microscope with cryo equipment) was installed at IIMCB, consisting of a 120 kV TECNAI Spirit microscope (FEI) equipped with a TVIPS CMOS 4Kx4K camera and all additional equipment that is required for cryo-EM work, such as a Vitrobot and cryo-holder (FEI). This equipment is suitable for tissue/cell imaging and single-particle EM sample preparation and characterization.

IIMCB received a ministerial **subsidy (1 710 000 PLN) for Biacore S200**, the newest model of the Surface Plasmon Resonance system from GE Healthcare, redefining state-of-the-art in this technology for studies of molecular interactions. Because of its unsurpassed sensitivity and flexibility, it will be primarily used for mid-throughput fragment screening (up to 384 compounds can be screened in a single unattended experiment) and thorough in-depth studies of molecular interactions between any biological molecules (proteins, nucleic acids, or low-molecular-weight ligands).

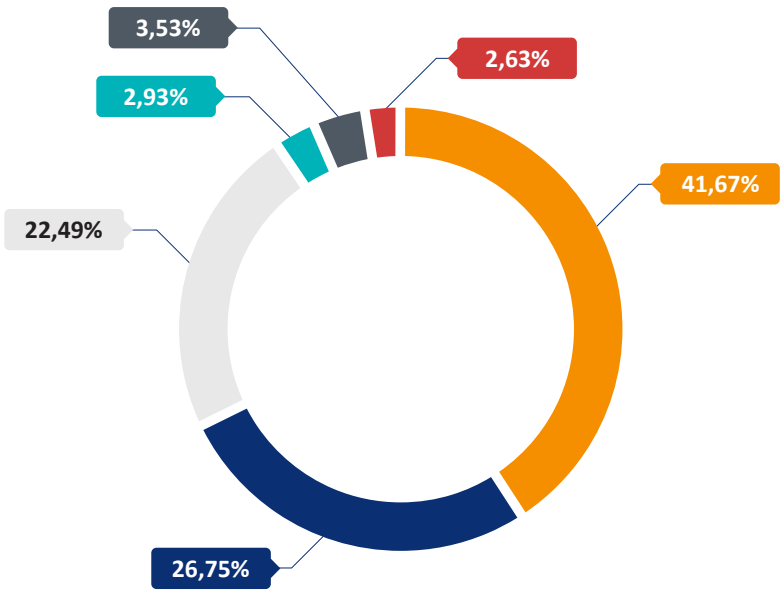
Restructuring subsidy to establish the *C. elegans* Core Facility (320 500 PLN) was granted to IIMCB. This will enable professional breeding of the model organism, the nematode *Caenorhabditis elegans*, and facilitate the implementation of research using this model.

IIMCB received a ministerial **subsidy (1 440 000 PLN) for maintenance of the Zebrafish Core Facility.** This funding enables professional maintenance of the constantly growing and the largest zebrafish collection held in Poland for scientific purposes. In addition, the subsidy facilitates the maintenance of the unique microscope equipment "Lightsheet.Z1" allowing to conduct long-term microscopic observations of *Danio rerio* transgenic lines and mutants labeled with fluorescent markers.

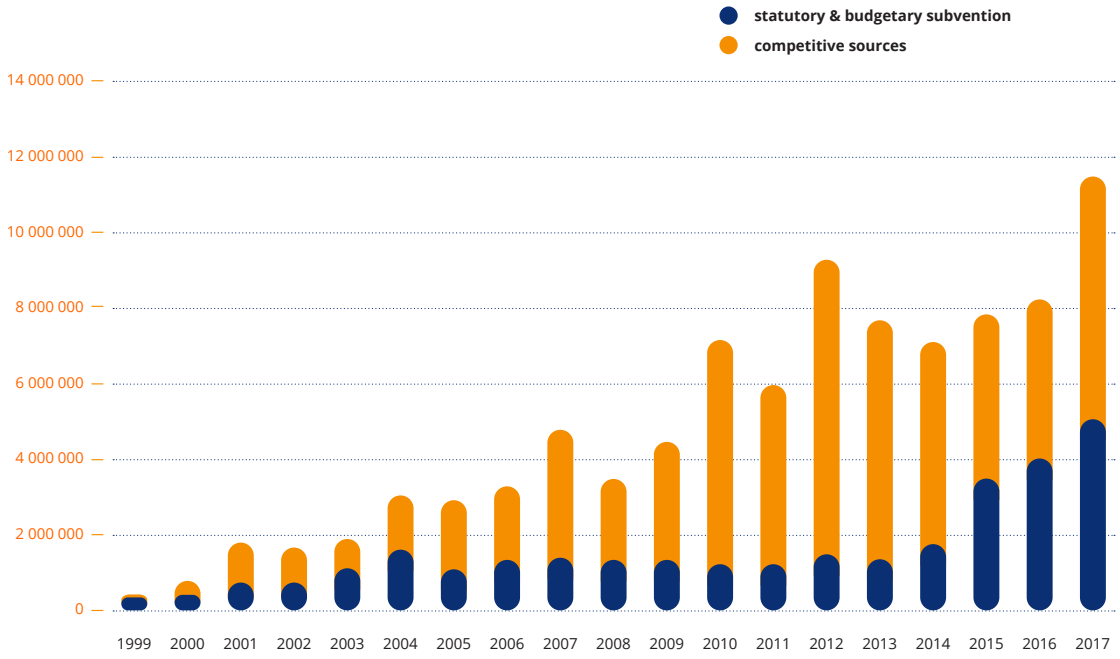
Diversity of Funding IIMCB'2017

Sources of Funding	PLN	EUR*
Statutory Subvention	20 187 510	4 840 085
Budgetary Subvention	1 274 000	305 450
Individual Domestic Grants	12 960 645	3 107 398
Structural Funds	10 893 878	2 611 877
Foreign Grants	1 418 620	340 123
Equipment Subsidy	1 710 000	409 983
Total	48 444 653	11 614 916

** 1 EUR - 4,1709 @ 31st Dec'2017*



Annual Income in EUR



RESEARCH GROUPS

Laboratory of Structural Biology

Senior Scientist

Honorata Czapińska, PhD (until May 2018)

Postdocs

Humberto Fernandes, PhD (IBB PAS)
Anna Fricke, PhD
Thomas Fricke, PhD
Joanna Krwawicz, PhD (until July 2018)
Małgorzata Perycz, PhD (until April 2018)

PhD Students

Marlena Kisiała, MSc (IBB PAS)
Norbert Osiński, MSc
Michał Pastor, MSc (IBB PAS)
Dominik Rafalski, MSc
Anton Slyvka, MSc
Anna Stroynowska-Czerwińska, MSc
Katarzyna Szafran, MSc

Technician

Agnieszka Olszewska (part-time)

Laboratory-Administrative Partner

Paulina Okafor, MSc (part-time)

Lab Leader

Matthias Bochtler, PhD, Professor

Curriculum Vitae

Degrees

2009 Professor of Biological Sciences, nomination by the President of the Republic of Poland

2006 DSc Habil, Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznań, Poland

1999 PhD in Biochemistry, Technical University of Munich, Germany

1995 MSc in Experimental Physics, Munich University, Germany

Research Training

1996-1999 Research Assistant, Max Planck Institute of Biochemistry, Martinsried, Germany

1995-1996 Internship, Medical Microbiology, University of Regensburg, Germany

1992-1993 Guest Student, Cambridge University, United Kingdom

1990-1992 Studies in physics, Munich University, Germany

Professional Employment

2011-Present Professor, Head of Laboratory of Structural Biology, International Institute of Molecular and Cell Biology and Laboratory of Genome Engineering, Institute of Biochemistry and Biophysics PAS, Warsaw, Poland

2007-2011 Part-time Director of Structural Biology, Cardiff University, United Kingdom

2001-2010 Head, Joint MPG-PAS Junior Research Group, IIMCB, Warsaw, Poland

2000 Patent training, Weickmann & Weickmann

1999-2000 Postdoctoral Fellow, Max Planck Institute of Biochemistry, Martinsried, Germany

Honors, Prizes, Awards

2011 Full Professor, Institute of Biochemistry and Biophysics PAS, Warsaw

2005 Pieńkowski Award

2004 EMBO/HHMI Young Investigator Award

2000 Crystal Award, Germany

1998 Crystal Award, Germany

1990-1992 Scholarship from Deutsche Studienstiftung and Bavarian State

Selected publications

(In bold authors with IIMCB affiliation)

Protein-nucleic acid interactions

- **Bochtler M**, **Kolano A**, Xu G-L. DNA demethylation pathways: Additional players and regulators. ***Bioessays***, 2017; 39(1):1-13
- **Slyvka A**, **Mierzejewska K**, **Bochtler M**. Nei-like 1 (NEIL1) excises 5-carboxylcytosine directly and stimulates TDG-mediated 5-formyl and 5-carboxylcytosine excision. ***Sci Rep***, 2017; 7(1):9001
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Our group is interested in DNA modifications, their specific recognition by proteins, and the machinery that is involved in altering DNA modifications. DNA methylation is a single-step reaction. In contrast, DNA demethylation proceeds in several steps. Methylated cytosines are first oxidized by ten eleven translocation (TET) enzymes and then excised by base excision repair or possibly other DNA repair pathways (Bochtler et al., *Bioessays,* 2017, review).

Structural biology projects

Highly specific, methylation-dependent DNA binding is surprising from a mechanistic point of view because methyl groups can only engage in weak attractive van der Waals interactions. In collaboration with the laboratory of Prof. Janusz Bujnicki, we demonstrated that the specific recognition of adenine methyl groups can surprisingly be achieved through *repulsion* rather than *attraction* (Mierzejewska et al., *Nucleic Acids Res*, 2014), but this mechanism is specific to adenine methylation and cannot be generalized to cytosine methylation. Therefore, we are currently studying model proteins that specifically bind cytosine C5-methylated DNA (in collaboration with Dr. Shuang-Yong Xu, New England Biolabs) and have already obtained diffracting crystals. In parallel, we are attempting to grow crystals of TET paralogues that have not yet been structurally characterized to understand their differing substrate preferences and aid the engineering projects that are described below.

Biochemical projects

Small molecule control of TET dioxygenases

Previous studies have shown that acute and chronic ablation of TET enzymes leads to very different phenotypes, apparently through epigenetic adaptations. Therefore, we are interested in developing small-molecule approaches to control TET activity. Inhibitors of TETs are already available, but one caveat of these inhibitors is that they are all mechanism-based and thus inhibit not only TET enzymes but also other α-ketoglutarate-dependent dioxygenases. By taking cues from "Shokat" kinases, we are attempting to design TET variants that can be specifically targeted by small molecules that will not affect other enzymes. We achieved the first examples of control in collaboration with Prof. Tomasz Jurkowski (University of Stuttgart). In collaboration with Prof. Olov Anderson (Karolinska Institute, Stockholm), we obtained TET2/TET3 heterozygote fish that can be crossed to generate TET2/TET3 null fish with a severe phenotype (i.e., lethality at the larval stage), which can serve as a test system for switchable TET dioxygenases.

Role of DNA glycosylases in the replacement of 5-formylcytosine and 5-carboxylcytosine

Thymine DNA glycosylase (TDG) and Nei-like 1 (NEIL1) have both been implicated in the base excision repair step of active DNA demethylation. The robust glycosylase activity of TDG on DNA substrates that contain 5-formylcytosine (5fC) or 5-carboxylcytosine (5caC) is universally accepted, but the mode of action of NEIL1 is still debated. Based on genetic experiments, the Leonhardt laboratory has suggested that NEIL1 acts redundantly with TDG and excises 5fC and 5caC directly. However, this result has been disputed. The Niehrs group suggested that NEIL1 is recruited by the monofunctional TDG for the 2'-deoxyribose excision step. Using purified human NEIL1 and its catalytically impaired P2T and E3Q variants as controls, we detected NEIL1 activity on 5caC but not a 5fC-containing dsDNA substrate. We confirmed the NEIL1 and TDG interaction and NEIL1-mediated 2' deoxyribose excision downstream of TDG glycosylase activity. NEIL1 acts downstream of TDG and stimulates TDG activity on 5fC- or 5caC-containing DNA. The NEIL1-mediated enhancement of TDG-mediated glycosylation was substrate-specific and did not occur for dsDNA with a T/G mismatch (Slyvka et al., *Sci Rep*, 2017).

Animal models

Hymenopterans as models of DNA methylation and demethylation

Honeybees exhibit developmental dimorphism. Depending on diet, diploids develop into either workers or queens. Our collaborator, Prof. Ryszard Maleszka (ANU, Canberra), previously showed that a "worker diet" in combination with DNA methylation inhibitors led to a "queen-like" phenotype with gonads. Together with Prof. Maleszka, we demonstrated that honeybees (and many other hymenopterans) possess a functional TET gene that catalyzes the oxidation of methylcytosine. We are now attempting to knock out hymenopteran TET genes to complement the gene expression and biochemical data with phenotypic information. In parallel, we characterized a component of the royal jelly that inhibited a model cytosine DNA methyltransferase. We are currently collaborating with Prof. Maleszka and Dr. Elżbieta Purta from the laboratory of Prof. Janusz Bujnicki (IIMCB) to express honeybee methyltransferase genes and test inhibition of the proteins by the royal jelly factor. If inhibition of the biologically relevant DNA methyltransferases and cell permeability are confirmed, then our data will help explain nutrition-dependent differences in development between honeybee workers and queens.

Zebrafish as a model for the "Jekyll and Hyde" role of TETs

Zebrafish appear to be a good model for studying oxidative DNA demethylation. We created TET-deficient zebrafish lines. In agreement with articles that were published while this work was ongoing, we found that the ablation of individual TET paralogues was well tolerated, but the combined loss of TET2 and TET3 led to lethality at the level stage. This clearly shows that 5methylcytosine oxidation plays an essential role in somatic tissue. At the same time, it prevents studies of the role of TET enzymes in the germline, where TETs have already been shown to be essential in mammals. Germline transplantation in zebrafish (in collaboration with Dr. Cecilia Winata, IIMCB) opens the possibility of circumventing this difficulty. Germ cells are defined early (prior to TET2/TET3 null lethality) and can thus be transplanted into wildtype embryos. We are currently in the process of introducing dominant germline markers into TET2/TET3 heterozygote embryos in preparation for the planned germline transplantation experiments. Because of the much easier accessibility of early fish embryos compared with mammalian embryos, we expect that it will be less difficult to study the role of maternal TET in early development in fish. Widespread 5mC oxidation is clearly essential, but it also represents a hazard because it reduces gene repression and can thus lead to the activation of mobile genetic elements. Our preliminary experiments in collaboration with Dr. Jose Luis Garcia-Perez (Edinburgh University) support the idea that TET activity indeed poses a genetic risk in somatic tissue. We seek to corroborate this finding and determine whether it also applies to the germline. If it does not, as we expect, then we will seek to understand the way in which the germline is protected.

Completion of several long-standing projects

In addition to the current focus on epigenomics and DNA stability/repair, we completed several long-term projects in the laboratory, which are now published (Piasecka et al., *J Mol Biol*, 2018; Perycz et al., *PLoS One,* 2017; Bochtler et al., *Front Microbiol*, 2018). We are currently also finalizing two additional projects: DNA endonucleases and methodological comparisons of differences between experimental densities that are obtained by X-ray crystallography and cryo-EM.

Laboratory of Bioinformatics and Protein Engineering

Senior Scientists

Elżbieta Purta, PhD
Filip Stefaniak, PhD

Postdocs

Michał Boniecki, PhD
Lucyna Budźko, PhD
Justyna Czarnecka, PhD (maternity leave)
Pritha Ghosh, PhD
Radosław Pluta, PhD
Tomasz Wirecki, PhD

PhD Students and Research Associates

Astha, MSc (fellowship abroad)
Błażej Bagiński, MSc
Pietro Boccaletto, MSc
Nithin Chandran, MSc
Chinju John, MSc (until March 2018)
Marcin Magnus, PhD (until March 2018)
Magdalena Orłowska, MSc
Diana Toczydłowska, MSc (fellowship abroad)
Adriana Żyła, MSc (until April 2018)

Research Technicians

Agata Bernat, MSc
Małgorzata Kurkowska, MSc
Katarzyna Merdas, MSc
Ewa Skowronek, PhD
Magdalena Sroka, MSc

MSc Students

Joanna Broniarek, BSc
Dharm Skandh Jain, BSc

Laboratory-Administrative Partner

Agnieszka Faliszewska, MSc (until April 2018)

Technician

Iwona Ptasiewicz (part-time)

Lab Leader

Janusz M. Bujnicki, PhD, Professor

Curriculum Vitae

Degrees

- **2009** Professor of Biological Sciences, nomination by the President of the Republic of Poland
- **2005** DSc Habil in Biochemistry, Institute of Biochemistry and Biophysics PAS, Warsaw, Poland
- **2001** PhD in Biology, University of Warsaw, Faculty of Biology, Poland
- **1988** MSc in Microbiology, University of Warsaw, Faculty of Biology, Poland

Professional Experience

- **2002-Present** Professor, Head of Laboratory of Bioinformatics and Protein Engineering, IIMCB, Warsaw, Poland (100% appointment)
- **2006 -Present** Associate Professor (extraordinarius) Bioinformatics Laboratory, Institute of Molecular Biology and Biotechnology, Adam Mickiewicz University, Poznań, Poland (currently 25% appointment)
- **2010-2011** Deputy Director, IIMCB (1 year rolling position)
- **2008** Visiting Professor, University of Tokyo, Japan (sabbatical)
- **2004-2006** Assistant Professor, Adam Mickiewicz University
- **2001** Visiting Scientist, National Center for Biotechnology Information, National Institutes of Health, Bethesda, Maryland, USA
- **1999-2002** Research Scientist, Bioinformatics Laboratory, IIMCB
- **1998-2000** Senior Research Assistant, Henry Ford Hospital, Detroit, Michigan, USA

Selected professional affiliations

- European Science Advisors Forum (member, 11.2017-Present)
- Group of Chief Scientific Advisors within the European Commission's Scientific Advice Mechanism (2015-Present)
- Scientific Policy Committee (2014-2018, chairman 04-09.2015 & 06-12.2016)
- Scientific Committee of the Innovative Medicines Initiative (2013-2016)
- Council of the National Science Congress (2016-2017)
- Science Europe: Life, Environmental and Geo Sciences (LEGS) Scientific Committee (2013-2015)
- Young Academy, Polish Academy of Sciences, AMU-PAS (2011-2016)
- Polish Academy of Sciences, corresponding member (2016-Present)
- Member: Polish Bioinformatics Society, PTBI (founding member, Vice-President 2007-2010, President 2011-2013), International Society for Computational Biology, RNA Society
- Executive Editor, Nucleic Acids Research (2013-Present)

Selected awards and fellowships of the lab leader

- **2016** Crystal Brussels Sprout – special award of the National Contact Point of the EU
- **2015** Parnas Award of the Polish Biochemical Society
- **2014** Award of the Polish National Research Center (NCN)
- **2014** Master Award from the Foundation for Polish Science
- **2014** Prime Minister Award for Outstanding Research Achievements
- **2014** Selected as one of "25 leaders for the next 25 years" by "Teraz Polska" magazine of the Polish Promotional Emblem Foundation
- **2014** Award of the Knight's Cross of the Order of Polonia Restituta
- **2014** Award in the Science category of the national plebiscite "Poles with Verve"
- **2012** Award for Outstanding Research Achievements, Ministry of Science and Higher Education
- **2010** ERC Starting Grant (2011-2015)
- **2009** Fellowship for Outstanding Young Scientists, Ministry of Science and Higher Education
- **2009** Award for Research Achievements, Ministry of Science and Higher Education
- **2006** Prime Minister Award for the habilitation thesis
- **2006** Young Researcher Award in Structural and Evolutionary Biology, Visegrad Group Academies of Sciences
- **2003, 2004** Fellowship for Young Scientists, Foundation for Polish Science
- **2002-2005** EMBO/Howard Hughes Medical Institute Young Investigator Program Award
- **2002** Award of the Polish Genetics Society (best Polish genetics-related publication in 2002)
- **2001** Award of the Polish Biochemical Society and Sigma-Aldrich (best Polish publication on nucleic acid biochemistry in 2000)

Doctorates defended under lab leader's supervision

Żylicz-Stachula A, Chmiel A, Cymerman I, Czerwoniec A, Gajda M, Pawłowski M, Sasin-Kurowska J, Kosinski J, Obarska-Kosińska A, Pawlak S, Purta E, Tkaczuk K, Kosciński Ł, Rother M, Potrzebowski W, Korneta I, Puton T, Kasprzak J, Tuszyńska I, Kozłowski Ł, Werner M, Kamaszewska A, Philips A, Milanowska K, Piętal M, Matelska D, Majorek K, Domagalski M, Osinski T, Machnicka M, Magnus M, Szczepaniak K.

Selected publications

(In bold authors with IIMCB affiliation)

- **Foik IP, Tuszynska I,** Feder M, **Purta E, Stefaniak F, Bujnicki JM.** Novel inhibitors of the rRNA ErmC' methyltransferase to block resistance to macrolides, lincosamides, streptogramine B antibiotics. ***Eur J Med Chem***, 2018; 146:60-67

- **Boccaletto P, Machnicka MA, Purta E, Piatkowski P, Baginski B, Wirecki TK,** de Crécy-Lagard V, Ross R, Limbach PA, Kotter A, Helm M, **Bujnicki JM**. MODOMICS: a database of RNA modification pathways: 2017 update. ***Nucleic Acids Res***, 2018; 46(D1):D303-D307

- **Boccaletto P, Magnus M, Almeida C, Zyla A, Astha, Pluta R, Baginski B, Jankowska E, Dunin-Horkawicz S, Wirecki T, Boniecki M, Stefaniak F, Bujnicki JM**. RNArchitecture: a database and a classification system of RNA families, with a focus on structural information. ***Nucleic Acids Res***, 2018; 46(D1):D202-D205

- **Piątkowski P, Jabłońska J, Żyła A, Niedziałek, Matelska D, Jankowska E, Waleń T, Dawson WK, Bujnicki JM**. SupeRNAlign: a new tool for flexible superposition of homologous RNA structures and inference of accurate structure-based sequence alignments. ***Nucleic Acids Res***, 2017; 45(16):e150

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- **Dawson WK**, **Maciejczyk M**, **Jankowska EJ**, **Bujnicki JM**. Coarsegrained modeling of RNA 3D structure. ***Methods***, 2016; 103:138-156

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- **Piatkowski P**, **Kasprzak JM**, **Kumar D**, **Magnus M**, **Chojnowski G**, **Bujnicki JM**. RNA 3D structure modeling by combination of templatebased method ModeRNA, template-free folding with SimRNA, and refinement with QRNAS. ***Methods Mol Biol***, 2016; 1490:217-235

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Our group is involved in theoretical and experimental research on sequence structure-function relationships in proteins, nucleic acids, and macromolecular complexes. Theoretical research involves the development of computer software for the analysis of biological macromolecules. We are currently focusing on developing software for the structural prediction and modeling of RNA and RNA protein complexes. To date, we have developed and made publicly available one of the first methods for the automated comparative (template-based) modeling of three-dimensional (3D) RNA structures (ModeRNA; http://iimcb.genesilico.pl/moderna/) and a method for de novo (template-free) RNA structure modeling (SimRNA; http://genesilico.pl/software/stand-alone/simrna, also available as a web server at http://genesilico.pl/SimRNAweb). We also developed a method for predicting metal ion binding sites in RNA structures (MetalionRNA; http://metalionrna.genesilico.pl), a method for modeling RNA-ligand complexes (LigandRNA; http://ligandrna.genesilico.pl), and a method for predicting the structure of RNA-protein complexes (http://genesilico.pl/NPDock). Other methods for RNA bioinformatics include a method for the classification of contacts in RNA 3D structures (ClaRNA; http://iimcb.genesilico.pl/clarna/) and a method for flexible superposition of RNA 3D structures and their fragments (SupeRNAlign; http://genesilico.pl/supernalign/). We also developed various databases, including a database of RNA modification pathways and enzymes (MODOMICS; http://modomics. genesilico.pl) and a database of RNA 3D motifs and their interactions (RNA Bricks; http://iimcb.genesilico.pl/rnabricks/).

Our suite of programs for the prediction and analysis of protein structures and macromolecular complexes includes the GeneSilico MetaServer (https://www.genesilico.pl/meta2/), methods for modeling large macromolecular complexes with the use of restraints that are derived from experimental data (PyRy3D; http://genesilico.pl/pyry3d/, and MinkoFit3D; http://iimcb.genesilico.pl/minkofit3d/), and a method for discriminating models according to their agreement with experimental data (FILTREST3D; http://filtrest3d.genesilico.pl/). We also developed methods for predicting order/disorder in protein structures (http://iimcb.genesilico.pl/metadisorder/).

Our experimental research focuses on elucidating sequence structure-function relationships in proteins and nucleic acids using biophysics, biochemistry, molecular biology, and cell biology. We tightly integrate theoretical and experimental research. We often experimentally test functional and structural predictions for proteins and RNAs and their complexes using computational methods. For structural studies, we combine X-ray crystallography and low-resolution methods, such as small angle X-ray scattering (SAXS), structure probing by chemical modification or crosslinking, mass spectrometry, circular dichroism, mutagenesis, etc. We also use experimental methods for protein engineering to obtain enzymes with new, useful features, particularly alterations in substrate specificity (e.g., nucleases that exhibit new substrate specificities).

Recent Highlights

RNArchitecture: a database and classification system of RNA families, with a focus on structural information

RNA molecules play fundamental roles in cellular processes. They have been long known to carry genetic information and synthesize proteins. They may detect the presence of ions or small molecules in the environment, regulate gene expression at various levels (from DNA to RNA, to proteins), and catalyze chemical reactions. Many RNAs that have been structurally characterized form compact, functional, 3D structures that determine their function and interactions with other molecules in a manner similar to sequence-structure-function relationships that have been well described for proteins. The need to compare and classify protein structures has led to the development of commonly used databases and hierarchical structural classifications, such as SCOP and CATH. Thanks to these and other computational resources, comparing and classifying proteins was demonstrated to be crucially important for function inference, and it continues to be used in many applications. The lack of similar computational tools for RNAs has prompted the Bujnicki group to develop a new hierarchical classification system, database of structures, and an associated web server. RNArchitecture (Boccaletto et al., Nucleic Acids Res 2018;46:D202-D205, published online 2017 Oct 23. doi: 10.1093/nar/gkx966) provides a comprehensive description of relationships between known families of structured non-coding RNAs (ncRNAs), with a focus on their structural similarities. The new classification organizes ncRNAs hierarchically with Family as the central level, which mainly builds on the Rfam catalog and groups together evolutionarily related RNAs with a conserved structure and detectable sequence similarity. A total of 2688 Families have been included in the initial version of the database, of which only 2.54% (74 Families) have a structural model that has been solved experimentally. Consensus structures of Families are described with a reduced secondary structure representation. For each Family with experimentally determined 3D structures, a representative set of atomic coordinates is provided. Families whose members exhibit structural variation are further subdivided into Subfamilies. Families with similar structures and functions and that are likely to be evolutionarily related (or at least converged to fulfill the same role in essentially the same way) are grouped into Superfamilies (which are more extensive than Clans that are currently described by Rfam). Superfamilies that share a similar core structure but that are not clear homologs are grouped into Architectures. The highest level, Class, organizes Families into very broad structural and functional categories, such as simple or complex structured RNAs. The coarse-graining of secondary structures in RNArchitecture is not much used at the "evolutionary" level of classification into Superfamilies but mostly at higher levels of Architecture and Class, which group RNAs according to structural similarities, which is analogous to Fold and Class in SCOP. The classification of Families into RNArchitecture is expected to evolve as new data become available.

RNArchitecture also serves as a repository for theoretical models of RNA 3D structures and is open for the submission of structural models by users. Compared with other databases, RNArchitecture is unique with regard to its focus on structure-based RNA classification and providing a platform for storing RNA 3D structure predictions. RNArchitecture can be accessed at http://iimcb.genesilico.pl/RNArchitecture/.

New project: toward flexible modeling of RNA interactions with small-molecule ligands

Recently, a new grant entitled, "Development of new computational methods for modeling RNA interactions with small molecule ligands, and its application to study and regulate the mechanism of action of viral and bacterial RNA molecules," was awarded within the TEAM program of the Foundation for Polish Science, co-financed by the European Union under the European Regional Development Fund.

Structures and functions of RNAs are often modulated by small chemical molecules, including naturally occurring molecules and compounds that are obtained by synthetic organic chemistry. Many RNA molecules are known or predicted targets of small-molecule drugs, and the continuous discovery of new functional RNAs that are involved in various biomedically important processes increases the demand for the development of new small molecules that target RNA and methods for analyzing RNA–small-molecule-ligand interactions. Unfortunately, the advancement of computational methods for predicting RNA-ligand interactions lags behind analogous methods for analyzing protein-ligand interactions. There is a dearth of computational methods for modeling the 3D structure and dynamics of RNA-ligand complexes. Currently, it is almost impossible to computationally predict structures of RNA-ligand complexes that involve large conformational changes of the RNA upon ligand binding or that are stable only in the presence of the ligand, unless very similar structures are already known.

The Bujnicki group has developed a method for the computational modeling of RNA 3D structures, termed SimRNA, which, according to independent tests, belongs to the best existing approaches for RNA 3D structure prediction. SimRNA, however, does not allow for the consideration of ligands. Independently, we also developed LigandRNA, a computational method that is used in the docking of small-molecule ligands to rigid RNA 3D structures. Together, these computational tools provide a starting point for the development of new approaches to model fully flexible interactions of RNA molecules with small-molecule ligands. The main goal of the new project is to develop and experimentally validate a general-purpose computational method for predicting RNA-ligand interactions that can model conformational changes. The new method, provisionally dubbed SimRNA-L, will enable simulations of conformational changes in RNA in response to ligand binding, such as those in riboswitches, which are currently beyond the reach of existing programs. It will also extend the range of applications that involve the prediction of potential ligands for target RNAs in the context of virtual screening.

Laboratory of Molecular and Cellular Neurobiology

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Ewa Liszewska, PhD
Matylda Macias, PhD (part-time)

Postdocs

Magdalena Błażejczyk, PhD
Agnieszka Brzozowska, PhD (since October 2017)
Aleksandra Janusz-Kamińska, PhD
Bartosz Tarkowski, PhD
Michalina Wężyk, PhD (since July 2017)
Justyna Zmorzyńska, PhD

Junior Researchers

Katarzyna Banasiak, BSc
Marcelina Firkowska, MSc
Magdalena Kędra, MSc
Agnieszka Kolka, MSc (until July 2017)
Alicja Kościelny, MSc
Kinga Kuchcińska, MSc (since July 2017)
Hadi Mirzapour Delavar, MSc (since October 2017)
Katarzyna Rydz, MSc
Katarzyna Świtoń, MSc
Aleksandra Tempes, MSc
Jan Węsławski, MSc (since September 2017)

Laboratory-Administrative Partner

Marcelina Firkowska, MSc

Technician

Alina Zielińska

Lab Leader

Jacek Jaworski, PhD, Professor

Curriculum Vitae

Degrees

2014 Professor of Biological Sciences, nomination by the President of the Republic of Poland

2010 DSc Habil in Molecular Biology, Warsaw University, Poland

2001 PhD in Molecular Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

1996 MSc in Biology, Department of Genetics, Warsaw University, Poland

Professional Experience

2010-2013 Deputy Director, International Institute of Molecular and Cell Biology, Warsaw, Poland

2005-Present Professor, Head of Laboratory of Molecular and Cellular Neurobiology, International Institute of Molecular and Cell Biology, Warsaw, Poland

Research Training

2016 Research visit (3 weeks) with Prof. William Harris, Cambridge University, Cambridge, UK

2011 Research visit (2 weeks) with Dr. Carlo Sala, CNR Institute of Neuroscience & Instituto Neurologico Carlo Besta, Milan, Italy

2006 Research visit (1 month) with Dr. C.C. Hoogenraad, Erasmus Medical Center, Rotterdam, Holland

2002-2005 Postdoctoral Associate with Prof. Morgan Sheng, Picower Center for Learning and Memory, Massachusetts Institute of Technology and Howard Hughes Medical Institute, Cambridge, MA, USA

2000 Research training (1 month) with Dr. J. Guzowski, ARL Division of Neural Systems, Memory and Aging, University of Arizona, Tucson, USA

1997-2001 Research training (7 months) with Prof. J. Mallet, Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs (LGN), UMR 9923, Centre National de la Recherche Scientifique, Paris, France

1996-2002 PhD student (until 2001) and Postdoctoral Associate (until May 2002) with Prof. L. Kaczmarek, Laboratory of Molecular Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

1995-1996 Master's degree, Prof. P. Węgleński, Department of Genetics, Warsaw University, Poland

Fellowships and Awards

2014 Foundation for Polish Science Professorial Subsidy Master

2011 Prime Minister Award for habilitation thesis

2009 2nd Division (Biological Sciences) of Polish Academy of Sciences Award for series of publications on MMP9 (together with teams of Prof. Kaczmarek and Dr. Wilczyński)

2005 Konorski Award for best publication of 2004 in the field of neuroscience (Kowalczyk et al., J Cell Biol, 2004; 167:209-213), Polish Neuroscience Society and Polish Academy of Sciences

2002 Prime Minister Award for PhD thesis

2001 Foundation for Polish Science National Scholarship for Young Investigators (1 year scholarship)

2000 EMBO Short-Term Fellowship

1999 Polish Network for Cell and Molecular Biology UNESCO/PAS Scholarship

1997 French Government Scholarship

Membership in Scientific Societies, Organizations, and Panels

2017 Vice President of Polish Neuroscience Society

2015 Warsaw Scientific Society, Corresponding Member

2015 Scientific Advisory Board to the Nencki Institute of Experimental Biology, PAS, Member

2011 Neurobiology Committee of the Polish Academy of Sciences, Member (terms 2011-2014; 2015-2018)

Awards, Honors and Titles (Lab members)

2017 A. Kościelny, V4 Young Researcher Award in Biomedicine

2017 A. Tempes, Travel grant of the Boehringer Ingelheim Fonds

Selected publications

(In bold authors with IIMCB affiliation)

Publications in 2016-2017

- **Urbanska M**, **Gozdz A**, **Macias M**, **Cymerman IA**, **Liszewska E**, Kondratiuk I, Devijver H, Lechat B, Van Leuven F, **Jaworski J**. GSK3β Controls mTOR and Prosurvival Signaling in Neurons. ***Mol Neurobiol***, 2017 Nov 15. Epub ahead of print

- **Koscielny A**, **Malik AR**, **Liszewska E**, **Zmorzynska J**, **Tempes A**, **Tarkowski B**, **Jaworski J**. Adaptor Complex 2 Controls Dendrite Morphology via mTOR-Dependent Expression of GluA2. ***Mol Neurobiol***, 2018; 55(2):1590-1606

- **Urbanska AS**, **Janusz-Kaminska A**, **Switon K**, Hawthorne AL, **Perycz M**, **Urbanska M**, Bassell GJ, **Jaworski J**. ZBP1 phosphorylation at serine 181 regulates its dendritic transport and the development of dendritic trees of hippocampal neurons. ***Sci Rep***, 2017; 7(1):1876

- **Gozdz A**, Nikolaienko O, **Urbanska M**, **Cymerman IA**, Sitkiewicz E, **Blazejczyk M**, Dadlez M, Bramham CR, **Jaworski J**. GSK3α and GSK3β Phosphorylate Arc and Regulate its Degradation. ***Front Mol Neurosci***, 2017; 10:192

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- **Switon K**, Kotulska K, **Janusz-Kaminska A**, **Zmorzynska J**, **Jaworski J**. Molecular neurobiology of mTOR. ***Neuroscience,*** 2017; 341:112-153

- **Blazejczyk M**, **Macias M**, Korostynski M, **Firkowska M**, Piechota M, **Skalecka A**, **Tempes A**, **Koscielny A**, **Urbanska M**, Przewlocki R, **Jaworski J**. Kainic Acid Induces mTORC1-Dependent Expression of Elmo1 in Hippocampal Neurons. ***Mol Neurobiol***, 2017; 54(4):2562-78

- Kondratiuk I, Łęski S, **Urbańska M**, Biecek P, Devijver H, Lechat B, Van Leuven F, Kaczmarek L, Jaworski T. GSK-3β and MMP-9 Cooperate in the Control of Dendritic Spine Morphology. ***Mol Neurobiol***, 2017; 54(1):200-211

- **Switon K**, Kotulska K, **Janusz-Kaminska A**, **Zmorzynska J**, **Jaworski J**. Tuberous sclerosis complex: From molecular biology to novel therapeutic approaches. ***IUBMB Life***, 2016; 68(12): 955-962

- **Skalecka A**, **Liszewska E**, Bilinski R, Gkogkas C, Khoutorsky A, **Malik AR,** Sonenberg N, **Jaworski J**. mTOR kinase is needed for the development and stabilization of dendritic arbors in newly born olfactory bulb neurons. ***Dev Neurobiol***, 2016; 76(12):1308-1327

- **Lipka J**, Kapitein LC, **Jaworski J**, Hoogenraad CC. Microtubule-binding protein doublecortin-like kinase 1 (DCLK1) guides kinesin-3-mediated cargo transport to dendrites. ***EMBO J***, 2016; 35(3):302-318

- Kevenaar JT, Bianchi S, van Spronsen M, Olieric N, **Lipka J**, Frias CP, Mikhaylova M, Harterink M, Keijzer N, Wulf PS, Hilbert M, Kapitein LC, de Graaff E, Ahkmanova A, Steinmetz MO, Hoogenraad CC. Kinesin-Binding Protein Controls Microtubule Dynamics and Cargo Trafficking by Regulating Kinesin Motor Activity. ***Curr Biol***, 2016; 26(7):849-861

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Other selected publications

- **Malik AR**, **Liszewska E**, **Skalecka A**, **Urbanska M**, Iyer AM, **Swiech LJ**, **Perycz M**, **Parobczak K**, **Pietruszka P**, **Zarebska MM**, **Macias M**, Kotulska K, Borkowska J, Grajkowska W, Tyburczy ME, Jozwiak S, Kwiatkowski DJ, Aronica E, **Jaworski J**. Tuberous sclerosis complex neuropathology requires glutamate-cysteine ligase. ***Acta Neuropathol Commun***, 2015; 3:48

- **Malik AR**, **Urbanska M**, **Gozdz A**, **Swiech LJ**, **Nagalski A**, **Perycz M**, **Blazejczyk M**, **Jaworski J**. Cyr61, a matricellular protein, is needed for dendritic arborization of hippocampal neurons. ***J Biol Chem***, 2013; 288(12):8544-59

- **Macias M**, **Blazejczyk M**, Kazmierska P, Caban B, **Skalecka A**, **Tarkowski B**, Rodo A, Konopacki J, **Jaworski J**. Spatiotemporal characterization of mTOR kinase activity following kainic acid induced status epilepticus and analysis of rat brain response to chronic rapamycin treatment. ***PLoS One***, 2013; 8(5): e64455

- Knapska E#, **Macias M**, Mikosz M, Nowak A, Owczarek D, Wawrzyniak M, **Pieprzyk M**, **Cymerman IA**, Werka T, Sheng M, Maren S, Jaworski J#, Kaczmarek L#. Functional anatomy of neural circuits regulating fear and extinction. ***Proc Natl Acad Sci***, 2012; 109(42):17093-8; # - corresponding authors

- **Urbanska M**, **Gozdz A**, **Swiech LJ**, **Jaworski J**. Mammalian target of rapamycin complex 1 (mTORC1) and 2 (mTORC2) control the dendritic arbor morphology of hippocampal neurons. ***J Biol Chem***, 2012; 287(36):30240-56

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- **Swiech L**, **Blazejczyk M**, **Urbanska M**, **Pietruszka P**, Dortland BR, **Malik AR**, Wulf PS, Hoogenraad CC, **Jaworski J**. CLIP-170 and IQGAP1 cooperatively regulate dendrite morphology. ***J Neurosci***, 2011; 31(12):4555-68

- **Jaworski J**, Kapitein LC, Montenegro Gouveia S, Dortland BR, Wulf PS, Grigoriev I, Camera P, Spangler SA, Di Stefano P, Demmers J, Krugers H, Defilippi P, Akhmanova A, Hoogenraad CC. Dynamic microtubules regulate dendritic spine morphology and synaptic plasticity. ***Neuron***, 2009; 61:85-100

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- **^Jaworski J**, Mioduszewska B, Sanchez-Capelo A, Figiel I, Habas A, Gozdz A, Proszynki T, Hetman H, Mallet J, Kaczmarek L. Inducible cAMP early repressor, an endogenous antagonist of cAMP responsive element-binding protein, evokes neuronal apoptosis *in vitro*. ***J Neurosci***, 2003; 23(11):4519-26

- **^Jaworski J**, Biederman IW, Lapinska J, Szklarczyk A, Figiel I, Konopka D, Nowicka D, Filipkowski RK, Hetman M, Kowalczyk A, Kaczmarek L. Neuronal excitation-driven and AP-1-dependent activation of timp1 gene expression in rodent hippocampus. ***J Biol Chem***, 1999; 274(40): 28106-12

^no IIMCB affiliation

Mammalian/mechanistic target of rapamycin (mTOR) is a serine-threonine kinase that is involved in almost every aspect of mammalian cell function. It forms two protein complexes, initially identified as regulating translation (mTORC1) or influencing the actin cytoskeleton (mTORC2). My postdoctoral work showed that the regulation of mTOR-dependent translation contributes to dendritogenesis (Jaworski et al., *J Neurosci,* 2005). However, the list of cellular processes that involve both mTORCs has expanded, and new ways of regulating mTORC activity, novel mTOR partners, and mTOR effectors have been discovered. Nonetheless, their contribution to the neuronal functions of mTOR and neuropathology is still poorly understood. Therefore, since the inception of our laboratory, we have sought to identify mTOR partners and regulated proteins that are involved in the neuronal development and characterization of mTOR dysfunction in neuropathology.

To achieve our scientific objectives, we have been using a well-established, relatively simple, and robust model of the dendritogenesis of neurons that are cultured *in vitro*. Using this approach, we previously performed both proof-of-principle experiments and unbiased screens that clearly showed that mTOR functions during neuronal development beyond the canonical control of translation (Swiech et al., *J Neurosci,* 2011; Urbanska et al., *J Biol Chem*, 2012; Malik et al., *J Biol Chem,* 2013). In one of these screens, we identified several proteins that are involved in various steps of membrane trafficking control. One of them is Vps35, a core component of retromer, a protein complex that is responsible for the retrieval of cargo from the endocytic pathway. Following this lead, we found that mTOR binds two important regulators of retromer, Rab7 and TBC1D5. TBC1D5 is a negative regulator of Rab7. Our experiments showed that it is a substrate of mTOR. Along these lines, we showed that mTOR can influence retromer function. We also found evidence that TBC1D5 phosphorylation by mTOR is needed for proper dendritogenesis (Kisielewska et al., in preparation). Our current efforts are focused on revealing the retromer cargo that is needed for mTOR-dependent dendritogenesis and verifying the role of mTOR-driven TBC1D5 phosphorylation beyond dendritogenesis control.

Our previous research showed that mTOR is also present outside the endocytic pathway (e.g., in nuclei of active neurons; Macias et al., *PLoS One,* 2013). However, our work until recent years provided no evidence of whether nuclear mTOR is active. Using live imaging approaches to monitor mTORC1 activity and localization, we obtained evidence that upon an increase in neuronal activity, mTOR moves to the nucleus where mTORC1 activity subsequently increases (Macias et al., in preparation). Therefore, the next task is to identify the nuclear targets of mTOR. Mass spectrometry analysis of mTOR that is immunoprecipitated from neuronal nuclei and the literature analysis indicates the potential involvement of mTOR in the regulation of chromatin organization. Thus, we are now using CHIP to discover which genes that are needed for neuronal plasticity are regulated by nuclear mTOR.

In 2017, we finalized several projects on another kinase, GSK3. We showed that GSK3 in neurons, unlike in several non-neuronal cells, positively controls the activity of mTORC1 and mTORC2 under certain conditions (Urbanska et al., *Mol Neurobiol,* 2017). For example, in transgenic mice that expressed an active form of GSK3β in neurons, we showed that disinhibition of the neuronal network using PTZ resulted in much stronger mTOR activation than in controls. The link between mTOR and GSK3 prompted us to investigate the effect of GSK3 on the levels of proteins that are locally translated in dendrites. One such protein is Arc. Although we did not observe an effect of GSK3 on *de novo* Arc synthesis, we discovered that Arc becomes a substrate of GSK3 upon NMDA receptor activation. Once phosphorylated by GSK3, Arc undergoes ubiquitination and degradation (Gozdz et al., *Front Mol Neurosci*, 2017). This process is important for the proper stability of dendritic spines (the structural equivalent of excitatory synapses) upon excessive neuronal stimulation and might be critical for protecting neurons from excitotoxicity.

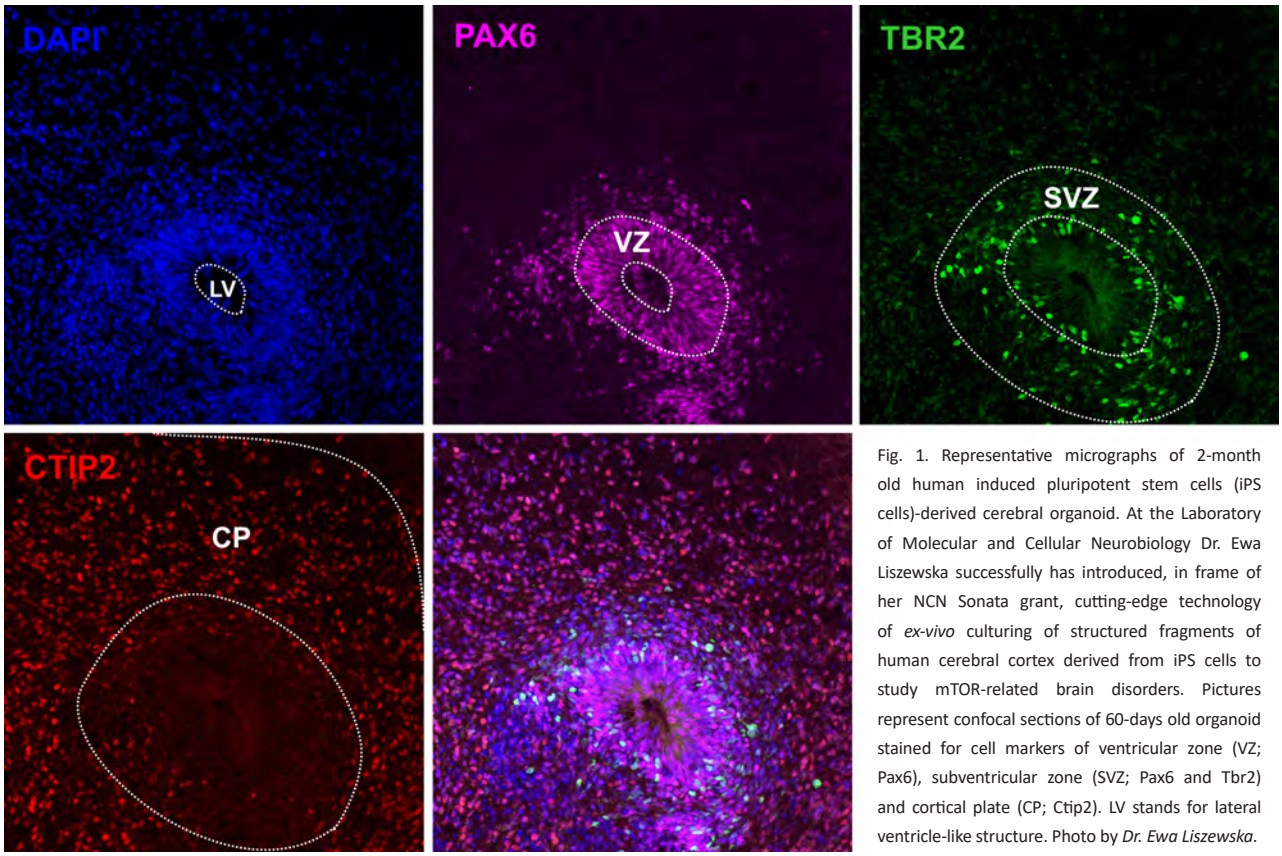

Fig. 1. Representative micrographs of 2-month old human induced pluripotent stem cells (iPS cells)-derived cerebral organoid. At the Laboratory of Molecular and Cellular Neurobiology Dr. Ewa Liszewska successfully has introduced, in frame of her NCN Sonata grant, cutting-edge technology of *ex-vivo* culturing of structured fragments of human cerebral cortex derived from iPS cells to study mTOR-related brain disorders. Pictures represent confocal sections of 60-days old organoid stained for cell markers of ventricular zone (VZ; Pax6), subventricular zone (SVZ; Pax6 and Tbr2) and cortical plate (CP; Ctip2). LV stands for lateral ventricle-like structure. Photo by *Dr. Ewa Liszewska.*

Laboratory of Neurodegeneration

Senior Scientist, Vice Head

Łukasz Majewski, PhD

Senior Scientists

Magdalena Czeredys, PhD
Joanna Gruszczyńska-Biegała, PhD
Vladimir Korzh, PhD
Smijin Karthully Soman, PhD
Małgorzata Wiweger, PhD

Senior Staff Scientist

Tomasz Węgierski, PhD (part-time)

Postdocs

Evgeny Gasanov, PhD (since July 2017)
Oksana Palchevska, PhD (since November 2017)

Research Assistant

Michał Bazała, MSc

PhD Students

Kinga Gazda, MSc Eng. (until March 2018)
Anna Jaworska, MSc (PhD defense May 30th, 2017)
Justyna Jędrychowska, MSc
Rishikesh Kumar Gupta, M Tech. (since January 2018)
Filip Maciąg, MSc Eng.
Iga Wasilewska, MSc

MSc Students

Anna Romaszko (until September 2017)
Klaudia Strucińska (since June 2017)

Trainees

Gulsevinc Ay (March-June 2017)
Weronika Jasińska (August 2017-March 2018)

Technician

Monika Matuszczyk (part-time)

Lab Leader

Jacek Kuźnicki, PhD, Professor

Curriculum Vitae

Degrees

1993 Professor, nomination by the President of the Republic of Poland

1987 DSc Habil, Nencki Institute of Experimental Biology, Polish Academy of Sciences (PAS)

1980 PhD in Biochemistry, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1976 MSc in Biochemistry, Warsaw University, Poland

Postdoctoral Training

July 2015 Visiting Professor, Laboratory of W. Harris, University of Cambridge, UK

July 2014 Visiting Professor, Laboratory of B.E. Snaar-Jagalska, Leiden University, The Netherlands

1992-1995 Visiting Professor, Laboratory of D. Jacobowitz, Mental Health at NIH, Bethesda, MD, USA

1981-1984 Visiting Fellow (postdoc), Laboratory of E.D. Korn, NIH, Bethesda, MD, USA

Professional Employment

2017-Present Deputy Chair of the Council of Provosts, 2nd Division, PAS

2001-Jan 2018 Director, IIMCB; Feb-Jun 2018 Acting Director, IIMCB

2001-Present Professor, Head of Laboratory of Neurodegeneration, IIMCB, Warsaw, Poland

2000-2001 Director, Centre of Excellence Phare Sci-Tech II, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1999-2001 Acting Director, IIMCB; Organizer and Director, Centenarian Program

1996-2002 Head, Lab of Calcium Binding Proteins, professor 2002-2014 Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1991-1992 Deputy Scientific Director, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1986-1992 Associate Professor and Head, Lab of Calcium Binding Proteins, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1984-1985 Research Associate, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1980-1981 Postdoctoral Fellow, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

1976-1980 PhD Student, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

Membership in Scientific Societies, Organizations, and Panels

2016-Present Member, International Advisory Board, Małopolska Centre of Biotechnology, Jagiellonian University

2011-Present Member, International Expert Council of the Research and Education Center, State Key Laboratory of Molecular and Cellular Biology in Ukraine

2011-2014 Member, Science Policy Committee, Ministry of Science & Higher Education, Rotating President Jul-Dec 2012

2008-Present Board Member, European Calcium Society

2008-Present Member of the Board of Directors, Biocentrum-Ochota Consortium; Rotating President, Jul-Dec 2016, Jul-Dec 2013, Jul-Dec 2010

2006-2011 Member, Advisory Group of the 7FP for Health, European Commission

2004-Present Corresponding Member of PAS

2004-Present Honorary chairman, one of the founders, BioEducation Foundation

2002-Present Head of the Program Board, Centre for Innovative Bioscience Education

1993-2014 Member, Scientific Council of the Nencki Institute of Experimental Biology PAS

1996-1998, 2000-2002 Vice-President Polish Biotechnology Committee

1989-1991 General Secretary, Polish Biochemical Society

Honors, Prizes, and Awards

2013 Award of the 2nd Division of Biological and Agricultural Sciences of PAS

2013 Crystal Brussels Prize for outstanding achievements in 7FP of the European Union

2011 Konorski Award by the Polish Neuroscience Society and Committee on Neurobiology of PAS

2008 Officer's Cross of the Order of Polonia Restituta by the President of the Republic of Poland

2003 Prime Minister Award for scientific achievement

2001 Award of the Division of Biological Sciences of PAS for work on calcium binding proteins

1998 Knight's Cross of the Order of Polonia Restituta by the President of the Republic of Poland

Doctorates

Filipek A, Kordowska J, Wojda U, Hetman J, Palczewska M, Nowotny M, Billing-Marczak K, Bojarski Ł, Michowski W, Misztal K, Figiel M, Honarnejad K, Jaworska A.

Selected publications

(In bold authors with IIMCB affiliation)

- **Korzh V**. Development of brain ventricular system. ***Cell Mol Life Sci***, 2018; 75(3):375-383

- **Gazda K**, **Kuznicki J**, **Wegierski T**. Knockdown of amyloid precursor protein increases calcium levels in the endoplasmic reticulum. ***Sci Rep***, 2017; 7(1):14512

- **Szewczyk LM**, Brozko N, **Nagalski A**, Röckle I, Werneburg S, Hildebrandt H, **Wisniewska MB, Kuznicki J**. ST8SIA2 promotes oligodendrocyte differentiation and the integrity of myelin and axons. ***Glia***, 2017; 65(1):34-49

- **Majewski Ł**, **Maciąg F**, Boguszewski PM, **Wasilewska I**, Wiera G, Wójtowicz T, Mozrzymas J, **Kuznicki J**. Overexpression of STIM1 in neurons in mouse brain improves contextual learning and impairs long-term depression. ***BBA Mol Cell Res***, 2017; 1864(6):1071-87

- **Misztal K**, **Brozko N**, **Nagalski A**, **Szewczyk LM**, **Krolak M**, **Brzozowska K**, **Kuznicki J**, **Wisniewska MB**. TCF7L2 mediates the cellular and behavioral response to chronic lithium treatment in animal models. ***Neuropharmacology***, 2017; 113(Pt A):490-501

- **Czeredys M**, **Maciag F**, Methner A, **Kuznicki J**. Tetrahydrocarbazoles decrease elevated SOCE in medium spiny neurons from transgenic YAC128 mice, a model of Huntington's disease. ***Biochem Biophys Res Commun***, 2017; 483(4):1194-1205

- Nagaraj S, Laskowska-Kaszub K, Dębski KJ, Wojsiat J, Dąbrowski M, Gabryelewicz T, **Kuźnicki J**, Wojda U. Profile of 6 microRNA in blood plasma distinguish early stage Alzheimer's disease patients from non-demented subjects. ***Oncotarget***, 2017; 8(10):16122-43

- **Soman S**, Keatinge M, Moein M, Da Costa M, Mortiboys H, Skupin A, Sugunan S, **Bazala M**, **Kuznicki J**, Bandmann O. Inhibition of the mitochondrial calcium uniporter rescues dopaminergic neurons in pink1$^{-/-}$ zebrafish. ***Eur J Neurosci***, 2017; 45(4):528-535

- Garcia-Lecea M, **Gasanov E, Jedrychowska J,** Kondrychyn I, Teh C, You M-S, **Korzh V**. Development of Circumventricular Organs in the Mirror of Zebrafish Enhancer-Trap Transgenics. ***Front Neuroanat***, 2017; 11:114

- Shen H, Shin EM, Lee S, Mathavan S, Koh H, Osato M, Choi H, Tergaonkar V, **Korzh V**. Ikk2 regulates cytokinesis during vertebrate development. ***Sci Rep***, 2017; 7(1):8094

- Koh CH, Wu J, Chung YY, Liu Z, Zhang RR, Chong K, **Korzh V**, Ting S, Oh S, Shim W, Tian HY, Wei H. Identification of a Na+/K+-ATPase inhibition-independent proarrhythmic ionic mechanisms of cardiac glycosides. ***Sci Rep***, 2017; 7(1):2465

- Tan SY, Teh C, Ang CY, Li M, Li P, **Korzh V**, Zhao Y. Responsive mesoporous silica nanoparticles for sensing of hydrogen peroxide and simultaneous treatment toward heart failure. ***Nanoscale***, 2017; 9(6):2253-61

- Woźniak A, Grześkowiak BF, Babayevska N, Zalewski T, Drobna M, Woźniak-Budych M, **Wiweger M**, Słomski R, Jurga S. ZnO@Gd(2)O(3) core/shell nanoparticles for biomedical applications: Physicochemical, in vitro and in vivo characterization. ***Mater Sci Eng C Mater Biol Appl***, 2017; 80:603-615.

- **Gruszczynska-Biegala J**, **Sladowska M**, **Kuznicki J**. AMPA Receptors Are Involved in Store-Operated Calcium Entry and Interact with STIM Proteins in Rat Primary Cortical Neurons. ***Front Cell Neurosci***. 2016; 10:251

- **Wegierski T**, **Gazda K**, **Kuznicki J**. Microscopic analysis of Orai-mediated store-operated calcium entry in cells with experimentally altered levels of amyloid precursor protein. ***Biochem Biophys Res Commun***. 2016; 478(3):1087-92

- **Nagalski A**, Puelles L, Dabrowski M, **Wegierski T**, **Kuznicki J**, **Wisniewska MB**. Molecular anatomy of the thalamic complex and the underlying transcription factors. ***Brain Struct Funct***. 2016; 221(5):2493-510

- **Goś D**, **Szymańska E**, **Białek-Wyrzykowska U**, **Wiweger M**, **Kuźnicki J**. Be Healthy as a Fish Educational Program at the International Institute of Molecular and Cell Biology in Warsaw, Poland. ***Zebrafish***, 2016; 13(4):266-271

- **Majewski L**, **Kuznicki J**. SOCE in neurons: Signaling or just refilling? ***BBA Mol Cell Res***, 2015; 1853(9):1940-52

- Brendel M, **Jaworska A**, Herms J, Trambauer J, Rötzer C, GildehausFJ, Carlsen J, Cumming P, Bylund J, Luebbers T, Bartenstein P, Steiner H, Haass C, Baumann K, Rominger A. Amyloid-PET predicts inhibition of de novo plaque formation upon chronic γ-secretase modulator treatment. ***Mol Psychiatry***. 2015; 20(10):1179-87

- Mills F, Bartlett TE, Dissing-Olesen L, **Wisniewska MB**, **Kuznicki J**, Macvicar BA, Wang YT, Bamji SX. Cognitive flexibility and long-term depression (LTD) are impaired following β-catenin stabilization in vivo. ***Proc Natl Acad Sci USA***, 2014; 111(23):8631-36

- Honarnejad K, Daschner A, Gehring AP, **Szybinska A**, Giese A, **Kuznicki J**, Bracher F, Herms J. Identification of tetrahydrocarbazolesas novel multifactorial drug candidates for treatment of Alzheimer's disease. ***Transl Psychiatry***. 2014; 4:e489

- **Czeredys M**, **Gruszczynska-Biegala J**, Schacht T, Methner A, **Kuznicki J**. Expression of genes encoding the calcium signalosome in cellular and transgenic models of Huntington's disease. ***Front Mol Neurosci***. 2013; 6:42

- Honarnejad K, Daschner A, Giese A, Zall A, Schmidt B, **Szybinska A**, **Kuznicki J**, Herms J. Development and implementation of a high-throughput compound screening assay for targeting disrupted ER calcium homeostasis in Alzheimer's disease. ***PLoS One***, 2013; 8(11):e80645

- **Gruszczynska-Biegala J**, **Kuznicki J**. Native STIM2 and ORAI1 proteins form a calcium-sensitive and thapsigargin-insensitive complex in cortical neurons. ***J Neurochem***. 2013; 126(6):727-738

- **Jaworska A**, Dzbek J, Styczynska M, **Kuznicki J**. Analysis of calciumhomeostasis in fresh lymphocytes from patients with sporadic Alzheimer's disease or mild cognitive impairment. ***BBA Mol Cell Res***. 2013; 1833(7):1692-9

- **Wojda U, Kuznicki J**. Alzheimer's disease modeling: ups, downs, and perspectives for human induced pluripotent stem cells. ***J Alzheimers Dis***. 2013; 34(3):563-588

- **Nagalski A**, Irimia M, Szewczyk L, Ferran JL, **Misztal K**, **Kuznicki J**, **Wisniewska MB**. Postnatal isoform switch and protein localization of LEF1 and TCF7L2 transcription factors in cortical, thalamic, and mesencephalic regions of the adult mouse brain. ***Brain Struct Funct***. 2013; 218(6):1531-49

- **Wisniewska MB**, **Nagalski A**, Dabrowski M, **Misztal K**, **Kuznicki J**. Novel β-catenin target genes identified in thalamic neurons encode modulators of neuronal excitability. ***BMC Genomics***, 2012; 13:635

- **Bialopiotrowicz E**, **Szybinska A**, **Kuzniewska B**, Buizza L, Uberti D, **Kuznicki J**, **Wojda U**. Highly pathogenic Alzheimer's disease presenilin 1 P117R mutation causes a specific increase in p53 and p21 protein levels and cell cycle dysregulation in human lymphocytes. ***J Alzheimers Dis***. 2012; 32(2):397-415

- **Misztal K**, **Wisniewska MB**, **Ambrozkiewicz M**, **Nagalski A**, **Kuznicki J**. WNT protein-independent constitutive nuclear localization of beta-catenin protein and its low degradation rate in thalamic neurons. ***J Biol Chem***. 2011; 286(36):31781-8

- **Gruszczynska-Biegala J**, Pomorski P, **Wisniewska MB**, **Kuznicki J**. Differential roles for STIM1 and STIM2 in store-operated calciumentry in rat neurons. ***PLoS One***. 2011; 6(4):e19285

- **Sobczak A, Debowska K, Blazejczyk M**, Kreutz MR, **Kuznicki J**, Wojda U. Calmyrin1 binds to SCG10 protein (stathmin2) to modulateneurite outgrowth. ***BBA Mol Cell Res***, 2011; 1813(5):1025- 37

- **Wisniewska MB**, **Misztal K**, **Michowski W**, Szczot M, Purta E, Lesniak W, Klejman ME, Dabrowski M, Filipkowski RK, **Nagalski A**, Mozrzymas JW, **Kuznicki J**. LEF1/beta-catenin complex regulates transcription of the Cav3.1 calcium channel gene (Cacna1g) in thalamic neurons of the adult brain. ***J Neurosci***. 2010; 30(14):4957-69

We are interested in the molecular mechanisms that are involved in neurodegeneration, with a special emphasis on the role of Ca^{2+} homeostasis and signaling. These processes are being studied at the genomic, proteomic, and cellular levels using zebrafish, rats, and mice as model organisms. The projects are focused on proteins that are involved in store-operated calcium entry (SOCE), the involvement of potassium channels in the brain ventricular system, and the *in vivo* analysis of calcium homeostasis in neurons using zebrafish models.

Role of STIM proteins in store-operated calcium entry in neurons

We previously showed that STIM1 is involved in thapsigargin-induced SOCE, whereas STIM2 is mostly active after the EGTA-driven depletion of extracellular calcium (Gruszczynska-Biegala et al., *PLoS One*, 2011; Gruszczynska-Biegala and Kuznicki, *J Neurochem*, 2013). We searched for new partners of STIM proteins other than ORAI channels and found that endogenous STIMs physically associate with GluA subunits of AMPA receptors. The SOCE inhibitors reduced AMPA-induced Ca^{2+} influx, and AMPA antagonists decreased neuronal SOCE. These results suggested the involvement of AMPA receptors in neuronal SOCE (Gruszczynska-Biegala et al., *Front Cell Neurosci*, 2016).

Dysregulation of calcium homeostasis in neurodegenerative diseases

The vast majority of available animal models of Alzheimer's disease (AD) are based on the β-amyloid/tau hypothesis. These mice overexpress one or more mutated proteins that are known to be responsible for early-onset familial Alzheimer's disease (FAD). Models of FAD, representing less than 5% of all human cases, appear to have little value for understanding the mechanisms of sporadic AD (SAD; for review, see Wojda and Kuznicki, *J Alzheimers Dis*, 2013). Thus, new models need to be developed that incorporate some features of SAD. We tested the hypothesis that brain dysfunction during ageing is induced by changes in Ca^{2+} homeostasis, which may predispose the brain to SAD pathologies. Transgenic mice that overexpressed key SOCE proteins (STIM1, STIM2, and Orai1) specifically in brain neurons under the Thy1 promoter were generated. Characterization of the STIM1 line (Majewski et al., *BBA Mol Cell Res*, 2017) and Orai1 line (Majewski et al., Society for Neuroscience, 2017, abstract no. 477.06/P6) has been reported. The double transgenic line that expressed STIM2 and Orai1 proteins in neurons was generated, and its phenotype is being characterized.

FAD mutations in presenilins were shown to alter both endoplasmic reticulum (ER) calcium signaling and SOCE, but the role of amyloid precursor protein (APP) and APP FAD mutants in intracellular calcium homeostasis is controversial. Our data indicate that APP and APP FAD mutants are not directly involved in SOCE (Wegierski et al., *Biochem Biophys Res Commun*, 2016). Instead, we found that APP knockdown resulted in an elevation of the resting levels of ER Ca^{2+}, reduced Ca^{2+} leakage, and delayed the translocation of STIM1 to Orai1 upon ER Ca^{2+} store depletion. Our data suggest a regulatory role for APP in ER Ca^{2+} (Gazda et al., *Sci Rep*, 2017).
To explore calcium homeostasis during the early stages of SAD and mild cognitive impairment (MCI), we investigated SOCE and inositol triphosphate receptor 3-mediated calcium release into the cytoplasm in unmodified B-lymphocytes from MCI subjects and SAD patients and compared them with non-demented subjects. We observed perturbed calcium homeostasis in peripheral cells from MCI and SAD patients, supporting the hypothesis that SAD is a systemic disease, and MCI is a risk factor for AD (Jaworska et al., *BBA Mol Cell Res*, 2013; for review, see Majewski and Kuznicki, *BBA Mol Cell Res*, 2015).

Using qRT-PCR, we compared microRNA (miRNA) profiles in blood plasma from MCI-AD patients (whose diagnoses were confirmed by cerebrospinal fluid [CSF] biomarkers) with AD patients and non-demented, age-matched controls. We adhered to standardized blood and CSF assays that are recommended by the JPND BIOMARKAPD consortium, and we employed commercially available Exiqonq RT-PCR-assays. Six miRNAs (three not yet reported in the context of AD and three reported in AD blood) were selected as the most promising biomarker candidates that can differentiate early AD from controls with the highest fold changes (Nagaraj et al., *Oncotarget*, 2017; patent pending, PCT/IB2016/052440).

We previously showed that a mutation of huntingtin (HTT) in YAC128 mice (i.e., a model of Huntington's disease) resulted in the higher expression of some components of the calcium signalosome, including huntingtin-associated protein 1 (HAP1) and calcyclin (S100A6) binding protein (CacyBP/SIP; Czeredys et al., *Front Mol Neurosci*, 2013). We detected greater activity of SOC channels in medium spiny neurons (MSNs) from YAC128 mice and found that some tetrahydrocarbazoles restored the disturbances in Ca^{2+} homeostasis and stabilized SOCE in YAC128 MSN cultures (Czeredys et al., *Biochem Biophys Res Commun*, 2017). The overexpression of HAP1 protein isoform A in MSNs from YAC128 mice was found to enhance the activity of SOC channels after the activation of IP3R1.

In collaboration with Prof. Oliver Bandmann (University of Sheffield), we used a pink1 mutant ($pink^{-/-}$) zebrafish line to study possible alterations of Ca^{2+} homeostasis (Flinn et al., *Ann Neurol*, 2013). A loss-of-function mutation of pink1 causes early-onset Parkinson's disease in humans. We found that both genetic and pharmacological inhibition of the mitochondrial Ca^{2+} uniporter rescued dopaminergic neurons in $pink1^{-/-}$ zebrafish by reversing mitochondrial respiratory chain function (Soman et al., *Eur J Neurosci*, 2016). This work is being continued to establish the role of calcium homeostasis in mitochondria in $pink1^{-/-}$ fish.

Brain ventricle project

Formation of the brain ventricular system (BVS) occurs during the early neural development of vertebrates (Korzh, *Cell Mol Life Sci*, 2018). Deficiency of the BVS has been linked to numerous neurodegenerative diseases. The BVS depends on many factors, including the crucial role of ependyma (i.e., cells that line the BVS cavity and circumventricular organs, including the choroid plexus; Garcia-Lecea et al., *Front Neuroanat*, 2017). We previously found that ependyma expresses subunits of the voltage-gated potassium channels Kcnb1 (Kv2.1) and Kcng4 (Kv6.4), which antagonize each other. The deficiency of Kcnb1 in zebrafish causes microcephaly, and the gain-of-function of Kcnb1 causes hydrocephalus. Kcng4 acts in a reverse manner (Shen et al., *Sci Rep,* 2016). To study the role of K^+ channels in the development of ependyma, we are currently designing and developing transgenic knockin zebrafish that express fluorescent proteins in ependyma under the control of Kcng4b regulatory elements and mutants of Kcng4b using the CRISPR-Cas9 mutagenesis system.

Laboratory of Cell Biology

Senior Scientists

Magdalena Banach-Orłowska, PhD
Ewelina Szymańska, PhD
Daria Zdżalik-Bielecka, PhD

Postdocs

Jarosław Cendrowski, PhD
Kamil Jastrzębski, PhD
Krzysztof Kolmus, PhD (since June 2017)
Lidia Wolińska-Nizioł, PhD
(maternity leave since May 2017)

PhD Students

Marta Kaczmarek, MSc
Małgorzata Maksymowicz, MSc
Agata Poświata, MSc
Karolina Wojciechowska, MSc (since October 2017)

Undergraduate Students

Kamila Kozik (since March 2017)
Michał Mazur, Eng.
Patryk Ślusarczyk, Eng.
Małgorzata Świątek, BSc (since January 2018)

Trainees

Paulina Nowak, MSc (since October 2017)
Renata Wyszyńska, MSc (since October 2017)

Laboratory-Administrative Partner

Paulina Okafor, MSc (part-time)

Technician

Monika Matuszczyk (part-time)

Lab Leader

Marta Miączyńska, PhD, Professor

Curriculum Vitae

Degrees

- **2013** Professor of Biological Sciences, nomination by the President of the Republic of Poland
- **2008** DSc Habil in Cell Biology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
- **1997** PhD in Genetics, University of Vienna, Austria
- **1993** MSc in Molecular Biology, Jagiellonian University, Cracow, Poland
- **1991** BSc in Biological Sciences, University of Wolverhampton, UK

Professional Employment

- **2013-2015** Deputy Director for Science, International Institute of Molecular and Cell Biology, Warsaw, Poland
- **2003-Present** Professor, Head of Laboratory of Cell Biology, International Institute of Molecular and Cell Biology, Warsaw, Poland

Research Training

- **2001-2005** Senior Postdoctoral Fellow, Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG), Dresden, Germany
- **1997-2002** Postdoctoral training, European Molecular Biology Laboratory, Heidelberg, Germany
- **1993-1996** PhD studies, Institute of Microbiology and Genetics, University of Vienna, Austria
- **1990-1991** Exchange Student, University of Wolverhampton, UK

Honors, Fellowships and Awards

- **2017** Elected EMBO Member
- **2016-Present** Member, Council of the National Science Centre, Poland
- **2007** Habilitation Fellowship of L'Oreal Poland for Women in Science
- **2006-2012** International Senior Research Fellowship, Wellcome Trust, UK
- **2006-2010** International Research Scholar, Howard Hughes Medical Institute, USA
- **2006-2010** Partner Group grant, Max Planck Society, Germany
- **2001-2004** Postdoctoral Fellowship, Max Planck Society, Germany
- **1999-2000** Long-Term Postdoctoral Fellowship, Human Frontier Science Program Organization (HFSPO)
- **1998-1999** Erwin Schrödinger Postdoctoral Fellowship, Austrian Science Fund (FWF)
- **1993-1966** Bertha von Suttner PhD Scholarship, Austrian Ministry of Science
- **1990-1991** Studentship, European Community Tempus Scheme

Selected publications

(In bold authors with IIMCB affiliation)

- **Szymanska E, Budick-Harmelin N, Miaczynska M**. Endosomal "sort" of signaling control: The role of ESCRT machinery in regulation of receptor-mediated signaling pathways. ***Semin Cell Dev Biol***, 2018; 74:11–20

- Tudek B, **Zdżalik-Bielecka D**, Tudek A, Kosicki K, Fabisiewicz A, Speina E. Lipid peroxidation in face of DNA damage, DNA repair and other cellular processes. ***Free Radic Biol Med***, 2017; 107:77-89

- **Jastrzębski K**, **Zdżalik-Bielecka D**, **Mamińska A**, Kalaidzidis Y, Hellberg C, **Miaczynska M**. Multiple routes of endocytic internalization of PDGFRβ contribute to PDGF-induced STAT3 signaling. ***J Cell Sci,*** 2017; 130:577-589

- **Mamińska A**, **Bartosik A**, **Banach-Orłowska M**, **Pilecka I**, **Jastrzębski K**, **Zdżalik-Bielecka D**, Castanon I, Poulain M, Neyen C, **Wolińska-Nizioł L**, **Toruń A**, **Szymańska E**, Kowalczyk A, Piwocka K, Simonsen A, Stenmark H, Fürthauer M, González-Gaitán M, **Miaczynska M**. ESCRT proteins restrict constitutive NF-κB signaling by trafficking cytokine receptors. ***Sci Signal***, 2016; 9:ra8

- **Szymanska E**, **Skowronek A**, **Miaczynska M**. Impaired dynamin 2 function leads to increased AP-1 transcriptional activity through the JNK/c-Jun pathway. ***Cell Signal***, 2016; 28:160-71

- **Cendrowski J**, **Mamińska A**, **Miaczynska M**. Endocytic regulation of cytokine receptor signaling. ***Cytokine Growth Factor Rev***, 2016; 32:63-73

- Song J, Mu Y, Li C, Bergh A, **Miaczynska M**, Heldin CH, Landström M. APPL proteins promote TGFβ-induced nuclear transport of the TGFβ type I receptor intracellular domain. ***Oncotarget***, 2016; 7:279-92

- Mikula M, Skrzypczak M, Goryca K, Paczkowska K, Ledwon JK, Statkiewicz M, Kulecka M, Grzelak M, Dabrowska M, Kuklinska U, Karczmarski J, Rumienczyk I, **Jastrzebski K**, **Miaczynska M**, Ginalski K, Bomsztyk K, Ostrowski J. Genome-wide co-localization of active EGFR and downstream ERK pathway kinases mirrors mitogen-inducible RNA polymerase 2 genomic occupancy. ***Nucleic Acids Res***, 2016; 44:10150-10164

- Kalaidzidis I, **Miaczynska M**, **Brewińska-Olchowik M**, **Hupalowska A**, Ferguson C, Parton RG, Kalaidzidis Y, Zerial M. APPL endosomes are not obligatory endocytic intermediates but act as stable cargo sorting compartments. ***J Cell Biol,*** 2015; 211:123-44

- **Toruń A**, **Szymańska E**, Castanon I, **Wolińska-Nizioł L**, **Bartosik A**, **Jastrzębski K**, **Miętkowska M**, González-Gaitán M, **Miaczynska M**. Endocytic adaptor protein Tollip inhibits canonical Wnt signaling. ***PLoS One***, 2015; 10:e0130818

- **Banach-Orłowska M**, **Szymanska E**, **Miaczynska M**. APPL1 endocytic adaptor as a fine tuner of Dvl2-induced transcription. ***FEBS Lett***, 2015; 589:532-9

- Kolanczyk M, Krawitz P, Hecht J, **Hupalowska A**, **Miaczynska M**, Marschner K, Schlack C, Emerich D, Kobus K, Kornak U, Robinson PN, Plecko B, Grangl G, Uhrig S, Mundlos S, Horn D. Missense variant in CCDC22 causes X-linked recessive intellectual disability with features of Ritscher-Schinzel/3C syndrome. ***Eur J Hum Genet***, 2015; 23:633-8

- **Sadowski Ł**, **Jastrzebski K**, Purta E, Hellberg C, **Miaczynska M**. Labeling of platelet-derived growth factor by reversible biotinylation to visualize its endocytosis by microscopy. ***Methods Enzymol***, 2014; 535:167-77

- **Miaczynska M**. Effects of membrane trafficking on signaling by receptor tyrosine kinases. (Review) ***Cold Spring Harb Perspect Biol***, 2013; 5:a009035

- **Sadowski Ł**, **Jastrzebski K**, Kalaidzidis Y, Heldin CH, Hellberg C, **Miaczynska M**. Dynamin Inhibitors Impair Endocytosis and Mitogenic Signaling of PDGF. ***Traffic***, 2013; 14:725-36

- **Pyrzynska B**, **Banach-Orlowska M**, **Teperek-Tkacz M**, Miekus K, Drabik G, Majka M, **Miaczynska M**. Multifunctional protein APPL2 contributes to survival of human glioma cells. ***Mol Oncol***, 2013; 7:67-84

- Winiarska M, Nowis D, Bil J, Glodkowska-Mrowka E, Muchowicz A, Wanczyk M, Bojarczuk K, Dwojak M, Firczuk M, Wilczek E, Wachowska M, Roszczenko K, **Miaczynska M**, Chlebowska J, Basak GW, Golab J. Prenyltransferases Regulate CD20 Protein Levels and Influence Anti-CD20 Monoclonal Antibody-mediated Activation of Complement-dependent Cytotoxicity. ***J Biol Chem***, 2012; 287:31983-93

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- **Hupalowska A**, **Pyrzynska B**, **Miaczynska M**. APPL1 regulates basal NF-κB activity by stabilizing NIK**.** ***J Cell Sci***, 2012; 125: 4090-102

- **Hupalowska A**, **Miaczynska M**. The new faces of endocytosis in signaling. (Review) ***Traffic***, 2012; 13:9-18

- **Urbanska A**, **Sadowski L**, Kalaidzidis Y, **Miaczynska M**. Biochemical Characterization of APPL Endosomes: The Role of Annexin A2 in APPL Membrane Recruitment. ***Traffic***, 2011; 12:1227-41

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- **Rashid S**, **Pilecka I**, **Torun A**, **Olchowik M**, **Bielinska B**, **Miaczynska M**. Endosomal Adaptor Proteins APPL1 and APPL2 Are Novel Activators of beta-Catenin/TCF-mediated Transcription. ***J Biol Chem***, 2009; 284:18115-28

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^ no IIMCB affiliation

LABORATORY OF **CELL BIOLOGY**

We study the ways in which intracellular signal transduction and membrane trafficking in endocytosis are integrated at the molecular level. We focus on proteins that play well-known roles in endocytosis to investigate their involvement in various signaling pathways and their impact on patterns of gene expression. Initially, our efforts were focused on studying the endosomal and nuclear roles of APPL proteins. In recent years, we broadened our interests to other multifunctional proteins that act in endocytosis and signaling. The specific projects that are developed by our group seek to answer the following questions:

- What is the role of endosomal compartments in the trafficking and signaling of growth factors and cytokines?
- How does the endocytic trafficking of receptors impinge on the patterns of gene expression in different signaling pathways?
- What are the consequences of endosomal dysfunction in the cell?

Endocytosis was first viewed simply as a mechanism of signal termination through the downregulation and degradation of surface receptors. However, more recent data indicate that endosomal compartments and their resident proteins play an important role in transmitting intracellular signals by transporting ligand-receptor complexes and affecting their activity inside the cell (Cendrowski et al., *Cytokine Growth Factor Rev*, 2016; Hupalowska and Miaczynska, *Traffic*, 2012; Miaczynska, *Cold Spring Harb Perspect Biol*, 2013; Miaczynska and Bar-Sagi, *Curr Opin Cell Biol*, 2010; Sadowski et al., *Exp Cell Res*, 2009; Szymanska et al., *Semin Cell Dev Biol*, 2018). Moreover, several endocytic proteins can undergo nucleocytoplasmic shuttling and interact with nuclear molecules that are involved in transcription or chromatin remodeling, changing their localization or activity, and thus may directly modulate the levels or specificity of gene transcription (Pilecka et al., *Eur J Cell Biol*, 2007). Importantly, some such dual-function endocytic and nuclear proteins affect cell proliferation or act as tumor suppressors, or their expression changes in human cancers (Pyrzyńska et al., *Mol Oncol*, 2009).

In a recently completed project, we systematically characterized the endocytic routes of platelet-derived growth factor receptor β (PDGFRβ) bound to its ligand PDGF-BB and uncovered the impact of PDGFRβ trafficking on its signaling. PDGFRβ is a receptor tyrosine kinase. PDGFRβ activation by PDGF-BB stimulates cell proliferation, migration, and angiogenesis. We previously described two modes of PDGFRβ endocytosis in human fibroblasts: dynamin-dependent and -independent internalization (Sadowski et al., *Traffic*, 2013). This indicated the complexity of the mechanisms that contribute to the uptake of PDGFRβ. Therefore, more recently, we extended this initial study to identify the routes that mediate the internalization of PDGFRβ and their molecular determinants. We first showed that PDGFRβ-PDGF complexes are internalized via parallel pathways of clathrin-mediated endocytosis (CME) and clathrin-independent endocytosis (CIE). The CME of PDGFRβ requires the canonical AP2 complex as a clathrin adaptor. However, CIE includes a number of routes with different molecular players and operating modes. We demonstrated that PDGFRβ uptake engages Cdc42 and RhoA GTPases, along with the RhoA effectors ROCK1 and ROCK2. Furthermore, the involvement of galectin-3 in PDGFRβ internalization suggested that this receptor can also undergo lectin-mediated endocytosis via clathrin-independent carriers (CLICs). Interestingly, different uptake mechanisms of PDGFRβ cannot fully substitute for each other, although they are partially interdependent. Finally, we found that the inhibition of any internalization mechanism selectively impairs the activation of STAT3 transcription factor but not the activation of other downstream effectors of PDGFRβ. Our studies generally demonstrate that multiple routes of internalization of PDGFRβ operate in parallel and contribute to a transcriptional and mitogenic response of cells to PDGF. Moreover, among several signaling effectors of PDGFRβ, only STAT3 activation depends on receptor internalization (Fig. 1).

In another line of research, we identified four components of endosomal sorting complexes required for transport (ESCRTs) as novel inhibitors of NF-κB signaling (Mamińska et al., *Sci Signal*, 2016). We found that the depletion of Tsg101, Vps28, UBAP1, and CHMP4B in the absence of cytokine stimulation potently activated both canonical and noncanonical NF-κB signaling. This led to upregulation of the expression of NF-κB target genes in cultured human cells, zebrafish embryos, and fat bodies in flies. These effects depended on cytokine receptors, such as lymphotoxin β receptor (LTβR) and tumor necrosis factor receptor 1 (TNFR1). Upon the depletion of ESCRT subunits, both receptors became concentrated on and signaled from endosomes. The endosomal accumulation of LTβR induced its ligand-independent oligomerization and inflammatory NF-κB signaling. We propose that ESCRTs constitutively control the distribution of cytokine receptors in their ligand-free state to restrict their signaling. Building upon this work, we are currently investigating the mechanisms of intracellular trafficking and inflammatory signaling by LTβR.

Moreover, the depletion of ESCRT proteins represents a model of endosomal dysfunction. In an ongoing TEAM grant from the Foundation for Polish Science, we are studying the consequences of impairments in endosomal function on cellular protein homeostasis and metabolism. In collaboration with scientists from the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, we are also investigating the function of endosomes in cancer cells and the possibility of its pharmacological modulation.

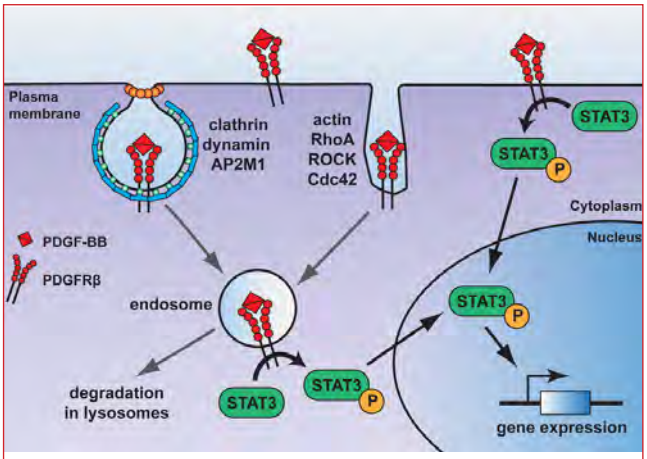

Fig. 1. Model of endocytosis and signaling by platelet-derived growth factor receptor β (PDGFRβ). PDGFRβ is internalized via multiple entry pathways, relying on the indicated molecular regulators for clathrin-dependent (left) and clathrin-independent (right) endocytosis. Full STAT3 activation that is induced by ligand binding to PDGFRβ requires receptor internalization into endosomes. Author: Kamil Jastrzębski.

Laboratory of Iron Homeostasis

- **PhD Students**
  Gabriela Jędruszewska, MSc
  Ewa Mandziak, MSc
- **MSc Student**
  Dawid Mąkosa
- **Technician**
  Marta Niklewicz (part-time)
- **Laboratory-Administrative Partner**
  Aleksandra Szybińska, MSc (part-time)

Lab Leader

Katarzyna Mleczko-Sanecka, PhD

Curriculum Vitae

Degrees

2011 PhD in Biology, European Molecular Biology Laboratory (EMBL) Heidelberg and Heidelberg University, Germany

2007 MSc in Biotechnology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Cracow, Poland

Research experience

2016-Present Professor, Head of Laboratory of Iron Homeostasis, International Institute of Molecular and Cell Biology in Warsaw, Poland

2011-2015 Post-doctoral research with Prof. Martina Muckenthaler and Prof. Matthias W. Hentze, Molecular Medicine Partnership Unit, EMBL Heidelberg and Heidelberg University, Germany

2007-2011 Doctoral research with Prof. Martina Muckenthaler and Prof. Matthias W. Hentze, Molecular Medicine Partnership Unit, EMBL Heidelberg and Heidelberg University, Germany

2006-2007 Master thesis research in the laboratory of Prof. Jozef Dulak and Prof. Alicja Jozkowicz, Department of Medical Biotechnology, Jagiellonian University, Cracow, Poland

2006 Undergraduate research during Erasmus fellowship at the Centre De Biophysique Moleculaire in Dr. Claudine Kieda's laboratory, CNRS, Orleans, France

2005 Undergraduate research in the laboratory of Prof. Jozef Dulak and Prof. Alicja Jozkowicz, Department of Medical Biotechnology, Jagiellonian University, Cracow, Poland

Achievements and honors

2015 NCN Polonez Fellowship (funded by Marie Sklodowska-Curie Actions)

2014 Independent research grant from the University of Heidelberg

2011 Invitation for the 61st Lindau Meeting of Nobel Laureates, Lindau, Germany

2015, 2014, 2011, 2010, 2009 Travel Grants to attend and present data at the International Bioiron Society Meetings: 2015 (Hangzhou, China), 2011 (Vancouver, Canada) and 2009 (Porto, Portugal) and the European Iron Club Meetings: 2014 (Verona, Italy) and 2010 (Nijmegen, Netherlands)

2007 The Louis-Jeantet PhD Scholarship for young researchers from Eastern Europe supporting PhD studies at EMBL

2006 ERASMUS Scholarship at the CNRS, Orleans, France

Selected publications

(In bold authors with IIMCB affiliation)

- Pasricha SR, Lim PJ, Duarte TL, Casu C, Oosterhuis D, **Mleczko-Sanecka K**,Suciu M, Da Silva AR, Al-Hourani K, Arezes J, McHugh K, Gooding S, Frost JN, Wray K, Santos A, Porto G, Repapi E, Gray N, Draper SJ, Ashley N, Soilleux E, Olinga P, Muckenthaler MU, Hughes JR, Rivella S, Milne TA, Armitage AE, Drakesmith H. Hepcidin is regulated by promoter-associated histone acetylation and HDAC3. ***Nat Commun***. 2017; 8(1):403

- **Mleczko-Sanecka K**, da Silva AR, Call D, Neves J, Schmeer N, Damm G,Seehofer D, Muckenthaler MU. Imatinib and spironolactone suppresshepcidin expression. ***Haematologica***, 2017; 102(7):1173-84

- Tejchman A, Lamerant-Fayel N, Jacquinet JC, Bielawska-Pohl A, **^Mleczko-Sanecka K**, Grillon C, Chouaib S, Ugorski M, Kieda C. Tumor hypoxia modulates podoplanin/CCL21 interactions in CCR7+ NK cell recruitment and CCR7+ tumor cell mobilization. ***Oncotarget***, 2017; 8(19):31876-87

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- Sonnweber T, Nachbaur D, Schroll A, Nairz M, Seifert M, Demetz E, Haschka D, Mitterstiller AM, Kleinsasser A, Burtscher M, Trübsbach S, Murphy AT, Wroblewski V, Witcher DR, **^Mleczko-Sanecka K**, Vecchi C, Muckenthaler MU, Pietrangelo A, Theurl I, Weiss G. Hypoxia induced downregulation of hepcidin is mediated by platelet derived growth factor BB. ***Gut***, 2014; 63(12):1951-9

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- Casanovas G, **^Mleczko-Sanecka K**, Altamura S, Hentze MW, Muckenthaler MU. Bone morphogenetic protein (BMP)-responsive elements located in the proximal and distal hepcidin promoter are critical for its response to HJV/BMP/SMAD. ***J Mol Med***, 2009; 87(5):471-80

- Jozkowicz A, Was H, Taha H, Kotlinowski J, **^Mleczko K**, Cisowski J, Weigel G, Dulak J. 15d-PGJ2 upregulates synthesis of IL-8 in endothelial cells through induction of oxidative stress. ***Antioxid Redox Signal***, 2008; 10(12):2035-46

- Funovics P, Brostjan C, Nigisch A, Fila A, Grochot A, **^Mleczko K**, Was H, Weigel G, Dulak J, Jozkowicz A. Effects of 15d-PGJ(2) on VEGF-induced angiogenic activities and expression of VEGF receptors in endothelial cells.

  Prostaglandins Other Lipid Mediat, 2006; 79(3-4):230-244

^ no IIMCB affiliation

Description of Current Research

Sufficient iron supplies are critical for vital cellular functions, such as energy production and RNA/DNA processing and repair. In the human body, the vast majority of iron is utilized for hemoglobin synthesis during the daily production of ~200 billion erythrocytes. However, excess free iron causes oxidative damage, leading to organ failure. The maintenance of an appropriate iron balance is essential for the proper functioning of cells and organisms. Broadening our knowledge of the genetic control of iron homeostasis is important for human health. The major objective of research in the Laboratory of Iron Homeostasis is to better understand the processes that impact systemic and cellular iron levels and identify new players in iron-regulatory pathways.

At the systemic level, more than 90% of daily iron needs are met by internal iron recycling from senescent erythrocytes by splenic macrophages. The iron pool in the body is largely preserved. Because iron excretion is unregulated, iron acquisition in the intestine and its release from splenic macrophage stores must be tightly controlled. In mammals, an appropriate iron balance in the body is chiefly ensured by the hepcidin-ferroportin (FPN) regulatory axis (Fig. 1A). Hepcidin is a small hormone that is produced by liver hepatocytes. It binds to the iron exporter FPN to trigger its degradation and inhibit iron release from specialized iron-exporting cells. Iron export via FPN determines iron saturation of the plasma protein transferrin. The uptake of transferrin-bound iron occurs via the ubiquitously expressed transferrin receptor 1 (TFR1), which constitutes a major route of cellular iron acquisition. Analyses of patients with iron-related disorders, complemented by mouse genetic studies, show that the key genetic regulators of systemic iron homeostasis are linked to the hepcidin-FPN-transferrin circuit. However, body iron status is a complex trait with a typical polygenic pattern of inheritance, and a proportion of its phenotypic variability remains not fully explained. Thus, elusive mechanisms that contribute to such processes as iron sensing, iron flux, and iron deposition still need to be elucidated.

When iron levels in the body increase, hepcidin production is enhanced to prevent further iron absorption from the diet. To gain insights into the genetic control of iron homeostasis, we previously designed and conducted large-scale RNAi screens for novel hepcidin regulators (Mleczko-Sanecka et al., *Blood*, 2010; Mleczko-Sanecka et al., *Blood*, 2014; Fig. 2). This work identified SMAD7 as an important hepcidin inhibitor and linked hepcidin control to proliferative signaling. Furthermore, our screens generated comprehensive lists of potential modifiers of iron homeostasis. One of our future goals is to employ this resource to better define the architecture of transcriptional complexes at the hepcidin promoter. Based on the screening data, we have also sought to identify and develop hepcidin-modifying drugs. Our recently published results demonstrate that a commonly used antihypertensive drug, spironolactone, which is prescribed for the treatment of heart failure, acne, and female hirsutism, and imatinib, a first-line, lifelong therapeutic option for some frequent cancer types, suppress hepcidin expression in cultured cells and in mice (Mleczko-Sanecka et al., *Haematologica,* 2017). We expect these findings to be relevant to patient management, which needs to be addressed in prospective clinical studies.

Bone morphogenetic protein (BMP) signaling is a key upstream pathway for iron-dependent hepcidin regulation. In recent years, BMP6 has emerged as a crucial endogenous BMP factor that is produced by liver sinusoidal endothelial cells, maintains body iron homeostasis, and stimulates hepcidin synthesis in hepatocytes under iron-rich conditions (Fig. 1B). Remaining unknown, however, is the way in which iron-related signals translate into increases in *Bmp6* mRNA levels. Therefore, one of our projects seeks to dissect iron-dependent regulatory mechanisms that control the expression of BMP6.

Dysregulation of the iron-sensing capacity of the BMP6-hepcidin axis leads to excessive tissue iron accumulation. This is a hallmark of the frequent iron overload disease hereditary hemochromatosis and some severe anemias (e.g. thalassemias) and is associated with several other diseases. When the iron saturation of transferrin exceeds its iron-binding capacity, non-transferrin bound iron (NTBI) starts to be generated in the circulation. This form of "free iron" is highly toxic and is currently considered a main contributor to the pathology of iron-overload disorders. We seek to understand the molecular processes that contribute to NTBI iron uptake in hepatocytes, the major cell type that accumulates iron in iron overload-related diseases. Specifically, we want to identify the regulatory network that modulates high hepatic expression levels of ZIP14 (encoded by *SLC39A14*), the key metal transporter that is responsible for NTBI uptake in the liver (Fig. 1B) This question will be primarily addressed using CRISPR/Cas9-based loss-of-function genetic screens, followed by functional characterization of the most interesting hits in cellular assays and in mice. As a tool for this project, we have employed gene editing techniques to generate reporter cells that are engineered to monitor endogenous levels of *SLC39A14* using a fluorescence-based readout. We aim to further validate and characterize such "new-generation" reporter systems, which could be applied to answer other interesting biological questions.

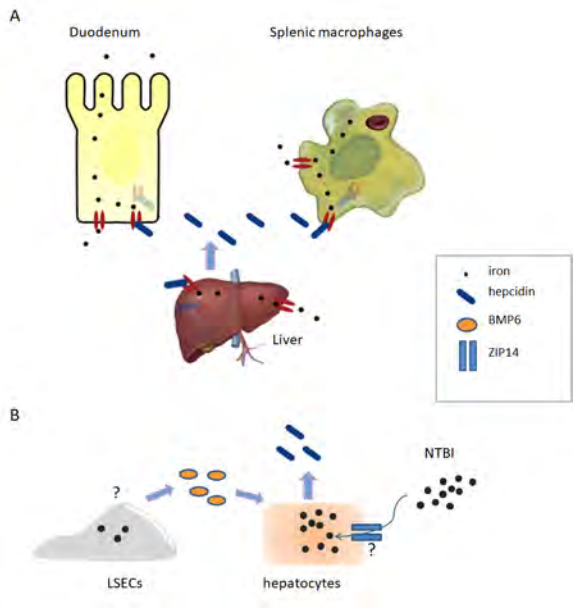

Fig. 1. Systemic iron homeostasis is maintained by the hepcidin/ferroportin axis. Under iron-rich conditions production of hepcidin is stimulated in hepatocytes by BMP6, an angiokine released from liver sinusoidal endothelial cells (LSECs). One aim of our research is to dissect mechanisms that control iron-triggered induction of BMP6, and thereby to better understand the process of iron-sensing in the liver. Another major objective of work in our laboratory is to seek for elusive mechanisms that control expression of ZIP14, an abundant hepatocytic transporter that is responsible for liver accumulation of non-transferrin bound iron (NTBI).

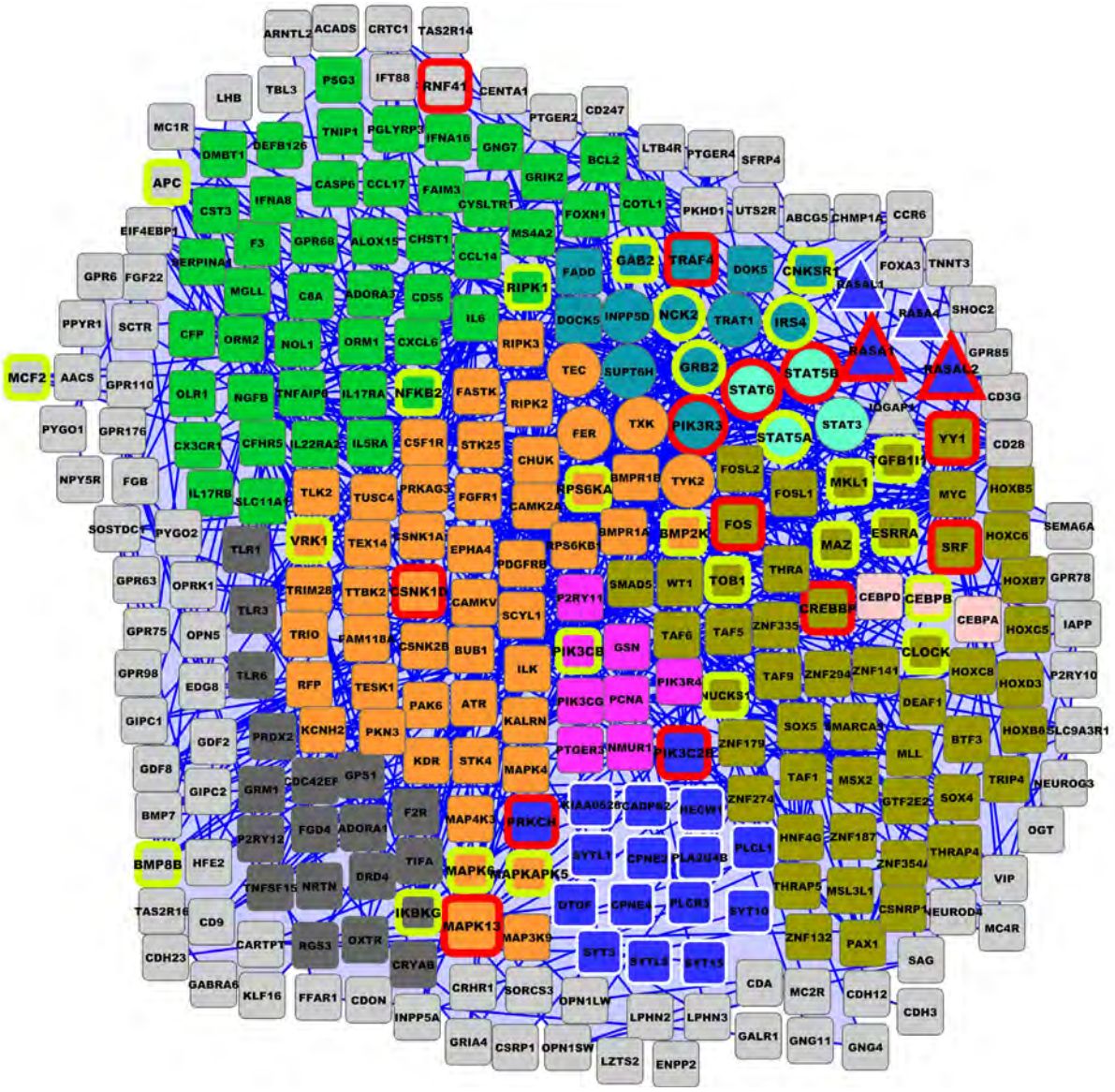

Fig. 2. An unbiased genome-wide RNAi screen provided new insights into genes and pathways that are involved in the regulation of hepcidin (Mleczko-Sanecka et al., 2014). The figure shows the interaction network of putative hepcidin activators, grouped within functional categories that were enriched in the screening data.

Laboratory of Protein Structure

Visiting Professor

Andrzej Wierzbicki, PhD
(University of Michigan, Ann Arbor)

Senior Scientist

Elżbieta Nowak, PhD

Postdocs

Mariusz Czarnocki-Cieciura, PhD
Małgorzata Figiel, PhD
Vineet Gaur, PhD
Filip Gołębiowski, PhD
Karolina Górecka, PhD
Zuzanna Kaczmarska, PhD (since March 2018)
Zbigniew Pietras, PhD (since August 2017)

PhD Students

Sebastian Chamera, MSc (since August 2017)
Marta Gapińska, MSc (since July 2017)
Deepshikha Malik, MSc
Marzena Nowacka, MSc
Michał Rażew, MSc

Research Technicians

Justyna Studnicka, MSc
Weronika Zajko, MSc

Technician

Iwona Ptasiewicz (part-time)

Laboratory-Administrative Partner

Kinga Adamska, MSc

Lab Leader

Marcin Nowotny, PhD, DSc Habil

Curriculum Vitae

Degrees

2013 DSc Habil in Molecular Biology, Institute of Biochemistry and Biophysics, Warsaw, Poland

2002 PhD magna cum laude in Biochemistry, under the supervision of Prof. Jacek Kuźnicki, Department of Molecular and Cellular Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

1998 MSc in Organic Chemistry and Biochemistry, Department of Chemistry, Warsaw University, Poland

Postdoctoral Training

2003-2008 Postdoctoral Fellow, Wei Yang Laboratory, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA

Professional Employment

2015-Present Deputy Director for Science, International Institute of Molecular and Cell Biology, Warsaw, Poland

2008-Present Professor, Head of the Laboratory of Protein Structure, International Institute of Molecular and Cell Biology, Warsaw, Poland

Honors, Prizes, Awards

2017 FNP TEAM grant

2015 Jan Karol Parnas Award for the best Polish biochemical publication (with the group of Prof. Janusz M. Bujnicki)

2013 Academia Europea Burgen Scholar

2013 Knight's Cross of the Order of Polonia Restituta

2012 Polish Prime Minister's Award for scientific achievement

2012 „Ideas for Poland" Award, Foundation for Polish Science

2012 Jan Karol Parnas Award for the best Polish biochemical publication

2012 Wellcome Trust Senior Research Fellowship (renewal)

2012 HHMI Early Career Scientist Award

2011 ERC Starting Grant

2007 EMBO Installation Grant

2007 Wellcome Trust Senior Research Fellowship

2003 Prime Minister's Award for PhD thesis

2001, 2002 Annual Stipend for Young Scientists, Foundation for Polish Science

Selected publications

(In bold authors with IIMCB affiliation)

- **Razew M**, Warkocki Z, Taube M, Kolondra A, **Czarnocki-Cieciura M**, **Nowak E**, Labedzka-Dmoch K, Kawinska A, Piatkowski J, Golik P, Kozak M, Dziembowski A, **Nowotny M**. Structural analysis of mtEXO mitochondrial RNA degradosome reveals tight coupling of nuclease and helicase components. ***Nat Commun***, 2018; 9(1):97
- **Figiel M**, Krepl M, Park S, Poznański J, Skowronek K, Gołąb A, Ha T, Šponer J, **Nowotny M**. Mechanism of polypurine tract primer generation by HIV-1 reverse transcriptase. ***J Biol Chem***, 2018; 293(1):191-202
- **Figiel M**, **Nowotny M**. Structural Studies of RNases H2 as an Example of Crystal Structure Determination of Protein-Nucleic Acid Complexes. ***Methods Enzymol***, 2017; 592:123-143
- Rydzik AM, Warminski M, Sikorski PJ, Baranowski MR, Walczak S, Kowalska J, Zuberek J, Lukaszewicz M, **Nowak E**, Claridge TDW, Darzynkiewicz E, **Nowotny M**, Jemielity J. mRNA cap analogues substituted in the tetraphosphate chain with CX2: identification of O-to-CCl2 as the first bridging modification that confers resistance to decapping without impairing translation. ***Nucleic Acids Res***, 2017; 45(15):8661-75
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- **Nowotny M**, **Gaur V**. Structure and mechanism of nucleases regulated by SLX4. ***Curr Opin Struct Biol***, 2016; 36:97-105
- **Gaur V**, Wyatt HDM, **Komorowska W**, Szczepanowski RH, de Sanctis D, **Gorecka KM**, West SC, **Nowotny M**. Structural and Mechanistic Analysis of the Slx1-Slx4 Endonuclease. ***Cell Rep***, 2015, 10(9):1467-76
- **Miętus M**, **Nowak E**, **Jaciuk M**, **Kustosz P**, **Studnicka J**, **Nowotny M**. Crystal structure of the catalytic core of Rad2: insights into the mechanism of substrate binding. ***Nucleic Acids Res***, 2014; 42(16):10762-75

Selected publications

- **Figiel M**, **Nowotny M**. Crystal structure of RNase H3-substrate complex reveals parallel evolution of RNA/DNA hybrid recognition. ***Nucleic Acids Res***, 2014; 42(14):9285-94
- **Nowak E**, Miller JT, Bona MK, **Studnicka J**, **Szczepanowski RH**, **Jurkowski J**, Le Grice SFJ§, **Nowotny M**§. Ty3 reverse transcriptase complexed with an RNA-DNA hybrid shows structural and functional asymmetry. ***Nat Struct Mol Biol,*** 2014; 21(4):389-396; §corresponding authors
- **Smietanski M***, Werner M*, Purta E, Kaminska KH, Stepinski J, Darzynkiewicz E, **Nowotny M**§, Bujnicki JM§. Structural analysis of human 2'-O-ribose methyltransferases involved in mRNA cap structure formation. ***Nat Commun,*** 2014; 5:3004; §corresponding authors, *equally contributing
- **Górecka KM**, **Komorowska W**, **Nowotny M**. Crystal structure of RuvC resolvase in complex with Holliday junction substrate. ***Nucleic Acids Res,*** 2013; 41(21):9945-55
- **Nowak E**, Potrzebowski W, Konarev P, Rausch J, Bona M, Svergun DI, Bujnicki JM, Le Grice SF, **Nowotny M**. Structural analysis of monomeric retroviral reverse transcriptase in complex with an RNA/DNA hybrid. ***Nucleic Acids Res,*** 2013; 41(6):3874-87
- **Figiel M**, Chon H, Cerritelli SM, **Cybulska M**, Crouch RJ, **Nowotny M**. The structural and biochemical characterization of human RNase H2 complex reveals the molecular basis for substrate recognition and Aicardi-Goutieres syndrome defects. ***J Biol Chem,*** 2011; 286(12):10540-50
- **Jaciuk M**, **Nowak E**, Skowronek K, **Tanska A**, **Nowotny M**. Structure of UvrA nucleotide excision repair protein in complex with modified DNA. ***Nat Struct Mol Biol,*** 2011; 18(2):191-197
- **Rychlik MP**, Chon H, Cerritelli SM, Klimek P, Crouch RJ, **Nowotny M**. Crystal structures of RNase H2 in complex with nucleic acid reveal the mechanism of RHAN-DNA junction recognition and cleavage. ***Mol Cell,*** 2010; 40(4):658-670
- **Nowotny M**, Yang W. Structural and functional modules in RNA interference (review). ***Curr Opin Struct Biol,*** 2009; 19(3):286-293
- **Nowotny M**. Retroviral integrase superfamily: the structural perspective (review). ***EMBO Rep,*** 2009; 10(2):144-151
- **^Nowotny M**, Gaidamakov SA, Ghirlando R, Cerritelli SM, Crouch RJ, Yang W. Structure of human RNase H1 complexed with an RNA/DNA hybrid: insight into HIV reverse transcription. ***Mol Cell,*** 2007; 28(2):264-276
- **^Nowotny M**, Gaidamakov SA, Crouch RJ, Yang W. Crystal structures of RNase H bound to an RNA/DNA hybrid: substrate specificity and metal-dependent catalysis. ***Cell,*** 2005; 121(7):1005-16

^ no IIMCB affiliation

Description of Current Research

Our laboratory focuses on structural and biochemical studies of nucleic acid enzymes using protein crystallography as a primary method. The key results that have been obtained recently by our group concern RNA turnover and reverse transcriptases (RTs).

Mechanism of mitochondrial RNA degradation

RNA metabolism, the regulation of gene expression, and the efficient removal of defective RNA molecules critically rely on RNA degradation pathways. This degradation is mainly achieved by the action of processive exoribonucleases that can act from either end of RNA molecules. They often form assemblies with other proteins to enhance their effectiveness. For example, exoribonucleases that exhibit 3'-to-5' directionality can work together with RNA helicases that are believed to facilitate substrate recruitment and help unwind structured RNAs. One example of such cooperation is the yeast mitochondrial RNA degradosome (mtEXO) complex. It is composed of two subunits: the metal-dependent 3'-to-5' exoribonuclease Dss1 and the nucleotide triphosphate (NTP)-dependent RNA helicase Suv3 that has the same directionality. Both proteins are encoded by nuclear genes. Mutations of either gene cause the accumulation of excision introns and RNA precursors, thus lowering the level of mature transcripts and consequently leading to loss of the mitochondrial genome. The mtEXO complex can be reconstituted *in vitro* with a 1:1 Dss1:Suv3 stoichiometry. Biochemical studies revealed that both subunits share a remarkable functional interdependence of their nuclease and helicase activity within the complex.

The aim of our research was to understand the mechanism of action of mtEXO and particularly the basis of the tight interdependence of the helicase and nuclease activities. We solved a crystal structure of Dss1 exoribonuclease from *Candida glabrata* (PDB ID: 6F3H), which showed that the enzyme is a unique member of the RNase II-like family with special N-terminal domains—β-barrel, winged-helix, and helix-turn-helix—that replaced the typically observed Cold Shock Domains. We also determined a crystallographic structure of the mtEXO complex from *Candida glabrata* (PDB ID: 6F4A), which for the first time showed the spatial orientation of both of its subunits within a functional complex. The arrangement of the two proteins enables the helicase motor to feed the free 3' end of the RNA molecule toward the exoribonuclease active site where efficient digestion of the substrate occurs. The protein-protein interface is formed between the RecA1 domain of Suv3 helicase and the two specialized domains of Dss1: winged-helix and helix-turn-helix. This allows the complex to accommodate conformational changes in the Suv3 ATPase cycle.

The cooperation of both activities is particularly important in the context of the degradation of structured RNA molecules that Dss1 nuclease is unable to digest. Only the unwinding of their secondary structure by the Suv3 helicase and the release of the free 3' end toward the Dss1 catalytic channel enables further degradation. This work was performed in collaboration with Prof. Andrzej Dziembowski and Prof. Paweł Golik (Razew et al., *Nat Commun*, 2018).

Reverse transcriptases

Reverse transcriptases catalyze the process of the conversion of single-stranded RNA to double-stranded DNA. This reaction is termed reverse transcription and a critical step in the proliferation of retroviruses, such as human immunodeficiency virus (HIV) and the most successful genetic mobile elements (i.e., retroelements). Two activities of RTs are required for reverse transcription: DNA polymerase synthesizes the new DNA, and RNase H degrades the RNA/DNA intermediate of the reaction. HIV RT is a heterodimer, and its larger subunit harbors both polymerase and RNase H activities. Our aim was to elucidate the mechanism of coordination of these two enzymatic activities of HIV-1 RT (Figiel et al., *Nucleic Acids Res*, 2017). A number of structures are available for the enzyme in complex with various nucleic acid substrates. In some of the structures, the substrate interacted with the polymerase active site, but none of them captured the catalytic interaction between the substrate and the RNase H domain. To characterize the conformation that corresponds to this catalytic interaction, we used an approach that combines chemical cross-linking between the protein and nucleic acid using molecular dynamics simulations. We found that the interaction between the substrate and RNase H domain involves conformational changes in both the protein and the nucleic acid

(i.e., untwisting of the double helix and narrowing of the minor groove). Importantly and contrary to the results of structural studies, when the substrate interacts with the RNase H active site, it can also be productively engaged at the polymerase active site. Such a configuration has not yet been captured in crystal structures and thus corresponds to a potential transient state of the protein-substrate complex. This demonstrates the existence of transient conformations that are essential for the mechanism of nucleic acid enzymes. This work was performed in collaboration with Prof. Jarosław Poznański (IBB, Polish Academy of Science) and were published online in 2017 (Figiel et al., *J Biol Chem*, 2018).

A critical yet poorly understood step of the reverse transcription reaction is the generation of the polypurine tract (PPT) primer for the synthesis of (+)-strand DNA. The PPT comprises 15 ribonucleotides, including a stretch of eight adenines with a single intervening guanine, followed by a stretch of six guanines. The PPT primer is generated by protecting its body from cleavage by RNase H and the introduction of specific cuts at the PPT termini. We prepared covalently tethered HIV-1 RT–PPT nucleic acid complexes. We found that recognition of the PPT occurred within these covalent complexes, indicating that the PPT is generated in the catalytic complex after its formation. We showed that two elements are involved in PPT recognition, and both rely on the specific sequence of the PPT. The first is RNase H sequence preference. The second is the inability of the poly-rA/dT tract of the PPT to adopt a conformation that is required for RNase H cleavage. The latter stems from the fact that the poly-rA/dT tract is rigid, and its deformations into an RNase H cleavage conformation lead to the base-pair slippage of its sequence. Our results demonstrated an unexpected mechanism by which the specific dynamic properties of the poly-rA/dT segment are involved in PPT recognition. The studies of HIV-1 RT have been performed in collaboration with Prof. Jarosław Poznański (IBB, Polish Academy of Science), the group of Jiri Šponer (Academy of Sciences of the Czech Republic), and the group of Taekjip Ha (Johns Hopkins University) and were published online in 2017 (Figiel et al., *J Biol Chem*, 2018).

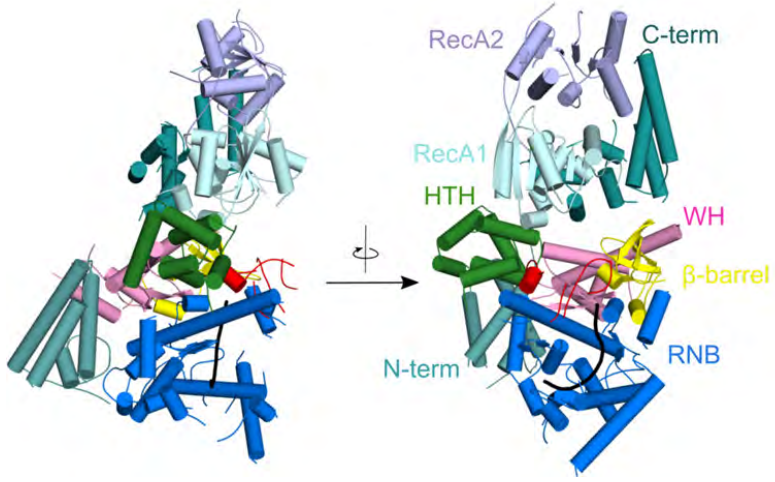

Fig. 1. The crystallographic structure of the mtEXO complex from Candida glabrata (PDB ID: 6F4A). Within the complex, the entry to the RNA-binding channel of Dss1 is occupied by the Suv3 helicase ring that interacts with the unique domains decorating the RNB catalytic domain of Dss1 (marked in blue). The co-crystallized RNA that is trapped inside the RNB domain is shown in black.

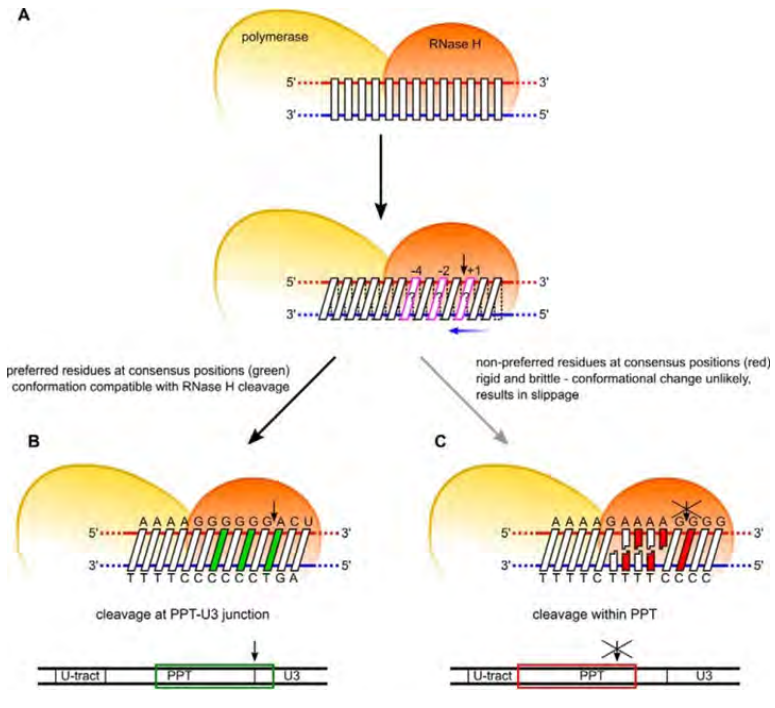

Fig. 2. Model of PPT recognition by HIV-1 RT. Comparison of interactions of RNase H domain with a preferred (PPT-U3 junction) and non-preferred (PPT) substrate. Preferred and non-preferred residues at the consensus positions of the substrate are shown in green and red, respectively. Deformation of the poly-A sequence of the substrate is represented by broken boxes.

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Curriculum Vitae

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Selected publications

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- Balaji V, **Pokrzywa W***, Hoppe T. Ubiquitylation Pathways In Insulin Signaling and Organismal Homeostasis. ***Bioessays***, 2018 Apr 3:e1700223 Epub ahead of print **Pokrzywa W**, Hoppe T. CHIPped balance of proteostasis and longevity. ***Oncotarget***, 2017; 8(57):96472-73

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- Stawiecka-Mirota M, ^**Pokrzywa W***, Morvan J, Zoladek T, Haguenauer-Tsapis R, Urban-Grimal D, Morsomme P. Targeting of Sna3p to the endosomal pathway depends on its interaction with Rsp5p and multivesicular body sorting on its ubiquitylation. ***Traffic***, 2007; 8(9):1280-96

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The proteome is defined as the entire set of proteins that are expressed in a given cell type or organism, which can vary with time and physiological status. Quality control networks support the integrity of the cellular proteome. The human protein homeostasis network (proteostasis) involves >1000 accessory factors and regulatory components that govern protein synthesis, folding, and degradation. Defective folding can result in the greater abundance of toxic protein aggregates, which can endanger the integrity of the entire proteome. With age, the ability of post-mitotic cells to maintain a balanced proteome is gradually compromised, particularly by the downregulation of molecular chaperones and lower efficiency of protein degradation. As such, impairments in proteostasis are a major hallmark of aging and associated with dementia, neurodegeneration, type 2 diabetes, cystic fibrosis, cancer, and cardiovascular disease (Labbadia and Morimoto, *Annu Rev Biochem*, 2015). One of the central nodes of the eukaryotic proteostasis network is the interaction between molecular chaperones and proteolytic machineries. To maintain the cellular proteome, molecular chaperones and ubiquitin-dependent degradation pathways (ubiquitin/proteasome system [UPS]) coordinate protein refolding and the removal of terminally damaged proteins. Irreversibly affected proteins are recognized by chaperone-assisted E3 ubiquitin ligases, which target them for degradation by the UPS or autophagy (Fig. 1).

Our research concentrates on the basic understanding of the spatiotemporal regulation of protein quality control activity and substrate processing. We use cell culture systems and *Caenorhabditis elegans* as an ideal animal model to study the organismal regulation of stress responses and proteostasis.

We focus mainly on the following projects:

Identification of signals that coordinate the function of distinct E3 ligases.

The UPS is a major proteolytic route that maintains the proteome during development, stress, and aging. Protein degradation is mainly mediated by the 26S proteasome upon the covalent attachment of ubiquitin to target proteins by E1 (activating), E2 (conjugating), and E3 (ligating) enzymes in a process known as ubiquitylation. Despite many structurally unrelated substrates, ubiquitin conjugation is remarkably selective. E3 ubiquitin ligases represent the largest group of proteins within the UPS, which is linked to their crucial role in substrate selection. A detailed analysis of several classes of E3 ligases identified specific proteins and molecular pathways that they regulate. Furthermore, the heterotypic oligomerization of E3 ligases might control the specificity and processivity of ubiquitylation. Recently, Scott and co-workers reported that two distinctive E3s could reciprocally monitor each other for the simultaneous and joint regulation of substrate ubiquitylation. Cullin-RING (CRL) ligase was shown to associate with a mechanistically distinct thioester-forming RBR-type E3, ARIH1, and rely on ARIH1 to directly add ubiquitin chains on CRL substrates (Scott et al., *Cell*, 2016). Therefore, the existence of cooperation between various E3 enzymes, which increases their molecular capabilities, appears to be highly probable but requires further exploration.

Our long-term objective is to understand the mechanistic and developmental aspects of protein degradation pathways that are defined by a specific pair of E3 enzymes. The combination of biochemical, microscopic, and genetic techniques with tissue-specific approaches in *C. elegans* will allow us to understand the ways in which alternative combinations of E3 proteins fine-tune proteolytic networks.

Stress-induced myosin folding and assembly mechanisms (Part Research Unit 2743 - Mechanical Stress Protection, financed by the German Research Foundation (DFG)).

The assembly and maintenance of myofilaments require a tightly balanced proteostasis network. One key player in myosin organization and muscle thick filament formation in health and disease is the Hsp90 co-chaperone UNC-45.

The activity and assembly of various myosin subtypes are coordinated by conserved UCS (UNC-45/CRO1/She4p) domain proteins. One founding member of the UCS family is the *Caenorhabditis elegans* UNC-45, a protein that is essential for the organization of striated muscle filaments (Price et al., *J Cell Sci*, 2002). Moreover, UNC-45 homologs exist in vertebrates, indicating a conserved requirement for myosin-specific co-chaperones (Price et al., *J Cell Sci*, 2002). Indeed, abnormal UNC-45 function is associated with severe muscle defects that result in skeletal and cardiac myopathies (Janiesch et al., *Nat Cell Biol,* 2007).

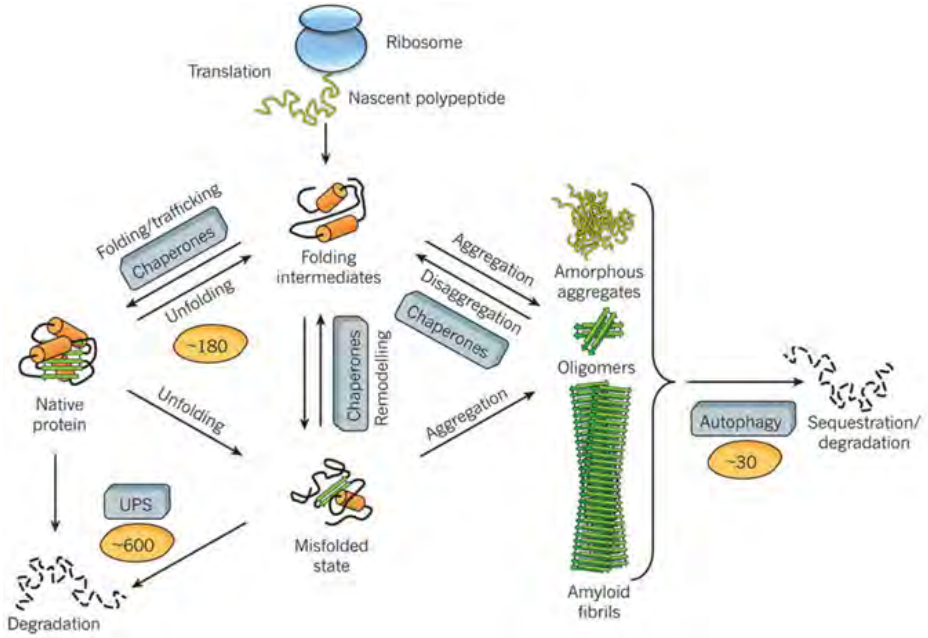

Fig. 1. The proteostasis network integrates chaperone pathways for the folding of newly synthesized proteins, for the remodeling of misfolded states, and for disaggregation with protein degradation that is mediated by the UPS and autophagy system. Approximately 180 different chaperone components and their regulators orchestrate these processes in mammalian cells, whereas the UPS comprises ~600 different components, and the autophagy system comprises ~30 different components. Figure from Harlt et al., *Nature*, 2011.

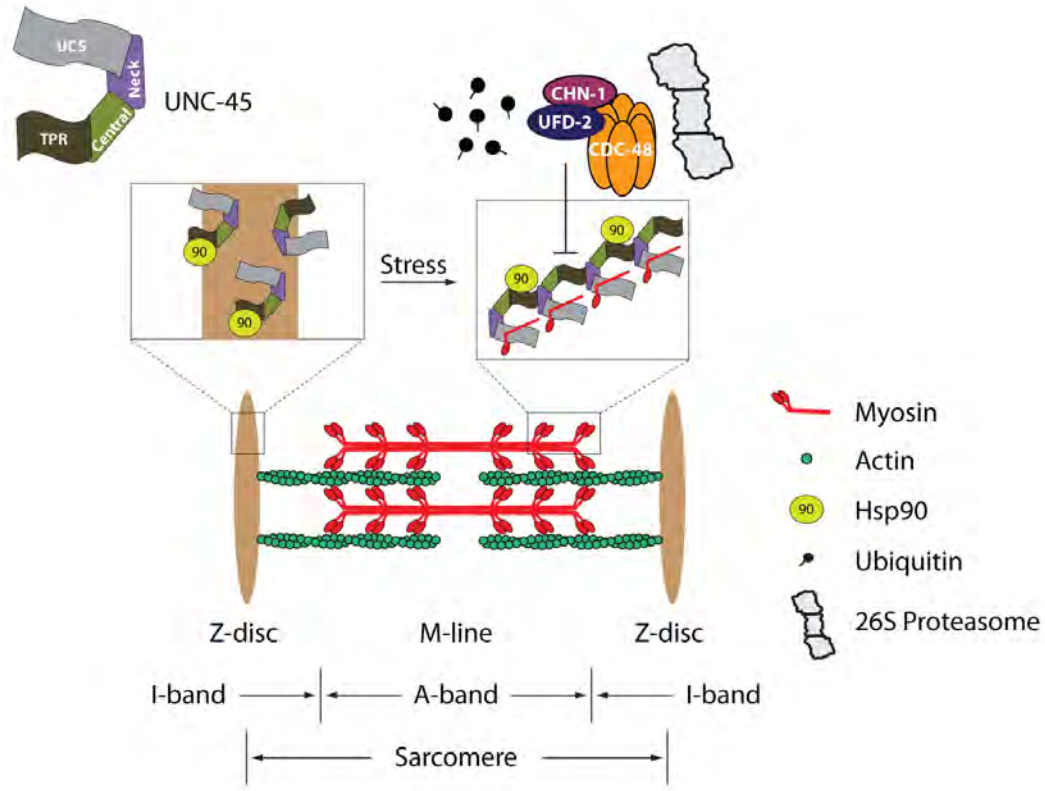

Fig. 2. Model for the UNC-45 polymerization in response to stress. The sarcomeric unit is defined by the distance between two Z-discs including the A-band, I-band, and M-line. UNC-45 composes tandem modules that allow the simultaneous binding of Hsp70/Hsp90 and myosin, enabling the folding and assembly of myosin in regular spacing. In the fully developed muscle, monomeric UNC-45 might be stored at the Z-disk, which anchors the thin actin filaments of the I-band. Under stress conditions, UNC-45 is relocated to damaged myosin filaments of the A-band and might assemble into short chaperone chains to maintain the sarcomeric structure especially during muscle regeneration and aging. The conserved CDC-48/UFD-2/CHN-1 ubiquitylation complex might influence the process of UNC-45 chain formation. The ubiquitylation of UNC-45 either reduces the pool of the monomeric form available for chain formation or inhibits UNC-45 polymerization directly by modifying the binding interface. Figure adapted from Pokrzywa and *Hoppe, Worm*, 2013.

The integrity of sarcomeric structures is permanently challenged upon muscle growth and mechanical stress. In response to eccentric exercise or damage to myofibers, UNC-45 and the chaperone Hsp90 shuttle between the impaired myofibers to support their repair (Fig. 2). However, little is known about the coordination of protein homeostasis pathways upon mechanical stress. Therefore, the long-term objective of this project is to understand the ways in which the balance between protein folding and degradation networks is coordinated with myosin assembly and muscle integrity. We combine genetic and biochemical approaches to study the conserved function of UNC-45 in myosin assembly and examine the ways in which this function is modulated during mechanical stress. Specifically, we plan to use targeted screening strategies to uncover mechanosensory proteins, chaperones, and UPS and autophagy components that are required for muscle function. The conserved regulation of proteostasis networks is studied in *C. elegans*, C2C12 mouse myoblasts, and human skeletal muscles. Finally, we want to investigate the remodeling of UNC-45 folding machinery under mechanical stress. A combination of genetic, biochemical, and *in vivo* imaging techniques will allow us to examine stress-induced changes in protein folding and degradation pathways. The proposed research will have broad implications for our understanding of myosin assembly, human myopathies, and proteostasis mechanisms in general.

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Honors and Awards

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Selected publications

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- **Winata CL**, **Łapiński M**, **Pryszcz L**, Vaz C, Bin Ismail MH, Nama S, Hajan HS, Lee SGP, **Korzh V**, Sampath P, Tanavde V, Mathavan S. Cytoplasmic polyadenylation-mediated translational control of maternal mRNAs directs maternal-to-zygotic transition. ***Development***, 2018; 145(1). pii: dev159566 Epub ahead of print
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Selected publications

- Korzh S, Pan X, Garcia-Lecea M, ^**Winata CL**, Pan X, Wohland T, Korzh V, Gong Z. Requirement of vasculogenesis and blood circulation in late stages of liver growth in zebrafish. ***BMC Dev Biol***, 2008; 8:84
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Description of Current Research

The aim of our research is to understand the mechanism of gene regulation during embryonic development *in vivo* using zebrafish (*Danio rerio*) as a model organism. Our main research interests center around the transcriptional and post-transcriptional regulation of gene expression in embryonic development. At the level of transcriptional regulation, we seek to understand the mechanism by which transcription factors (TFs) and the chromatin landscape interact to regulate the development of an organ. To understand the mechanisms of translational control, we investigate the transcriptome-wide distribution and biological consequences of post-transcriptional modifications on maternal mRNAs, which include cytoplasmic polyadenylation and RNA editing.

Selected Highlights

Elucidating the genome-wide regulatory landscape of heart development

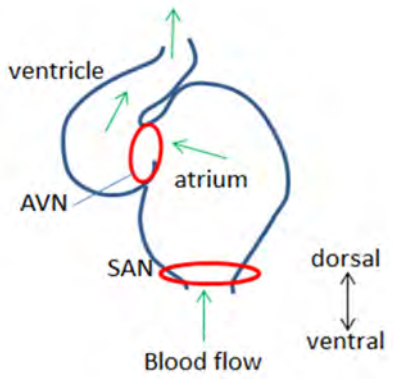

Fig. 1. ***Diagram of zebrafish heart with the cardiac conduction system (CCS) marked in red.*** *Note the sinoatrial node (SAN) that is located at the point of blood entry in the atrium and the atrioventricular node (AVN) at the atrioventricular junction. A network of fibers that is formed from specialized cardiomyocytes rapidly conducts electrical impulses between the two nodes and throughout heart muscle tissues.*

Our first line of research attempts to understand the mechanism of transcriptional regulation through the interaction between TFs and the epigenetic landscape in the process of heart development and disease. The vertebrate heart is a crucial organ that is required for blood circulation. The heart muscle or myocardium comprises most of the heart tissue and is mainly responsible for its function to contract and pump blood throughout the entire body. Heart muscle cells or cardiomyocytes (CMs) are specified early during embryogenesis from a pool of mesodermal progenitors. Upon the completion of gastrulation, these progenitors can be found as bilateral cell clusters that are located at the anterior portion of the embryonic lateral plate mesoderm. As development progresses, heart progenitors migrate to the midline and form a tube structure, known as the primitive heart tube. This structure subsequently expands by means of cell division and the addition of more cells that originate from the progenitor pool. Looping of the heart tube then gives rise to distinct chambers of the heart, namely the atria and ventricle. Although the heart in different species of vertebrates can have two to four chambers, the step-wise morphogenesis of progenitor specification, migration, tube formation, and looping has been shown to be highly conserved. At the core of the machinery that regulates each step of heart morphogenesis are cardiac TFs whose coordinated actions regulate the expression of downstream target genes. We ask three key questions. (1) How do cardiac TFs cooperatively interact to regulate the transcription of heart genes throughout the continuous heart development process? (2) How does the epigenomic landscape dynamically change throughout heart development and disease? (3) What is the nature of interaction between TFs and the epigenomic landscape, and how do interaction dynamics translate into biological processes in heart development?

To gain a comprehensive view of the gene regulatory network in heart development, we initiated two lines of investigation of two distinct cell types of the heart: CMs and cardiac pacemaker cells. These two cell types originate from the same progenitor population but are set apart early in the course of heart development through the induction of expression of distinct TFs, resulting in their different properties. The parallel studies in these two cell types will provide an additional interesting dimension of differential gene regulation in the context of cell type specification.

Transcriptional regulatory landscape in developing cardiomyocytes

Heart muscle cells or CMs are specified early during embryogenesis from a pool of mesodermal progenitors. At the core of the machinery that regulates each step of heart morphogenesis are cardiac TFs, including Nkx2.5, Gata5, Tbx5, and Hand2. These TFs are known to play a role in establishing the CM identity of mesodermal progenitor cells, regulating the formation and looping of the heart tube and the specification of atrial and ventricular CMs. To elucidate the dynamics of the transcriptional regulatory landscape during heart development, we employed a combination of transcriptome profiling (RNA-seq) and an assay for chromatin accessibility (ATAC-seq) at several key stages of heart development. From zebrafish transgenic lines with CM-specific green fluorescent protein (GFP) expression, we isolated CMs using FACS (in collaboration with Katarzyna Piwocka, Nencki Institute, Poland) and performed RNA-seq to profile transcriptome dynamics across three developmental stages. In collaboration with Piero Carninci (RIKEN Center for Life Science Technologies, Japan), we performed bioinformatics analyses of the RNA-seq data. We also performed ATAC-seq to profile the chromatin accessibility regions in samples that were stage-matched to the RNA-seq experiment. Analyses of the ATAC-seq dataset identified open chromatin regions at promoters of genes that are known to be involved in heart development and at distal intergenic regions that suggest regulatory elements. Current ongoing efforts focus on combinatorial analyses to identify gene expression dynamics and associated changes in the chromatin landscape across developmental stages. Ultimately, we aim to characterize the contribution of the dynamic transcriptional regulatory landscape to heart development and identify novel elements (both genic and non-genic) that are associated with heart defects.

To characterize the molecular mechanism and downstream regulatory network of cardiac TFs, we apply ChIP-seq methodology to identify genome-wide binding sites of Nkx2.5, Gata5, Tbx5, and Hand2 during key phases of heart development. In addition to applying conventional ChIP methodology to manually isolate heart cells using custom-generated antibodies, we are developing alternative tools that are based on the endogenous tagging of proteins of interest using the CRISPR/Cas9 system in collaboration with Tatjana Sauka-Spengler (University of Oxford, UK). This strategy circumvents the problem of availability of ChIP-grade antibodies against specific TFs, which remains a major obstacle in ChIP-seq experiments.

Genomics dissection of pacemaker development

Apart from CMs, the heart consists of other types of specialized cells that are central to its function. These include the cardiac conduction system, which is responsible for generating and propagating the electrical impulses that are required for the contraction of heart muscle tissues. The cardiac conduction system consists of pacemaker cells, specialized heart muscle cells that serve to ensure rhythmic contractions of the heart. Pacemaker cells possess distinctive morphological and electrophysiological properties that are specialized for their function. They are set apart early in the course of heart development through the induction of expression of core TFs, such as Tbx2, Tbx3, Tbx18, and Isl1, which prevents their differentiation into CMs. Once specified, pacemaker progenitor cells further develop low conductance properties through the expression of gap junction proteins that are distinct from CMs. Despite the knowledge of key genetic factors that are required for pacemaker cell specification, the molecular mechanisms that regulate their development are still insufficiently understood. Important questions remain with regard to the ways in which the underlying molecular mechanism translates into the proper functioning of pacemaker cells and the consequences of their dysregulation. Moreover, inherited forms of arrhythmia are often associated with more common forms of congenital heart malformations that affect other tissue types of the heart, including CMs, implying interconnectivity of the gene regulatory networks that govern their development and function.
The zebrafish heart exhibits remarkable similarities to the human heart in terms of basal heart rate, electrophysiological properties, and action potential shape and duration. Thus, it is an ideal model organism to study the heart pacemaker and model human clinical conditions that affect pacemaker function. Mutants of heart ion channels in the zebrafish have been reported to possess phenotypes that closely resemble various forms of human arrhythmia, suggesting the high conservation of molecular pathways that regulate heart conduction. Importantly, zebrafish have the potential to allow large-scale pharmaceutical screening to discover new therapies for heart disease, particularly those that affect the pacemaker. In collaboration with Vladimir Korzh (IIMCB), we utilize the transgenic lines ET33mi59B, ET33mi28, and ET31, which express GFP in subpopulations of pacemaker cells, to characterize the morphology of the zebrafish pacemaker and to isolate pacemaker cells for further genomic analyses to elucidate gene regulatory networks in pacemaker development. Ultimately, we aim to establish zebrafish as a model for pacemaker dysfunction through the identification of novel genetic elements that may be implicated in pacemaker-related human diseases and the generation of new mutant lines for functional studies of these factors.

Developmental control through post-transcriptional regulation of maternal mRNA expression

During embryogenesis, a silent transcriptional period exists from the moment of fertilization to the time of zygotic genome activation, known as the mid-blastula transition (MBT) in zebrafish and frogs. During this period of transcriptional silence, development is regulated by maternally deposited mRNAs that undergo various forms of posttranscriptional modifications to regulate their expression.

Translational control by cytoplasmic polyadenylation

The animal oocyte contains an abundant supply of maternal mRNAs that drive various stages of oogenesis and the earliest phases of embryonic development prior to zygotic genome activation. These maternal mRNAs are initially deposited in the immature oocyte in a translationally dormant state, with a very short poly(A) tail. Two major waves of cytoplasmic polyadenylation occur during oocyte maturation and upon fertilization, resulting in the translational activation of distinct subpopulations of maternal mRNAs. Previously, we identified two subpopulations of maternal mRNAs: those that already exist in a polyadenylated form at fertilization and those with an initially very short or no poly(A) tail that are gradually polyadenylated as development progresses (Aanes et al., *Genome Res,* 2011). The latter cohort is thought to undergo translational control by cytoplasmic polyadenylation. Supporting this, their 3'-UTR contains cytoplasmic polyadenylation sequence elements. Subsequently, through profiling of the polysome-associated transcriptome, we discovered that cytoplasmically polyadenylated maternal mRNAs are increasingly associated with polysomes, which demonstrates the coupling of translation to cytoplasmic polyadenylation. Furthermore, we found that the translational regulation of maternal mRNAs by cytoplasmic polyadenylation is required for the progression of embryonic development by ensuring the activation and clearance of key factors that determine zygotic genome activation. Thus, we established cytoplasmic polyadenylation as a prominent mode of the temporal activation of maternal mRNAs that is necessary for MBT (Winata et al., *Development*, 2018).
The current work in the laboratory focuses on studying the mechanistic basis of cytoplasmic polyadenylation through functional analyses of cytoplasmic polyadenylation element binding proteins (CPEBs) that are known to regulate cytoplasmic polyadenylation and translation. The transcripts of at least three different CPEBs (*cpeb1b*, *cpeb4a*, and *cpeb4b*) are present as maternal mRNAs and associated with polysomes between fertilization and MBT. Functional studies of these CPEBs are currently underway, and we are developing methods and tools for the analysis of RNA binding by these factors in the form of CRISPR-generated transgenic lines.

RNA editing of maternal mRNAs

RNA editing refers to the post-transcriptional modification of RNA sequences, the most common form of which is A-to-I conversion that occurs through the deamination of adenosine (A) at the C6 position, converting it to an inosine (I). In humans, the misregulation of A-to-I RNA editing in somatic tissues may lead to neurological and metabolic disorders, autoimmune diseases, and cancer. A mode of post-transcriptional gene regulation, such as RNA modification, would nicely fit into the scenario that occurs at the earliest stages of embryonic development, during which the embryo contains an abundant supply of maternal mRNAs and zygotic transcription is still absent. Surprisingly, despite this, RNA editing has been seldom considered in the context of embryonic development. In collaboration with the Bochtler lab (IIMCB), we aim to elucidate the biological function of A-to-I RNA editing in early embryonic development using zebrafish as a model organism.

According to our previous studies (Aanes et al., *Genome Res,* 2011; Winata et al., *Development,* 2018), two paralogs of the A-to-I RNA editing enzyme, *adar* and *adarb1*, are present in the form of maternally deposited transcript at the earliest stages of development. We conducted a pilot study in which we sequenced the genomes of a pair of adult zebrafish and transcriptomes of their embryonic offspring. To reliably detect RNA editing events, we developed a new method for RNA editing discovery that performed better than the existing method. Our preliminary analyses confirmed the presence of RNA editing in both maternally deposited and zygotic transcripts. We identified ~19,000 sites in the transcriptome of each stage, and the majority of these were stage-specific. Differential patterns of RNA editing throughout embryo development suggests that RNA editing may have some function during embryo development. Currently, we are generating a zebrafish line that carries a mutation of the endogenous *adar* locus using CRISPR/Cas9. This line will be used for more detailed functional studies of RNA editing. Furthermore, in collaboration with the Bujnicki laboratory (IIMCB), we are also planning to identify a correlation between RNA editing and structure through the prediction of secondary structures in conserved domains in selected mRNA candidates that will be identified through comparative transcriptome analyses with several closely related fish species from the Carp family. The transcriptome profiling and *de novo* assembly of these related species of fish are ongoing and promise to be a valuable resource for various fields of study.

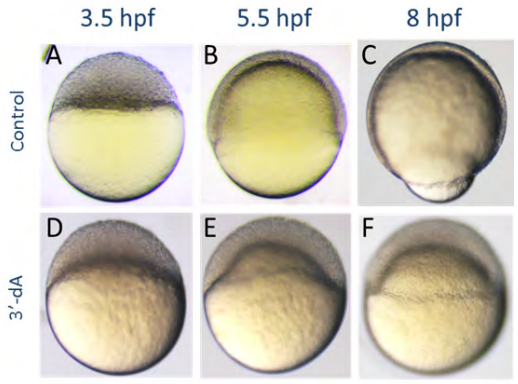

Fig. 2. ***Epiboly defects caused by 3'dA and CHX treatments.*** *(A-C) Untreated control embryos. (D-F) Embryos that were treated with 3'-dA from the 1-cell stage to 3.5 hpf undergo developmental arrest and cytolysis before 24 hpf.*

Laboratory of Biomolecular Interactions and Transport UAM/IIMCB in Poznań

PhD Students

Carlos Eduardo Sequeiros Borja, MSc
Bartłomiej Surpeta, MSc

Lab Leader

Jan Brezovsky, PhD

Curriculum Vitae

Degrees

20011 PhD in Environmental Chemistry, Faculty of Science, Masaryk University, Brno, Czech Republic

2006 MSc in Biophysics, Faculty of Science, Masaryk University, Brno, Czech Republic

Research experience

2016-Present Head of the joint Laboratory, International Institute of Molecular and Cell Biology in Warsaw, and Institute of Molecular Biology and Biotechnology, Faculty of Biology, Adam Mickiewicz University in Poznań, Poland

2016 Assistant Professor, Department of Experimental Biology, Masaryk University, Brno, Czech Republic

2015-2016 Postdoctoral Researcher, International Clinical Research Center of St. Anne's University Hospital, Brno, Czech Republic

2014 Research visit to the group of Professor Rebecca Wade, Heidelberg Institute of Theoretical Science, Germany

2012-2016 Leader of Research Team, Loschmidt Laboratories, Faculty of Science, Masaryk University, Czech Republic

2009-2011 Research Assistant, Loschmidt Laboratories, Department of Experimental Biology, Faculty of Science, Masaryk University, Brno, Czech Republic

2007-2008 Research Assistant, National Centre for Biomolecular Research, Faculty of Science, Masaryk University, Brno, Czech Republic

Achievements and honors

2018 SONATA BIS 7 grant from National Science Centre, Poland

2017 OPUS 13 grant from National Science Centre, Poland

2016 GACR grant from Czech Science Foundation

2015-2016 Elected member of the national node committee of European Life-Science Infrastructure for Biological Information, Czech Republic (ELIXIR-CZ)

2011 5th place at national competition Chemistry Prize of Jean-Marie Lehnen

2011 Dean's prize for outstanding PhD research, Masaryk University, Brno, Czech Republic

2007 Research grant from Masaryk University, Brno, Czech Republic

Selected publications

(In bold authors with IIMCB affiliation)

- ^**Brezovsky J***, Babkova P*, Degtjarik O, Fortova A, Gora A, Iermak I, Rezacova P, Dvorak P, Smatanova IK, Prokop Z, Chaloupkova R, Damborsky J. Engineering a de novo transport tunnel. ***ACS Catal,*** 2016; 6(11):7597-610

- Bendl J, Musil M, Stourac J, Zendulka J, Damborsky J, ^**Brezovsky J#**. PredictSNP2: A unified platform for accurately evaluating SNP effects by exploiting the different characteristics of variants in distinct genomic regions. ***PLoS Comput Biol,*** 2016; 12(5):e1004962

- Bendl J, Stourac J, Sebestova E, Vavra O, Musil M, ^**Brezovsky J#**, Damborsky J#. HotSpot Wizard 2.0: automated design of site-specific mutations and smart libraries in protein engineering. ***Nucleic Acids Res,*** 2016; 44:W479-487

- Daniel L, Buryska T, Prokop Z, Damborsky J, ^**Brezovsky J#.** Mechanismbased discovery of novel substrates of haloalkane dehalogenases using in silico screening. ***J Chem Inf Model,*** 2015; 55(1):54-62

- Sykora J*, ^**Brezovsky J***, Koudelakova T*, Lahoda M, Fortova A, Chernovets T, Chaloupkova R, Stepankova V, Prokop Z, Smatanova IK, Hof M, Damborsky J. Dynamics and hydration explain failed functional transformation in dehalogenase design. ***Nat Chem Biol,*** 2014; 10(6):428-430

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- Prokop Z*, Sato Y*, ^**Brezovsky J***, Mozga T, Chaloupkova R, Koudelakova T, Jerabek P, Stepankova V, Natsume R, Leeuwen JGE, Janssen DB, Florian J, Nagata Y, Senda T, Damborsky J. Enantioselectivity f Haloalkane Dehalogenases and its Modulation by Surface Loop Engineering. ***Angew Chem Int Ed Engl,*** 2010; 49(35):6111-15

* equal contribution; # corresponding author, ^ no IIMCB affiliation

Description of Current Research

Research in our laboratory is mostly oriented toward answering fundamental questions about the mechanism of action of various proteins that have biomedical and biotechnological importance. We investigate the mechanisms that enable the migration of ligands to and from functional sites that are deeply buried within protein structures. We also investigate the implications of such processes for the functions of living cells. To achieve these goals, we develop new computational protocols and tools and apply them to the analysis of biomedically and biotechnologically relevant proteins.

At any given moment, living systems contain several thousand small organic molecules, both endogenous and exogenous, comprising the metabolome. To exert their function, the hosts of molecules need to arrive at their sites of action, mostly represented by protein surfaces or internal cavities. The transport of the metabolome is mainly governed by protein tunnels and channels (Fig. 1). Such tunnels and channels secure the transport of ligands between different regions and connect inner protein cavities with the protein surface, connect two or more different cavities, or connect even different cellular environments, such as in membrane proteins. The presence of very sophisticated transport processes markedly contributes to the symbiotic co-existence of individual chemical species within a single compartment or whole cell without the presence of overly disruptive interference.

Protein channels facilitate the regulated and very selective transport of ions and ligands across a membrane between different cellular compartments. Both tunnels and channels are often equipped with additional dynamical elements, called molecular gates, that can provide yet another level of control over transport processes. The role of channels in the function of various proteins has been the focus of intense research for years. Their importance is illustrated by the identification of many diseases that are caused by channel mutations. Such channel pathologies can severely impair the function of many physiological systems, manifested as various diseases, including epilepsy, hypertension, cystic fibrosis, diabetes, and cancer. To counter these malfunctions, many inhibitors or activators that affect transport through these channels have been identified.

Tunnels connect buried functional sites to the bulk solvent, enabling the access of substrates and release of products. Many additional functions that are essential for the proper function of proteins that are exposed to interference from individual species that are present in the metabolome of the living cell are provided by tunnels. Tunnels enable the access of preferred substrates and deny access of non-preferred substrates. Tunnels can prevent damage to enzymes that contain transition metals through ligation and damage to the cell that is caused by the release of toxic intermediates to the cellular environment. Tunnels also enable reactions that require the absence of water and allow the temporal and spatial synchronization of reactions. Most enzymes likely possess tunnels. In fact, the presence of tunnels was already described for enzymes from six Enzyme Commission classes and four structural classes of proteins. Moreover, in many cases, tunnels are transient, meaning they cannot be readily identified from static crystal structures. Therefore, we can expect the discovery of tunnels in many other protein families. Recognizing the importance of transport processes for enzymatic catalysis, several protein engineering studies have successfully modified tunnels to improve enzymatic activity, specificity, enantioselectivity, and stability. Tunnels were established as important functional factors in enzyme catalysis relatively recently, but their role in cellular biochemistry and tunnel mutations in disease etiology has been largely overlooked. However, many enzymes that are known to contain tunnels have been associated with the development of various ailments, including cancer, neurodegenerative disorders, autoimmune diseases, and inflammation. Inhibitors of some of these enzymes have been shown to bind to tunnels exclusively, thus confirming the proposed role of tunnels in disease etiology and treatment.

To fill gaps in our knowledge of ligand transport phenomena, our research focuses on answering the following questions:

1. **What are the structures, properties, and dynamics of tunnel networks in biologically relevant proteins?**
2. **Which tunnels are traveled by particular ligands?**
3. **How are relevant ligands transported through these tunnels?**
4. **To what extent are tunnels influenced by their environment (e.g., solvents, small molecules, etc.)?**
5. **What are the consequences of mutations of these tunnels?**

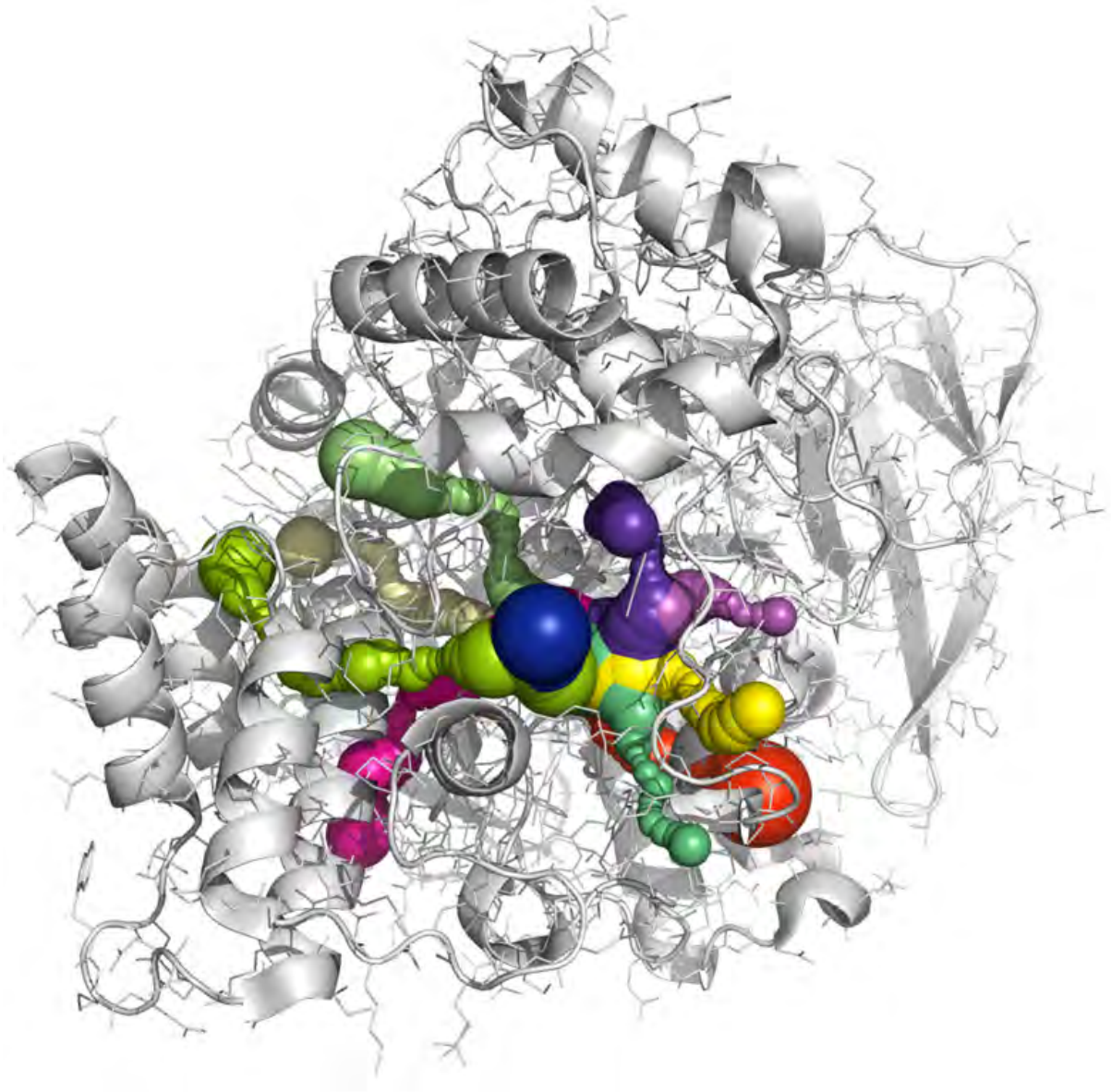


Fig. 1. Network of prospective ligand-transport pathways (tunnels) in acetylcholinesterase from *Torpedo californica*


PROJECTS
OUTSIDE
RESEARCH
LAB TEAMS

Auresine Project

Head

Izabela Sabała, PhD

Senior Scientist

Elżbieta Jagielska, PhD

Postdoc

Piotr Małecki, PhD (from February 2018)

PhD Students

Paweł Mitkowski, MSc
Alicja Wysocka, MSc (from December 2017)

Technican

Weronika Augustyniak, MSc (from February 2018)

Volunteer

Magdalena Orłowska, MSc (until February 2018)

This project develops commercial applications for a patented enzyme, Auresine (Aurezyna) that has potent bacteriolytic activity. Auresine can be used in diagnostic tests, as a food bioprotectant, to decontaminate various surfaces in industry and hospitals, and as a component of hygiene products for animals and humans. Our basic research focuses on the further structural and biochemical characterization of the protein to broaden our knowledge of the regulation of activity and determination of enzyme specificity, and provide a scientific basis for structure-designed enzyme engineering.

Main achievements in 2017:

1. Our research has been presented at prestigious national and international meetings, including the Great Wall Symposium in Portugal.
2. We were invited to give lectures on our research at the international Eurobiotech conference in Cracow.
3. We continued our outreach activities by participating in a radio broadcast to present our research and giving a lecture to the general public in the BoostBiotech series.
4. We were awarded the TeamTech grant financed by the Foundation for Polish Science, which focuses on developing new-generation wound dressings that are functionalized with bacteriolytic enzymes.
5. Our team received three Quest for Commercialization grants (founded by IIMCB) to leverage commercialization of Auresine.
6. We continued collaboration with our business partner to test the implementation of Auresine in industry.
7. We out-licensed our enzyme to a Polish biotech company.
8. We signed a distribution agreement with a global supplier of R&D chemicals.
9. We continue to develop our network of internal and external collaborations in Poland (University of Warsaw, Medical University of Warsaw, and Warsaw University of Life Sciences) and abroad (University of Nottingham, UK; University of Sheffield, UK; ITQB-UNL, Portugal).

Study on Ageing and Longevity

Head

Małgorzata Mossakowska, PhD, DSc Habil

Project Assistant

Aleksandra Szybalska, MSc

IT Specialist

Przemysław Ślusarczyk (until 2017)

A study on ageing and longevity was launched at IIMCB by the PolStu99 project that was commissioned by the Committee for Scientific Research (KBN), called "Genetic and environmental factors of longevity of Polish centenarians" (PolStu2001).

The PolSenior project, carried out in 2007-2012, was the largest gerontology research project in Poland and one of the largest in Europe. The results of PolSenior served as the basis for recommendations that were developed with regard to public health and social policies for the elderly population, both at the national and local levels. A comprehensive approach to the problems of the ageing population is consistent with the assumptions of policies that target senior citizens and provides a solid academic foundation for pursuing these policies.

The PolSenior project resulted in the detailed characterization of the elderly population in Poland and created a bank of biological samples and a database that includes all information from questionnaires and biochemical and genetic analyses. This enables comparisons with other studies and data gathering from projects that are conducted in other countries for pooled analyses of large populations.

In 2017, the PolSenior Study Group continued its activities as a member of the NCD Risk Factor Collaboration (NCD-RisC), a network of health scientists around the world that provides rigorous and timely data on major risk factors for non-communicable diseases for all of the world's countries. The results of this cooperation were published in the following research papers:

- Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults, ***Lancet***, 2017; 390(10113):2627-2642

- Contributions of mean and shape of blood pressure distribution to worldwide trends and variations in raised blood pressure: a pooled analysis of 1018 population-based measurement studies with 88.6 million participants, ***Int J Epidemiol***, 2018; Epub ahead of print

In 2017, the PolSenior Study Group continued analyses of the collected data and published the following papers:

- Sulicka J, Pac A, Puzianowska-Kuźnicka M, Zdrojewski T, Chudek J, Tobiasz-Adamczyk B, **Mossakowska M**, Skalska A, Więcek A, Grodzicki T. Health status of older cancer survivors-results of the PolSenior study. ***J Cancer Surviv***, 2018; Epub ahead of print

- Wyskida M, Owczarek A, **Szybalska A**, Brzozowska A, Szczerbowska I, Wieczorowska-Tobis K, Puzianowska-Kuźnicka M, Franek E, **Mossakowska M**, Grodzicki T, Więcek A, Olszanecka-Glinianowicz M, Chudek J. Socio-economic determinants of vitamin D deficiency in the older Polish population: results from the PolSenior study. ***Public Health Nutr***, 2018; Epub ahead of print

- **Szybalska A,** Broczek K, Ślusarczyk P, Kozdroń E, Błędowski P, Chudek J, **Mossakowska M**. The utilization of health resort treatment services by older people in Poland – results of the PolSenior study. ***Gerontol Pol***, 2018; 26(1):7-13

- Kozak-Szkopek E, Broczek K, **Slusarczyk P**, Wieczorowska-Tobis K, Klich-Raczka A, **Szybalska A**, **Mossakowska M**. Prevalence of chronic pain in the elderly Polish population: results of the PolSenior study. ***Arch Med Sci,*** 2017; 13(5):1197-1206

- Łabuz-Roszak B, Machowska-Majchrzak A, Skrzypek M, **Mossakowska M**, Chudek J, Więcek A, Wawrzyńczyk M, Łącka-Gaździk B, Pierzchała K. Antiplatelet and anticoagulant therapy in elderly people with type 2 diabetes mellitus in Poland (based on the PolSenior Study). ***Arch Med Sci,*** 2017; 13(5):1018-1024

- Łabuz-Roszak B, Skrzypek M, Machowska-Majchrzak A, **Mossakowska M**, Chudek J, Więcek A, Pierzchała K, Łącka-Gaździk B, Grodzicki T. Pharmacological stroke prevention in the elderly with atrial fibrillation in Poland: results of PolSenior study. ***Neurol Neurochir Pol,*** 2017; 51(5):382-387

- Majerczyk M, Choręza P, Bożentowicz-Wikarek M, Brzozowska A, Arabzada H, Owczarek A, **Mossakowska M**, Grodzicki T, Zdrojewski T, Więcek A, Olszanecka-Glinianowicz M, Chudek J. Increased plasma RBP4 concentration in older hypertensives is related to the decreased kidney function and the number of antihypertensive drugs: results from the PolSenior substudy. ***J Am Soc Hypertens,*** 2017; 11(2):71-80

Currently, the group that is led by M. Mossakowska is examining the socioeconomic factors related to medical rehabilitation services that are utilized by Polish seniors.

The group also investigates the prevalence of diabetes, anemia, and depression among Polish older adults in cooperation with other PolSenior consortium members.

The implementation of the PolSenior2 project began in 2017. A coordinator of the survey is the Medical University of Gdańsk. Financial resources were obtained from the Ministry of Health. The study will be carried out with the support and expertise of researchers who are involved in the PolSenior project that is coordinated by IIMCB.

As a result of the cooperation with the Polish Association Supporting People with Inflammatory Bowel Disease „J-elita", the indirect costs of IBD in Poland, as well as preferences of drug administration routes have been described in three papers:

- Holko P, Kawalec P, **Mossakowska M**. Quality of life related to oral, subcutaneous, and intravenous biologic treatment of inflammatory bowel disease: a time trade-off study. ***Eur J Gastroenterol Hepatol***, 2018; 30(2):174-180

- Kawalec P, Stawowczyk E, **Mossakowska M**, Pilc A. Disease activity, quality of life, and indirect costs of ulcerative colitis in Poland. ***Prz Gastroenterol,*** 2017; 12(1):60-65

- Holko P, Kawalec P, **Mossakowska M**, Pilc A. Health-Related Quality of Life Impairment and Indirect Cost of Crohn's Disease: A Self-Report Study in Poland. ***PLoS One***, 2016; 11(12):e0168586

Budget: 12 million PLN
Number of publications: 63
Total Impact Factor: 324,373
Published in:
Lancet, Annals of Neurology, International Journal of Epidemiology, eLife, Ageing Research Reviews, Journal of Hypertension, Aging, Metabolism: Clinical and Experimental, Journal of Alzheimer's Disease, Experimental Gerontology, Nephrology Dialysis Transplantation, PLoS One, Clinical Endocrinology, Biogerontology, Progress in Neuro-Psychopharmacology & Biological Psychiatry, Journal of Nutrition, Health and Aging, Gerontology, Journal of Cancer Survivorship, Clinical Chemistry and Laboratory Medicine, Kidney and Blood Pressure Research, Immunity & Ageing, Journal of the American Society of Hypertension, Clinica Chimica Acta, Clinical Biochemistry, Gene, Public Health Nutrition, Geriatrics & Gerontology International, Neuroscience Letters, Polish Archives of Internal Medicine, Archives of Gerontology and Geriatrics, European Journal of Gastroenterology & Hepatology, Archives of Medical Science, European Review for Medical and Pharmacological Sciences, Scandinavian Journal of Clinical and Laboratory Investigation, BMC Cardiovascular Disorders, Minerva Endocrinologica, European Geriatric Medicine, Journal of Applied Genetics, Endokrynologia Polska, Neurologia i Neurochirurgia Polska, Gerontologia Polska


CORE
FACILITIES

Core Facility

Head

Alicja Żylicz, PhD, Professor

Vice Head

Roman Szczepanowski, PhD

Senior Staff Scientists

Matylda Macias, PhD (part-time)
Katarzyna Misztal, PhD
Krzysztof Skowronek, PhD, DSc Habil
Tomasz Węgierski, PhD (part-time)

The goal of the Core Facility is to support innovative research at IIMCB, giving investigators access to a broad range of cutting-edge research technology platforms that are extensively used in such diverse areas as structural biology, bioinformatics, and molecular and cell biology. The Core Facility is run by experienced scientists who devote their time to maintaining the most sophisticated equipment and are top authorities in research applications for such equipment. More than 50 pieces of equipment are grouped into several units according to leading technologies and applications.

The Macromolecule Crystallography Unit is one of the most advanced in Poland. Proteins are purified with several chromatographic FPLC systems and subjected to crystallization using two crystallization robots and ~1,000 crystallization conditions (buffers). The crystallization process is performed in a crystallization hotel at 4°C or 18°C, and progress is tracked by a CCD camera. The crystals are analyzed using an X-ray generator (Proteum Bruker) that is equipped with a CCD detector (Platinum 135) and cryostream cooler (Oxford Cryosystems series 700). This facility allows the collection of a complete set of diffraction data within a few hours.

The Biochemical and Biophysical Analysis of Proteins and Nucleic Acids Unit is equipped with analytical instruments for in-depth analyses of proteins and nucleic acids using different methods. Interactions between molecules are studied using several complementary techniques: microcalorimetry (VP-DSC and VP-ITC) and analytical ultracentrifugation AUC (Beckman Coulter ProteomeLab XL-I). We use the Anton Paar DMA 5000 M and rolling-ball viscometer Lovis 2000 M, the world's most accurate density meter, to precisely determine buffer properties. The size of the macromolecular complexes is measured by size exclusion chromatography with a multiangle light-scattering (SEC-MALS) detector and analytical ultracentrifugation. We are also equipped with a wide selection of spectrometers, including spectrophotometers, a spectrofluorometer, a CD spectropolarimeter, and an FT-IR spectrometer. The list of instruments has recently been broadened by a new Biacore S200 surface plasmon resonance instrument, the most sensitive equipment of this class, which replaced the Biacore 3000.

The Mass Spectrometry of Proteins and Nucleic Acids Unit has two mass spectrometers: MALDI-TOF-TOF (ultrafleXtreem, Bruker) and LC-ESI-Ion Trap (amaZon speed ETD, Bruker). In addition to prompt standard proteomics analysis (protein identification and protein integrity assays) for internal users, which are vital for crystallography projects, we provide non-standard analyses of macromolecules other than proteins, particularly analyses of RNA samples and nucleosides. The use of MS analysis for RNA targets makes this facility a unique entity nationwide.

The Microscopy Bioimaging Unit offers fluorescence-based imaging systems that are suited for cell biology applications. Our microscopes either work in wide-field mode or use one of several optical sectioning techniques: confocal, two-photon, lightsheet, and TIRF. The newest acquisitions are a Zeiss LSM800 confocal microscope with a high-resolution Airyscan detector and an electrophysiology and fluorescence imaging station based on a Zeiss Examiner.Z1 upright stand. Other equipment includes a Zeiss LSM710 NLO dual confocal/multiphoton microscope for the live imaging of cells and tissues, a Leica TCS SP2 confocal microscope for live cell imaging and FRAP experiments, an Andor Revolutions XD system for real-time spinning-disk confocal microscopy and TIRF imaging, a Zeiss Lightsheet Z.1 single-plane illumination microscope (SPIM) for the imaging of fluorescently labeled zebrafish larvae, an Olympus CellR/ScanR imaging station for intracellular calcium measurements and the semi-high-throughput quantitative analysis of fluorescence signals, and a Nikon 80i Eclipse microscope with a scanning stage for the mosaic imaging of histochemically or fluorescently stained tissue sections. The unit also has a BD FACSCalibur for the quantitative analysis of fluorescence signals in suspension cells.

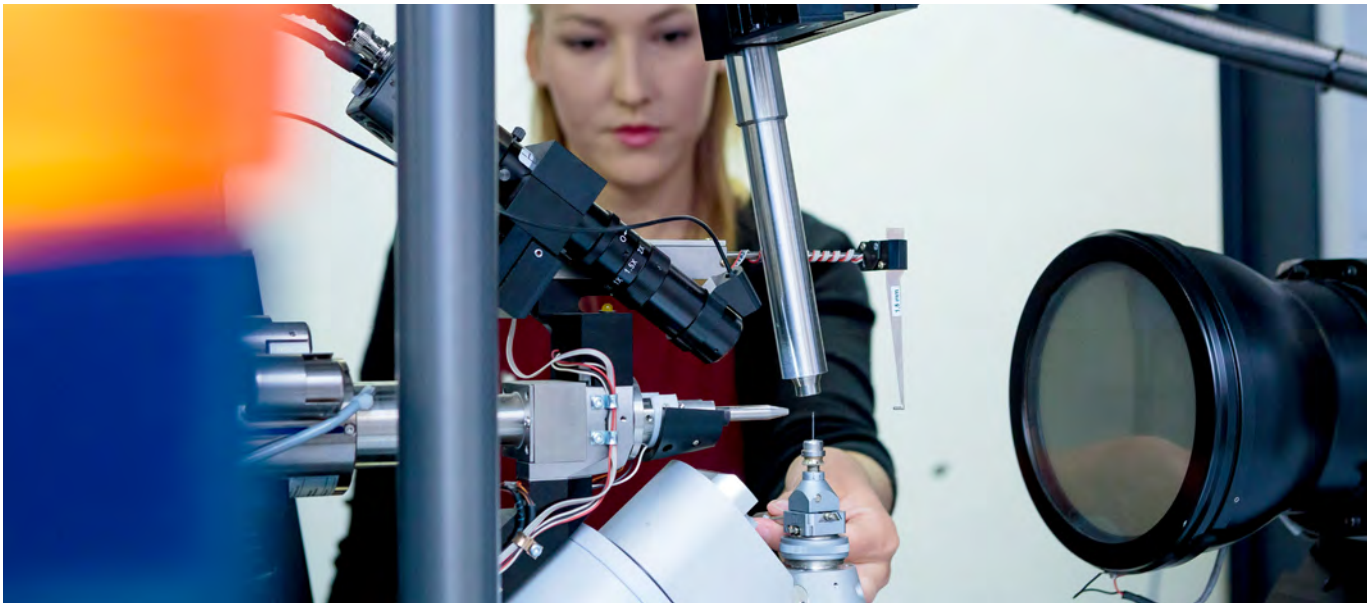
FEI Tecnai T12 Transmission Electron Microscope. In combination with the TemCam F-Series camera, the T12 microscope is used for biological research. It allows the analysis of structural biology and protein complexes both conventionally and with cryo-EM. One of the greatest advantages of cryo-EM relative to conventional structural biology techniques is its ability to analyze large, complex, and flexible structures, which oftentimes cannot be crystallized. The T12 microscope can be used not only for biological samples but also for such tasks as investigations of polymers, thin films, fibers, ceramics, powders, and single crystals.
The unit also has supplemental tools for EM sample preparation. The Quorum Q150T ES is a compact, easy-to-use glow discharge system that is used for the hydrophilization (wetting) of TEM support films and grids. The Q150T ES also allows the deposition of layers of carbon on grids. As part of our Cryo-TEM workflow, we have a Vitrobot FEI, which offers fully automated vitrification. It performs the cryo-fixation process under constant physical and mechanical conditions, including temperature, relative humidity, blotting conditions, and freezing velocity. This ensures high-quality cryo-fixation results and high sample preparation throughput prior to cryo-TEM observations.

The Next Generation Sequencing (NGS) Unit is equipped with a NextSeq 500 sequencer (Illumina). The Core Facility also provides instrumentation for complete sample preparation for sequencing, including a system for precise DNA/RNA and chromatin shearing and size selection (Covaris M220 and BioRuptor Pico, BluePippin), as well as a system for nucleic acid quality and quantity measurements (TapeStation, NanoDrop 3300 Fluorospectrometer and Quantus). The NGS system is already intensively used for the genomic, transcriptomic, and genome methylation sequencing of higher eukaryotes. The purchase of the NGS unit was supported by a Polish Ministry of Science and Higher Education equipment grant for the scientific consortium of IIMCB and Museum and Institute of Zoology Polish Academy of Sciences. We also operate one MinION unit (third-generation sequencing) in the Oxford Nanopore MinION access program.

The Core Facility provides flexible assistance with methodological principles, experimental design, initial training, procedures that are needed for specific experiments, data analysis, and final interpretation, serving as a link between

scientists and state-of-the-art technology. The Core Facility is also available to scientists from other institutions. IIMCB emphasizes cooperation with rapidly developing biotech companies in Poland. Within the framework of bilateral agreements, IIMCB laboratories collaborated with biotech companies, such as Adamed, Celon Pharma, Fermentas, BIOVECTIS, Glia, Polfa, OncoArendi, and Helix ImmunoOncology.

The biophysical part of the Core Facility is one of the founding members of the Association of Resources for Biophysical Research in Europe (ARBRE) and Core Technologies for Life Sciences (CTLS) network. We represent Poland on the Management Committee of the new COST Action "MOBIEU" ("Between Atom and Cell: Integrating Molecular Biophysics Approaches for Biology and Healthcare"). This year (March 19-21, 2018), we organized an annual plenary meeting of this action: "Talking molecules: The networks that shape the living world."



Zebrafish Core Facility

The Zebrafish Core Facility (ZCF) has existed since 2012. It is a licensed breeding and research facility (District Veterinary Inspectorate in Warsaw registry no. PL14656251; Ministry of Science and Higher Education record no. 064 and 051). The facility was established to introduce a new vertebrate model to research that is conducted at IIMCB.

Zebrafish, a small (3-5 cm) tropical freshwater fish, is an excellent model for biomedical research because of its high genetic similarity to humans, transparent embryos, very short reproduction cycle, access to experimental manipulations, large collection of mutant/transgenic animals, and low maintenance cost. Therefore, zebrafish are an attractive alternative to mammalian in vivo models and can be used to implement the "3R" principles (reduction, replacement, and refinement). In 2013, approximately 6000 fish (30 lines) were kept in the ZCF in 300 tanks (50 tanks in quarantine and 250 tanks in the main system). Currently, our zebrafish collection consists of more than 19,000 fish, including four wildtype lines and more than 100 genetically modified lines (see examples in the table on the next page). Numerous zebrafish mutants were generated using methods that are based on engineered endonucleases, such as transcription activator-like effector nucleases (TALENs) and the bacterial type II clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) system. Among the ZCF collection are animals that express modified genes that are involved in the mTOR signaling pathway, mitochondrial processes, heart development, and neurodegenerative disorders. The ZCF and research groups use zebrafish in innovative projects on genetics, developmental biology, and molecular mechanisms of human diseases. Currently, seven research groups from IIMCB use zebrafish and equipment resources of the ZCF. In 2017, the ZCF also served external users, including research groups from the Centre of New Technologies at the University of Warsaw, Medical University of Warsaw, Warsaw University of Life Sciences, Nencki Institute of Experimental Biology, Medical University of Lublin, University of Warmia and Mazury in Olsztyn, and Institute of Industrial Organic Chemistry in Pszczyna.

Maintaining such a large number of fish would not be possible without a suitable infrastructure. Our fish are currently housed in almost 1100 tanks (eight independent, automated aquatic systems) that are manufactured by Techniplast. Moreover, the ZCF is equipped with incubators, microscopes, injectors, a thermocycler, and a microinjection system for zebrafish embryos. In addition, ZCF users have at their disposal a laboratory that is dedicated to behavioral testing. The room is equipped with a housing system and two automated systems for observations and tracking of larval and adult zebrafish. The ZCF also performs sperm freezing and in vitro fertilization to guarantee the preservation of zebrafish genetic lines. The veterinarian continuously monitors the health of the fish colonies.

Scientists who use zebrafish for research purposes are obligated by law (Act of 15 January 2015 on the Protection of Animals Used for Scientific or Educational Purposes) to possess appropriate qualifications to work with an animal model. All of the research and breeding activities at the ZCF are performed in compliance with fundamental ethical principles (Act of 15 January 2015 and European/International guidelines on animal welfare, including Directive 2010/63/EU on the Protection of Animals Used for Scientific Purposes and the instructions of the Federation of European Laboratory Animal Science Associations [FELASA]).

ZCF personnel provide training courses to new users of the facility, including practical elements of handling, husbandry, breeding, fin clipping, microinjections, and behavioral testing. The ZCF is open for zebrafish users 5 days per week: Monday to Thursday from 8 AM to 5 PM and Friday from 8 AM to 4 PM.

Website:
www.iimcb.gov.pl/en/equipment-facilities/zebrafish-core-facility

2013 YEAR

300 tanks (6 racks)

2 individual aquatic systems

6 000 fish

30 lines

2017 YEAR

1200 tanks (23 racks)

8 individual aquatic systems

more than **18 000** fish

more than **100** lines

WILD TYPE LINES	MUTANT LINES				TRANSGENIC LINES
Name	Name	Affected genomic region	Allele	Molecular change	Name
AB	albino	slc45a2	unknown	unknown	Tg(ath5:gap43GFP)
TL	casper	(roy x nacre)	unknown	unknown	Tg(brn3c:mGFP)
ABTL	dackel	ext2	to273b	point mutation	Tg(cmlc2:GFP)
TU	fmr1	fmr1	hu2787	point mutation	Tg(cmlc2:mRFP)
	gata5	gata5	tm236a	point mutation	Tg(CMV:GFP-map1lc3b)
	gba1	gba1	sh391	small deletion	Tg(fabp10a:dsRed)
	hand2	hand2	Hanc99	insertion	Tg(fli:eGFP)
	nacre	mitfa	unknown	unknown	Tg(flt1BAC:YFP)
	ogr	tbx5	Hst^{m21}	unknown	Tg(gata1:dsRed)
	pink1	pink1	sh397	point mutation	Tg(gata1:dsRed;globin:GFP)
	pinscher	slc35b2	to216z	point mutation	Tg(-14.8gata4:GFP)
	CR2:stim2b	stim2b		insertion	Tg(hand2:GFP)
	tbx5	tbx5	Hst^{m21}	point mutation	Tg(kdr-l:mCherry-CAAX)
	tet1	tet1	g.74453	deletion	Tg(mnx1:TagRFP-T)
	tet2	tet2	g.23316	deletion	Tg(myl7:eGFP)
	tet3	tet3	g.52494	deletion	Tg(nkx2.5:eGFP)
	tsc2	tsc2	vu242	point mutation	Tg(ptf1a:GFP)
	mtor(ztor)	mtor(ztor)	xu015	transgenic insertion	Tg(vas:eGFP)

PRO Biostructures

- **Co-founder, Chief Scientific Officer**
  Marcin Nowotny, PhD, DSc Habil
- **Co-founder, Chief Executive Officer**
  Paweł Kustosz, MSc

- **Researchers**
  Agnieszka Napiórkowska, MSc
  Aneta Bartłomiejczak, MSc
- **Internship PhD Student**
  Malwina Hyjek, MSc
- **Technician**
  Iwona Ptasiewicz (part-time)

PRO Biostructures, IIMCB Structural Biology Center, is a dedicated commercial laboratory with a mission to utilize the scientific excellence of IIMCB scientists to support drug discovery for the treatment of diseases. PRO Biostructures specializes in consulting and providing services in structural biology using X-ray crystallography. The offer includes a full range of protein crystallography research, called "gene to structure", that can be divided into three separate phases:

1. Preparation of expression constructs.
2. Recombinant protein production in bacteria (E. coli), yeast, insects, and mammalian cells.
3. Bio-crystallography of protein or protein-ligand complexes.

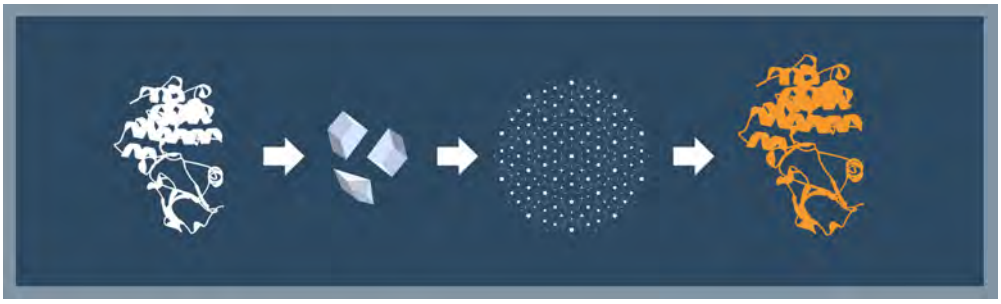
The laboratory has experience in the 3D structure determination of protein-ligand complexes in structure-based drug design. It cooperates closely with various pharmaceutical companies, such as UbiQ Bio, Celon Pharma, and OncoArendi Therapeutics (as a commercial services provider or partner on NCBiR grants). The results supported drug discovery efforts for such diseases as cancer, asthma, and depression. Some of the small molecules whose development PRO Biostructures had the opportunity to support are in clinical trials, and they may soon become medications that are available on the global market. In addition to profitable commercial projects, the Structural Biology Center also scientifically cooperates with foreign companies from the biotechnology and pharmaceutical sectors, such as IONIS from the United States and UbiQ Bio from the Netherlands. Such collaborations are an investment in promoting the laboratory by presenting its scientific potential, expertise in R&D projects, and flexible approach to cooperation with industry. These activities are focused on introducing new services and obtaining patents but can also lead to long-term international trade cooperation.

The success of PRO Biostructures results from very high levels of expertise in science, advanced skills, and the excellent quality of the services that are rendered. It offers the extensive experience of top scientists in biomedicine research with significant scientific output (publications in such journals as Cell, Molecular Cell, and Nature Structural and Molecular Biology) and recipients of prestigious research grants. The laboratory also actively promotes its operations through biotechnology and pharmaceutical industry conferences and events, such as BioEurope, BioEurope Spring, BioJapan, and BioFIT.

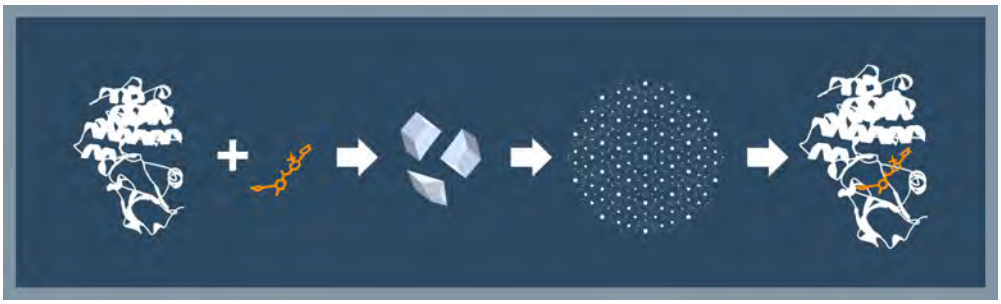
The competitive advantage PRO Biostructures is built on the premise of top-quality research expertise. It responds to the needs of business clients in state-of-the art, flexible, and custom-made projects and ensures the Intellectual Property rights of the clients in each project.

PRO Biostructures offer

Solving protein structures

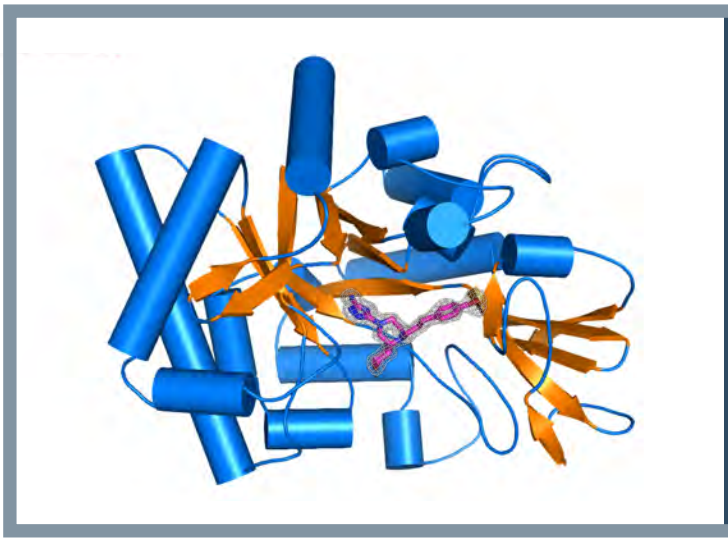


Drug discovery support



Consulting and sharing insider know-how

An example of a crystal structure of a protein-inhibitor complex



One of the thirteen crystal structures of protein-inhibitor complex solved by PRO Biostructures for OncoArendi Therapeutics SA from July 2015

Biotech Innovations Ltd

Chief Executive Officer

Iwona Cymerman, PhD

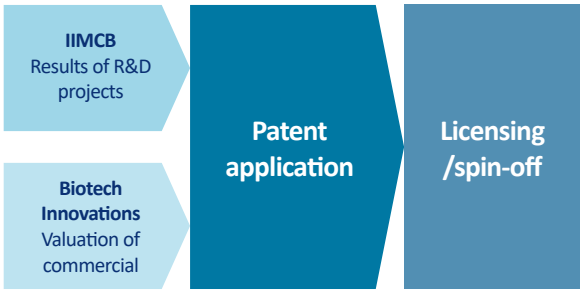
BioTech innovations

Mission

Biotech Innovations Ltd is a special-purpose vehicle that is funded by IIMCB. It is the successor to the "Bio&Technology Innovations Platform" Technology Transfer Office. Biotech Innovations is committed to turning scientific progress into marketable products and technologies and returning income to inventors and IIMCB to support further research. The company manages a portfolio of patents and patent applications and supports the development of the most commercially advanced projects in the economic environment.

Activities

Our work begins with disclosures of inventions of IIMCB scientists. We review new inventions to learn about their applicability and commercial potential. We then define value propositions for industry licensees. Together with the inventors, we look for companies that might be interested in the invention. We also support scientists who wish to stay actively involved in the further development of their invention and seek to set up a spin-off company.



To raise awareness among academics about intellectual property rights and possibilities of transferring R&D results to industry, we regularly hold seminars on "IP Policy for Management and Use of Intellectual Property of IIMCB."

To encourage IIMCB scientists to undertake steps toward validating the applicability of their discoveries in industry, we also designed and launched the internal grant program "Commercialization Quest." In 2017, a total of PLN 133 000 was awarded to five researchers to boost commerciality of the following projects

- Elżbieta Jagielska: "Optimization and scaling up of low cost Auresine production"
- Elżbieta Jagielska: "Auresine trademark registration and its graphic identity designing"
- Marek Kuźbicki: "eRNAse industry road show"
- Izabela Sabała: "Market analysis for implementation of Auresine enzyme in skin care products against acne"
- Aleksandra Tempes: "Validation of selected molecular blood marker potential to predict progression and clinical treatment effectiveness in neurological disorders"

Website:
biotech-innovations.com

Contact:
contact@biotech-innovations.com

IT Unit

Head

Roman Szczepanowski, PhD

IT Specialists

Łukasz Munio (part-time)
Jakub Skaruz

System Administrator

Michał Romiszewski

Computer Administrators

Tomasz Jarzynka (part-time)
Jan Kogut (part-time)

The tasks of the IT Unit focus on supporting various scientific activities at IIMCB and assisting administrative staff with their core responsibilities. These objectives embrace many diverse and highly technical fields, including:

- Maintenance and administration of the computer network.
- Administration of the email system, DNS, DHCP, and proxy servers.
- Helpdesk that provides user support and assistance with the installation of hardware and software.
- Ensuring the security of computer and email data.
- Maintaining and updating the anti-spam filter.
- Administration of IIMCB's web servers.
- Maintenance of intranet service.
- Providing secure wireless connections for employees and guests.
- Providing remote external user access to computing resources at IIMCB over the VPN protocol.
- Creation and administration of diary information (e.g., task diaries that contain information about the availability and use of scientific equipment).
- Administration and continuous updating of financial and accounting software.
- Providing back-ups of strategic computer servers.
- Purchasing and managing computer software and ensuring it is legally licensed.
- Providing IT support for seminars and conferences that are organized by IIMCB.
- Hardware purchase coordination: consultation and preparation of tender specifications.
- Maintaining and updating multimedia information services.
- Setting up dedicated websites that are designated for conferences that are organized by IIMCB.

IIMCB has a modern computer network (1 Gb/s) that is connected by fiber-optic structured cabling and provides both wired and wireless access to computers and mobile devices. The network is composed of 150 computers, both personal computers and dedicated units that support research equipment.

To improve quality of the network, the IT Unit recently launched the following services:

1. Virtual servers that provide key network services (email, DNS, anti-spam, file services).

2. New file servers:
- 3 new Dell Poweredge R630 servers to support key research projects.
- Dell Storage SCv2000 Series array and Dell Storage SC120 expansion enclosure.
- Personal network drive with 10 GB of storage for each user.
- Shared network drive available for departments and project groups.
- Previous Versions: allows making automatic backup copies or snapshots of files and folders on specific volumes at any point in time.

3. New version of backup and archive software, which provides better support for offsite backup, archiving, and replication.

4. Dell/EMC Isilon storage array that was recently expanded to 840 TB to facilitate NGS data storage and processing on the HPC cluster.

5. Upgrade of the virtualization environment, which provides IIMCB's scientific web services to the public, now implementing High Availability and disaster recovery across multiple storage devices.

The facility that is described above includes both the main servers of IIMCB and servers that belong to individual research groups. Particularly noteworthy are resources of the Laboratory of Bioinformatics and Protein Engineering. They include a computer cluster that consists of more than 2200 cores, with a file system that is built on the basis of SSD storage, 100 TB of backup memory, and 14 multiprocessor computing and application servers.

Also located in the server room are crystallographic servers that are used by the Laboratory of Protein Structure and Laboratory of Structural Biology, storage servers for data from the Zeiss Lightsheet SPIM microscope, and a high-performance computing system that supports the Illumina NextSeq 500 NGS system. This is where the databases of the PolSenior and PolStu centenarian projects can be accessed.


FACTS &
FIGURES

Publications in 2017 & Q1 2018

List of papers with IIMCB-affiliated main authors (first and/or corresponding)

No	Year	Publication	5 Year IF	Journal Category	Journal Rank in Category / Total Journals in Category	Quartile in Category
		2017				
1	2017	**Figiel M**, Krepl M, Poznanski J, **Golab A**, Šponer J, **Nowotny M**. Coordination between the polymerase and RNase H activity of HIV-1 reverse transcriptase. Nucleic Acids Res. 2017; 45(6):3341-3352	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
2	2017	**Piątkowski P**, Jabłońska J, **Żyła A, Niedziałek, Matelska D, Jankowska E**, Waleń T, **Dawson WK, Bujnicki JM**. SupeRNAlign: a new tool for flexible superposition of homologous RNA structures and inference of accurate structure-based sequence alignments. Nucleic Acids Res. 2017; 45(16):e150	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
3	2017	**Pruszko M**, Milano E, Forcato M, Donzelli S, Ganci F, Di Agostino S, De Panfilis S, Fazi F, Bates DO, Bicciato S, **Zylicz M, Zylicz A**, Blandino G, Fontemaggi G. The mutant p53-ID4 complex controls VEGFA isoforms by recruiting lncRNA MALAT1. EMBO Rep. 2017; 18(8):1331-1351	7,977	BIOCHEMISTRY & MOLECULAR BIOLOGY	22/290	1
4	2017	Gold VA, **Chroscicki P, Bragoszewski P, Chacinska A**. Visualization of cytosolic ribosomes on the surface of mitochondria by electron cryo-tomography. EMBO Rep. 2017; 18(10):1786-1800	7,977	BIOCHEMISTRY & MOLECULAR BIOLOGY	22/290	1
5	2017	**Mleczko-Sanecka K**, da Silva AR, Call D, Neves J, Schmeer N, Damm G, Seehofer D, Muckenthaler MU. Imatinib and spironolactone suppress hepcidin expression. Haematologica. 2017; 102(7):1173-1184	6,372	HEMATOLOGY	4/70	1
6	2017	**Szewczyk LM**, Brozko N, **Nagalski A**, Röckle I, Werneburg S, Hildebrandt H, **Wisniewska MB, Kuznicki J**. ST8SIA2 promotes oligodendrocyte differentiation and the integrity of myelin and axons. Glia. 2017; 65(1):34-49	5,971	NEUROSCIENCES	24/259	1
7	2017	**Urbanska M, Gozdz A, Macias M, Cymerman IA, Liszewska E**, Kondratiuk I, Devijver H, Lechat B, Van Leuven F, **Jaworski J**. GSK3β Controls mTOR and Prosurvival Signaling in Neurons. Mol Neurobiol. Epub 2017 Nov 15.	5,767	NEUROSCIENCES	25/259	1
8	2017	**Blazejczyk M, Macias M**, Korostynski M, **Firkowska M**, Piechota M, **Skalecka A, Tempes A, Koscielny A, Urbanska M**, Przewlocki R, **Jaworski J**. Kainic Acid Induces mTORC1-Dependent Expression of Elmo1 in Hippocampal Neurons. Mol Neurobiol. 2017; 54(4):2562-2578	5,767	NEUROSCIENCES	25/259	1
9	2017	**Wasilewski M, Chojnacka K, Chacinska A**. Protein trafficking at the crossroads to mitochondria. Biochim Biophys Acta - Molecular Cell Research. 2017; 1864(1):125-137	5,374	BIOCHEMISTRY & MOLECULAR BIOLOGY	61/290	1
10	2017	**Majewski Ł, Maciąg F**, Boguszewski PM, **Wasilewska I**, Wiera G, Wójtowicz T, Mozrzymas J, **Kuznicki J**. Overexpression of STIM1 in neurons in mouse brain improves contextual learning and impairs long-term depression. Biochim Biophys Acta - Molecular Cell Research. 2017; 1864(6):1071-87	5,374	BIOCHEMISTRY & MOLECULAR BIOLOGY	61/290	1
11	2017	**Tracz-Gaszewska Z, Klimczak M**, Biecek P, Herok M, Kosinski M, **Olszewski MB**, Czerwińska P, **Wiech M**, Wiznerowicz M, **Zylicz A, Zylicz M**, Wawrzynow B. Molecular chaperones in the acquisition of cancer cell chemoresistance with mutated TP53 and MDM2 up-regulation. Oncotarget, 2017; 8(47):82123-82143	5,312	ONCOLOGY	44/217	1
12	2017	**Pokrzywa W**, Hoppe T. CHIPped balance of proteostasis and longevity. Oncotarget, 2017; 8(57):96472-96473	5,312	ONCOLOGY	44/217	1
13	2017	**Jastrzębski K, Zdżalik-Bielecka D, Mamińska A**, Kalaidzidis Y, Hellberg C, **Miaczynska M**. Multiple routes of endocytic internalization of PDGFRβ contribute to PDGF-induced STAT3 signaling. J Cell Sci. 2017; 130(3):577-589	5,247	CELL BIOLOGY	61/190	2
14	2017	**Slyvka A, Mierzejewska K, Bochtler M**. Nei-like 1 (NEIL1) excises 5-carboxylcytosine directly and stimulates TDG-mediated 5-formyl and 5-carboxylcytosine excision. Sci Rep. 2017; 7(1):9001	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
15	2017	**Urbanska AS, Janusz-Kaminska A, Switon K**, Hawthorne AL, **Perycz M, Urbanska M**, Bassell GJ, **Jaworski J**. ZBP1 phosphorylation at serine 181 regulates its dendritic transport and the development of dendritic trees of hippocampal neurons. Sci Rep. 2017; 7(1):1876	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
16	2017	**Gazda K, Kuznicki J, Wegierski T**. Knockdown of amyloid precursor protein increases calcium levels in the endoplasmic reticulum. Sci Rep. 2017; 7(1):14512	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
17	2017	**Bragoszewski P, Turek M, Chacinska A**. Control of mitochondrial biogenesis and function by the ubiquitin-proteasome system. Open Biol. 2017; 7(4). pii: 170007	4,831	BIOCHEMISTRY & MOLECULAR BIOLOGY	98/290	2
18	2017	**Gozdz A**, Nikolaienko O, **Urbanska M, Cymerman IA**, Sitkiewicz E, **Blazejczyk M**, Dadlez M, Bramham CR, **Jaworski J**. GSK3α and GSK3β Phosphorylate Arc and Regulate its Degradation. Front Mol Neurosci. 2017; 10:192	4,740	NEUROSCIENCES	42/259	1
19	2017	**Misztal K**, Brozko N, Nagalski A, Szewczyk LM, Królak M, **Brzozowska K, Kuznicki J**, Wisniewska MB. TCF7L2 mediates the cellular and behavioral response to chronic lithium treatment in animal models. Neuropharmacology. 2017, 113(Pt A):490-501	4,681	NEUROSCIENCES	44/259	1
20	2017	**Bochtler M, Kolano A**, Xu G-L. DNA demethylation pathways: Additional players and regulators. Bioessays. 2017; 39(1):1-13	4,597	BIOCHEMISTRY & MOLECULAR BIOLOGY	63/290	1
21	2017	**Klimczak M**, Czerwińska P, Mazurek S, Sozańska B, Biecek P, Mackiewicz A, Wiznerowicz M. TRIM28 epigenetic corepressor is indispensable for stable induced pluripotent stem cell formation. Stem Cell Research. 2017; 23:163–172	4,079	BIOTECHNOLOGY & APPLIED MICROBIOLOGY	30/160	1

22	2017	García-Lecea M, Gasanov E, **Jedrychowska J, Kondrychyn I**, Teh C, You MS, **Korzh V**. Development of Circumventricular Organs in the Mirror of Zebrafish Enhancer-Trap Transgenics. Front Neuroanat. 2017; 11:114	3,531	NEUROSCIENCES	101/259	2
23	2017	**Perycz M, Krwawicz J, Bochtler M**. A TALE-inspired computational screen for proteins that contain approximate tandem repeats. PLoS One. 2017; 12(6):e0179173	3,394	MULTIDISCIPLINARY SCIENCES	15/64	1
24	2017	**Switon K**, Kotulska K, **Janusz-Kaminska A, Zmorzynska J, Jaworski J**. Molecular neurobiology of mTOR. Neurosci. 2017; 341:112-153	3,318	NEUROSCIENCES	100/259	2
25	2017	**Soman S**, Keatinge M, Moein M, DaCosta M, Mortiboys H, Skupin A, **Sugunan S, Bazala M, Kuznicki J**, Bandmann O. Inhibition of the mitochondrial calcium uniporter (MCU) rescues dopaminergic neurons in pink1-/- zebrafish. Eur J Neurosci, 2017; 45(4):528-535	3,288	NEUROSCIENCES	127/259	2
26	2017	**Czeredys M, Maciag F**, Methner A, **Kuznicki J**. Tetrahydrocarbazoles decrease elevated SOCE in medium spiny neurons from transgenic YAC128 mice, a model of Huntington's disease. Biochem Biophys Res Commun. 2017; 483(4):1194-1205	2,354	BIOCHEMISTRY & MOLECULAR BIOLOGY	164/290	3
27	2017	**Figiel M**, **Nowotny M**. Structural Studies of RNases H2 as an Example of Crystal Structure Determination of Protein-Nucleic Acid Complexes. Methods Enzymol. 2017; 592:123-143	2,259	BIOCHEMICAL RESEARCH METHODS	52/78	3
28	2017	Piven OO, **Winata CL**. The canonical way to make a heart: β-catenin and plakoglobin in heart development and remodeling. Exp Biol Med (Maywood). 2017; 242(18):1735-1745	2,512	MEDICINE, RESEARCH & EXPERIMENTAL	59/128	2
29	2017	Kozak-Szkopek E, Broczek K, **Slusarczyk P**, Wieczorowska-Tobis K, Klich-Raczka A, **Szybalska A, Mossakowska M**. Prevalence of chronic pain in the elderly Polish population – results of the PolSenior study. Arch Med Sci, 2017; 13(5):1197–1206	1,904	MEDICINE, GENERAL & INTERNAL	46/155	2
		Q1 2018				
1	2018	**Razew M**, Warkocki Z, Taube M, Kolondra A, **Czarnocki-Cieciura M, Nowak E**, Labedzka-Dmoch K, Kawinska A, Piatkowski J, Golik P, Kozak M, Dziembowski A, **Nowotny M**. Structural analysis of mtEXO mitochondrial RNA degradosome reveals tight coupling of nuclease and helicase components. Nat Commun. 2018; 9(1):97	13,092	MULTIDISCIPLINARY SCIENCES	3/64	1
2	2018	**Topf U**, Suppanz I, **Samluk L, Wrobel L**, Böser A, **Sakowska P**, Knapp B, **Pietrzyk MK, Chacinska A**, Warscheid B. Quantitative proteomics identifies redox switches for global translation modulation by mitochondrially produced reactive oxygen species. Nat Commun. 2018; 9(1):324	13,092	MULTIDISCIPLINARY SCIENCES	3/64	1
3	2018	**Boccaletto P, Magnus M, Almeida C, Zyla A, Astha, Pluta R, Baginski B, Jankowska E, Dunin-Horkawicz S, Wirecki T, Boniecki M, Stefaniak F, Bujnicki JM**. RNArchitecture: a database and a classification system of RNA families, with a focus on structural information. Nucleic Acids Res. 2018; 46(D1):D202-D205	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
4	2018	**Boccaletto P, Machnicka MA, Purta E, Piatkowski P, Baginski B, Wirecki TK**, de Crécy-Lagard V, Ross R, Limbach PA, Kotter A, Helm M, **Bujnicki JM**. MODOMICS: a database of RNA modification pathways. 2017 update. Nucleic Acids Res. 2018; 46(D1):D303-D307	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
5	2018	Wawrzynow B, **Zylicz A, Zylicz M**. Chaperoning the guardian of the genome. The two-faced role of molecular chaperones in p53 tumor suppressor action. Biochim Biophys Acta - Reviews on Cancer. 2018; 1869(2):161-174	8,661	BIOCHEMISTRY & MOLECULAR BIOLOGY	18/290	1
6	2018	**Winata CL, Łapiński M, Pryszcz L**, Vaz C, Bin Ismail MH, Nama S, Hajan HS, Lee SGP, **Korzh V**, Sampath P, Tanavde V, Mathavan S. Cytoplasmic polyadenylation-mediated translational control of maternal mRNAs directs maternal to zygotic transition. Development. 2018; 145(1). pii: dev159566	6,216	DEVELOPMENTAL BIOLOGY	5/41	1
7	2018	**Szymanska E, Budick-Harmelin N, Miaczynska M**. Endosomal „sort" of signaling control: The role of ESCRT machinery in regulation of receptor-mediated signaling pathways. Semin Cell Dev Biol. 2018; 74:11-20	6,124	CELL BIOLOGY	36/190	1
8	2018	**Koscielny A, Malik AR, Liszewska E, Zmorzynska J, Tempes A, Tarkowski B, Jaworski J**. Adaptor Complex 2 Controls Dendrite Morphology via mTOR-Dependent Expression of GluA2. Mol Neurobiol, 2018; 55(2):1590-1606	5,767	NEUROSCIENCES	25/259	1
9	2018	**Korzh V**. Development of brain ventricular system. Cell Mol Life Sci. 2018; 75(3):375-383	5,643	BIOCHEMISTRY & MOLECULAR BIOLOGY	40/290	1
10	2018	**Bochtler M**, Mizgalska D, Veillard F, Nowak ML, Houston J, Veith P, Reynolds EC, Potempa J. The Bacteroidetes Q-Rule: Pyroglutamate in Signal Peptidase I Substrates. Front Microbiol. 2018; 9:230	4,526	MICROBIOLOGY	26/125	1
11	2018	**Figiel M**, Krepl M, Park S, Poznański J, Skowronek K, Gołąb A, Ha T, Šponer J, **Nowotny M**. Mechanism of polypurine tract primer generation by HIV-1 reverse transcriptase. J Biol Chem. 2018; 293(1):191-202	4,323	BIOCHEMISTRY & MOLECULAR BIOLOGY	74/290	2
12	2018	**Foik IP, Tuszynska I, Feder M, Purta E, Stefaniak F, Bujnicki JM**. Novel inhibitors of the rRNA ErmC' methyltransferase to block resistance to macrolides, lincosamides, streptogramine B antibiotics. Eur J Med Chem. 2018; 146:60-67	4,187	CHEMISTRY, MEDICINAL	4/60	1
13	2018	Piasecka A, **Czapinska H**, Vielberg M-T, **Szczepanowski RH**, Kierfersauer R, Reed S, Groll, M, **Bochtler M**. The Y. bercovieri Anbu crystal structure sheds light on the evolution of highly (pseudo)symmetric multimers. J Mol Biol. 2018; 430(5):611-627	3,910	BIOCHEMISTRY & MOLECULAR BIOLOGY	57/290	1

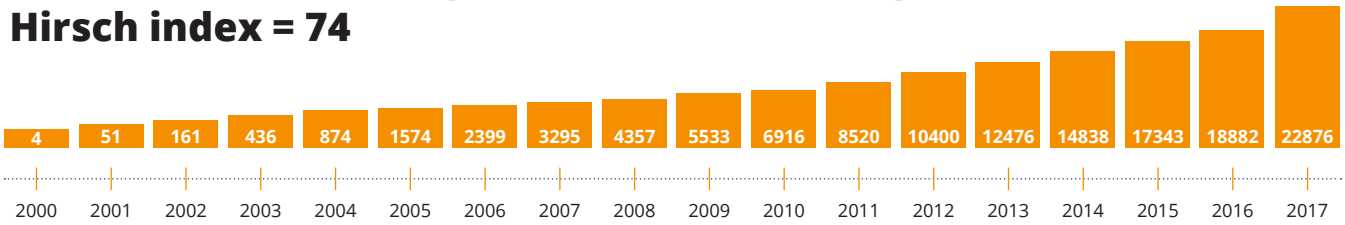
List of papers without IIMCB-affiliated main authors (first and/or corresponding)

No	Year	Publication	5 Year IF	Journal Category	Journal Rank in Category / Total Journals in Category	Quartile in Category
		2017				
1	2017	1040 Authors within **Mossakowska M** and **Slusarczyk P.** Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017; 390(10113):2627-2642	48,082	MEDICINE, GENERAL & INTERNAL	2/155	1
2	2017	NCD Risk Factor Collaboration (NCD-RisC) **Mossakowska M, … Slusarczyk P.** Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. Lancet. 2017; 389(10064):37-55	48,082	MEDICINE, GENERAL & INTERNAL	2/155	1
3	2017	**Potente M**, Mäkinen T. Vascular heterogeneity and specialization in development and disease. Nat Rev Mol Cell Biol. 2017; 18(8):477-494	43,310	CELL BIOLOGY	1/190	1
4	2017	Gross B, **Pawlak M**, Lefebvre P, Staels B. PPARs in obesity-induced T2DM, dyslipidaemia and NAFLD. Nat Rev Endocrinol. 2017; 13(1):36-49	17,146	ENDOCRINOLOGY & METABOLISM	2/138	1
5	2017	**Potente M**, Carmeliet P. The Link Between Angiogenesis and Endothelial Metabolism. Annu Rev Physiol. 2017; 79:43-66	15,313	PHYSIOLOGY	2/84	1
6	2017	Kononenko NL, Claßen GA, Kuijpers M, Puchkov D, Maritzen T, **Tempes A, Malik AR, Skalecka A**, Bera S, **Jaworski J**, Haucke V. Retrograde transport of TrkB-containing autophagosomes via the adaptor AP-2 mediates neuronal complexity and prevents neurodegeneration. Nat Commun. 2017, 8:14819	13,092	MULTIDISCIPLINARY SCIENCES	3/64	1
7	2017	Pasricha SR, Lim PJ, Duarte TL, Casu C, Oosterhuis D, **Mleczko-Sanecka K**, Suciu M, Da Silva AR, Al-Hourani K, Arezes J, McHugh K, Gooding S, Frost JN, Wray K, Santos A, Porto G, Repapi E, Gray N, Draper SJ, Ashley N, Soilleux E, Olinga P, Muckenthaler MU, Hughes JR, Rivella S, Milne TA, Armitage AE, Drakesmith H. Hepcidin is regulated by promoter-associated histone acetylation and HDAC3. Nat Commun. 2017; 8(1):403	13,092	MULTIDISCIPLINARY SCIENCES	3/64	1
8	2017	Andrade J, **Potente M**. New Q(ues) to keep blood vessels growing. EMBO J. 2017; 36(16):2315-2317	9,853	BIOCHEMISTRY & MOLECULAR BIOLOGY	16/290	1
9	2017	Rydzik AM, Warminski M, Sikorski PJ, Baranowski MR, Walczak S, Kowalska J, Zuberek J, Lukaszewicz M, **Nowak E**, W Claridge TD, Darzynkiewicz E, **Nowotny M**, Jemielity J. mRNA cap analogues substituted in the tetraphosphate chain with CX2: identification of O-to-CCl2 as the first bridging modification that confers resistance to decapping without impairing translation. Nucleic Acids Res. 2017; 45(15):8661-8675	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
10	2017	Charbonnel C, Niazi AK, Elvira-Matelot E, **Nowak E**, Zytnicki M, de Bures A, Jobet E, Opsomer A, Shamandi N, **Nowotny M**, Carapito C, Reichheld J-P, Vaucheret H, Saez-Vasquez J. The siRNA suppressor RTL1 is redox-regulated through glutathionylation of a conserved cysteine in the double-stranded-RNA-binding domain. Nucleic Acids Res. 2017; 45(20):11891-11907	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
11	2017	Chawla M, Chermak E, Zhang Q, **Bujnicki JM**, Oliva R, Cavallo L. Occurrence and stability of lone pair-π stacking interactions between ribose and nucleobases in functional RNAs. Nucleic Acids Res. 2017; 45(19):11019-11032	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
12	2017	Kalisiak K, Kuliński TM, Tomecki R, Cysewski D, **Pietras Z**, Chlebowski A, Kowalska K, Dziembowski A. A short splicing isoform of HBS1L links the cytoplasmic exosome and SKI complexes in humans. Nucleic Acids Res. 2017; 45(4):2068-2080	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
13	2017	Petrov AI, Kay SJE, Kalvari I, Howe KL, Gray KA, Bruford EA, Kersey PJ, Cochrane G, Finn RD, Bateman A, Kozomara A, Griffiths-Jones S, Frankish A, Zwieb CW, Lau BY, Williams KP, Chan PP, Lowe TM, Cannone JJ, Gutell RR, **Machnicka MA, Bujnicki JM**, Yoshihama M, Kenmochi N, Chai B, Cole JR, Szymanski M, Karlowski WM, Wood V, Huala E, Berardini TZ, Zhao Y, Chen R, Zhu W, Paraskevopoulou MD, Vlachos IS, Hatzigeorgiou AG, SILVA team , Ma L, Zhang Z, Puetz J, Stadler PF, McDonald D, Basu S, Fey P, Engel SR, Cherry JM, Volders P, Mestdagh P, Wower J, Clark M, Quek XC, Dinger ME. RNAcentral: a comprehensive database of non-coding RNA sequences. Nucleic Acids Res.2017; 45(D1):D128-D134	9,338	BIOCHEMISTRY & MOLECULAR BIOLOGY	14/290	1
14	2017	Tan SY, Teh C, Ang CY, Li M, Li P, **Korzh V**, Zhao Y. Responsive mesoporous silica nanoparticles for sensing of hydrogen peroxide and simultaneous treatment toward heart failure. Nanoscale. 2017; 9(6) 2253-2261	7,668	CHEMISTRY, MULTIDISCIPLINARY	21/166	1
15	2017	de Hoz L, Gierej D, Lioudyno V, **Jaworski J, Blazejczyk M**, Cruces-Solís H, Beroun A, Lebitko T, Nikolaev T, Knapska E, Nelken I, Kaczmarek L. Blocking c-Fos Expression Reveals the Role of Auditory Cortex Plasticity in Sound Frequency Discrimination Learning. Cereb Cortex, Epub 2017 Mar 17.	6,943	NEUROSCIENCES	21/259	1
16	2017	Brendel M, Focke C, Blume T, Peters F, Deussing M, Probst F, **Jaworska A**, Overhoff F, Albert N, Lindner S, von Ungern-Sternberg B, Bartenstein P, Haass C, Kleinberger G, Herms J, Rominger A. Time Courses of Cortical Glucose Metabolism and Microglial Activity Across the Life Span of Wild-Type Mice: A PET Study. J Nucl Med. 2017; 58(12):1984-1990	6,459	RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING	5/127	1
17	2017	Tudek B, **Zdżalik-Bielecka D**, Tudek A, Kosicki K, Fabisiewicz A, Speina E. Lipid peroxidation in face of DNA damage, DNA repair and other cellular processes. Free Radic Biol Med. 2017; 107:77-89	5,886	BIOCHEMISTRY & MOLECULAR BIOLOGY	42/290	1

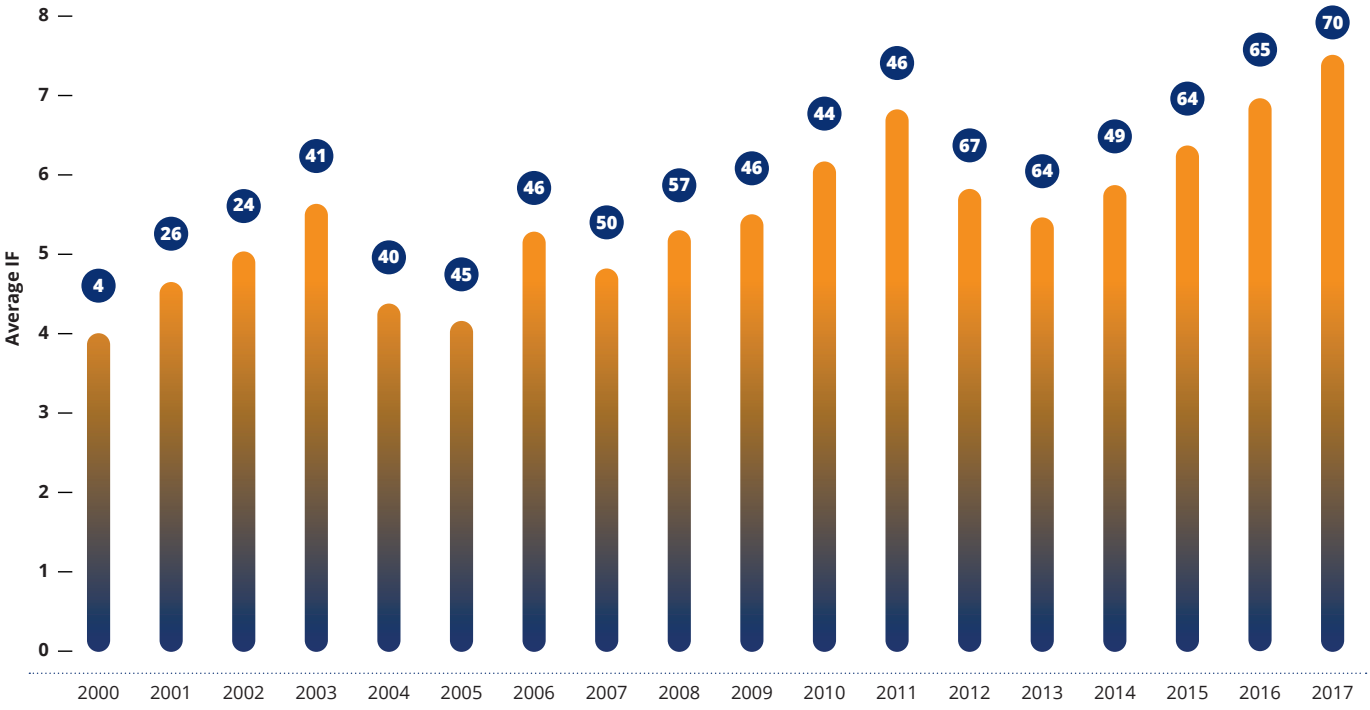
18	2017	Macioła AK, Pietrzak MA, Kosson P, **Czarnocki-Cieciura M**, Śmietanka K, Minta Z, Kopera E. The Length of N-Glycans of Recombinant H5N1 Hemagglutinin Influences the Oligomerization and Immunogenicity of Vaccine Antigen. Front Immunol. 2017; 8:444	5,849	IMMUNOLOGY	21/151	1
19	2017	Kondratiuk I, Łęski S, **Urbańska M**, Biecek P, Devijver H, Lechat B, Van Leuven F, Kaczmarek L, Jaworski T. GSK-3β and MMP-9 Cooperate in the Control of Dendritic Spine Morphology. Mol Neurobiol. 2017; 54(1):200-211	5,767	NEUROSCIENCES	25/259	1
20	2017	Aksoy I, Utami KH, **Winata CL**, Hillmer AM, Rouam SL, Briault S, Davila S, Stanton LW, Cacheux V. Personalized genome sequencing coupled with iPSC technology identifies GTDC1 as a gene involved in neurodevelopmental disorders. Hum Mol Genet. 2017; 26(2):367-382	5,689	BIOCHEMISTRY & MOLECULAR BIOLOGY	46/290	1
21	2017	Nagaraj S, Laskowska-Kaszuba K, Dębski KJ, Wojsiat J, Dąbrowski M, Gabryelewicz T, **Kuźnicki J**, Wojda U. Profile of 6 microRNA in blood plasma distinguish early stage Alzheimer's disease patients from non-demented subjects. Oncotarget. 2017; 8(10):16122-16143	5,312	ONCOLOGY	44/217	1
22	2017	Budzko L, Jackowiak P, Kamel K, Sarzynska J, **Bujnicki JM**, Figlerowicz M. Mutations in human AID differentially affect its ability to deaminate cytidine and 5-methylcytidine in ssDNA substrates in vitro. Sci Rep. 2017; 7(1):3873	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
23	2017	Koh CH, Wu J, Chung YY, Liu Z, Zhang RR, Chong K, **Korzh V**, Ting S, Oh S, Shim W, Tian HY, Wei H. Identification of a Na+/K+-ATPase inhibition-independent proarrhythmic ionic mechanisms of cardiac glycosides. Sci Rep. 2017; 7(1) 2465	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
24	2017	Shen H, Shin EM, Lee S, Mathavan S, Koh H, Osato M, Choi H, Tergaonkar V, **Korzh V**. Ikk2 regulates cytokinesis during vertebrate development. Sci Rep. 2017; 7(1):8094	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
25	2017	Cillingová A, Zeman I, Tóth R, Neboháčová M, Dunčková I, Hölcová M, Jakúbková M, Gérecová G, **Pryszcz LP**, Tomáška Ľ, Gabaldón T, Gácser A, Nosek J. Eukaryotic transporters for zydroxyderivatives of benzoic acid. Sci Rep. 2017; 7(1):8998	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
26	2017	Kozłowska M, Tarczewska A, Jakób M, Bystranowska D, Taube M, Kozak M, **Czarnocki-Cieciura M**, Dziembowski A, Orłowski M, Tkocz K, Ożyhar A. Nucleoplasmin-like domain of FKBP39 from Drosophila melanogaster forms a tetramer with partly disordered tentacle-like C-terminal segments. Sci Rep. 2017; 7:40405	4,847	MULTIDISCIPLINARY SCIENCES	10/64	1
27	2017	Brendel M, Kleinberger G, Probst F, **Jaworska A**, Overhoff F, Blume T, Albert NL, Carlsen J, Lindner S, Gildehaus FJ, Ozmen L, Suárez-Calvet M, Bartenstein P, Baumann K, Ewers M, Herms J, Haass C, Rominger A. Increase of TREM2 during Aging of an Alzheimer's Disease Mouse Model Is Paralleled by Microglial Activation and Amyloidosis. Front. Aging Neurosci., 2017: 9:8	4,602	NEUROSCIENCES	59/259	1
28	2017	Miao Z, Adamiak RW, Antczak M, Batey RT, Becka A, Biesiada M, **Boniecki MJ, Bujnicki JM**, Chen S, Cheng CY, Chou F, Ferré-D'Amaré AR, Das R, **Dawson WK**, Ding F, Dokholyan NV, **Dunin-Horkawicz S**, Geniesse C, Kappel K, Kladwang W, Krokhotin A, **Lach GE**, Major F, Mann TH, **Magnus M**, Pachulska-Wieczorek K, Patel DJ, Piccirilli JA, Popenda M, Purzycka KJ, Ren A, Rice GM, Santalucia J Jr, Sarzynska J, Szachniuk M, Tandon A, Trausch JJ, Tian S, Wang J, Weeks KM, Williams B II, Xiao Y, Xu X, Zhang D, Zok T, Westhof E. RNA-Puzzles Round III: 3D RNA structure prediction of five riboswitches and one ribozyme. RNA. 2017; 23(5):655-672	4,392	BIOCHEMISTRY & MOLECULAR BIOLOGY	58/290	1
29	2017	Karlowicz A, Wegrzyn K, Gross M, Kaczynska D, Ropelewska M, Siemiątkowska M, **Bujnicki JM**, Konieczny I. Defining the Crucial Domain and Amino Acid Residues in Bacterial Lon Protease for DNA Binding and Processing of DNA-interacting Substrates. J Biol Chem. 2017; 292(18):7507-7518	4,323	BIOCHEMISTRY & MOLECULAR BIOLOGY	74/290	3
30	2017	**Szybińska A**, Leśniak W. P53 Dysfunction in Neurodegenerative Diseases – The Cause or Effect of Pathological Changes? Aging and Disease, 2017; 8(4):506-518	4,100	GERIATRICS & GERONTOLOGY	6/49	1
31	2017	Woźniak A, Grześkowiak BF, Babayevska N, Zalewski T, Drobna M, Woźniak-Budych M, **Wiweger M**, Słomski R, Jurga S. ZnO@Gd_2O_3 core/shell nanoparticles for biomedical applications: Physicochemical, in vitro and in vivo characterization. Mater Sci Eng C Mater Biol Appl. 2017; 80:603-615	3,926	MATERIALS SCIENCE, BIOMATERIALS	9/33	2
32	2017	Patel T, Chojnowski G, **Astha**, Koul A, McKenna S, **Bujnicki JM**. Structural studies of RNA-protein complexes: A hybrid approach involving hydrodynamics, scattering and computational methods. Methods. 2017; 118-119:146-162	3,880	BIOCHEMICAL RESEARCH METHODS	21/78	2
33	2017	García-Lecea M, Gasanov E, **Jedrychowska J, Kondrychyn I**, Teh C, You MS, **Korzh V**. Development of Circumventricular Organs in the Mirror of Zebrafish Enhancer-Trap Transgenics. Front Neuroanat. 2017; 11:114	3,531	NEUROSCIENCES	101/259	2
34	2017	Kevei É, **Pokrzywa W**, Hoppe T. Repair or Destruction: An Intimate Liaison Between Ubiquitin Ligases and Molecular Chaperones in Proteostasis. FEBS Lett. 2017; 591(17):2616-2635	3,424	BIOPHYSICS	18/73	2
35	2017	Dzananovic E, **Astha**, Chojnowski G, Deo S, Booy EP, Padilla-Meier P, McEleney K, **Bujnicki JM**, Patel TR, McKenna SA. Impact of the structural integrity of the three-way junction of adenovirus VA(I) RNA on PKR inhibition. PLoS One. 2017; 12(10):e0186849	3,394	MULTIDISCIPLINARY SCIENCES	15/64	1
36	2017	Prabucka B, Mielecki M, Chojnacka M, Bielawski W, **Czarnocki-Cieciura M**, Orzechowski S. Structural and functional characterization of the triticale (x Triticosecale Wittm.) phytocystatin TrcC-8 and its dimerization-dependent inhibitory activity. Phytochemistry. 2017; 142:1-10	3,349	BIOCHEMISTRY & MOLECULAR BIOLOGY	119/290	2
37	2017	Majerczyk M, Choręza P, Bożentowicz-Wikarek M, Brzozowska A, Arabzada H, Owczarek A, **Mossakowska M**, Grodzicki T, Zdrojewski T, Więcek A, Olszanecka-Glinianowicz M, Chudek J. Increased plasma RBP4 concentration in older hypertensives is related to the decreased kidney function and the number of antihypertensive drugs-results from the PolSenior substudy. J Am Soc Hypertens. 2017; 11(2):71-80	3,032	PERIPHERAL VASCULAR DISEASE	24/63	2

38	2017	Mazurek T, Kobylecka M, Zielenkiewicz M, **Kurek A**, Kochman J, Filipiak KJ, Mazurek K, Huczek Z, Królicki L, Opolski G. PET/CT evaluation of F-18-FDG uptake in pericoronary adipose tissue in patients with stable coronary artery disease: Independent predictor of atherosclerotic lesions' formation? Journal of Nuclear Cardiology, 2017; 24(3):1075–1084	2,996	RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING	18/127	1
39	2017	Owczarz M, Budzinska M, Domaszewska-Szostek A, Borkowska J, Polosak J, Gewartowska M, **Slusarczyk P**, Puzianowska-Kuznicka M. miR-34a and miR-9 are overexpressed and SIRT genes are downregulated in peripheral blood mononuclear cells of aging humans. Exp Biol Med (Maywood). 2017; 242(14):1453-1461	2,512	MEDICINE, RESEARCH & EXPERIMENTAL	59/128	2
40	2017	Łabuz-Roszak B, Machowska-Majchrzak A, Skrzypek M, **Mossakowska M**, Chudek J, Więcek A, Wawrzyńczyk M, Łącka-Gaździk B, Pierzchała K. Antiplatelet and anticoagulant therapy in elderly people with type 2 diabetes mellitus in Poland (based on the PolSenior Study). Arch Med Sci. 2017; 13(5):1018–1024	1,904	MEDICINE, GENERAL & INTERNAL	46/155	2
41	2017	Dowierciał A, Jarmuła A, Wilk P, Rypniewski W, **Kowalska M**, Frączyk T, Cieśla J. Mouse thymidylate synthase does not show the inactive conformation, observed for the human enzyme. Struct Chem. 2017; 28:667-674	1,372	CHEMISTRY, MULTIDISCIPLINARY	94/166	3
42	2017	Łabuz-Roszak B, Skrzypek M, Machowska-Majchrzak A, **Mossakowska M**, Chudek J, Więcek A, Pierzchała K, Łącka-Gaździk B, Grodzicki T. Pharmacological stroke prevention in the elderly with atrial fibrillation in Poland - Results of PolSenior study. Neurol Neurochir Pol. 2017; 51(5):382-387	0,774	CLINICAL NEUROLOGY	175/194	4
		Q1 2018				
1	2018	NCD Risk Factor Collaboration (NCD-RisC) within **Mossakowska M. and Slusarczyk P**. Contributions of mean and shape of blood pressure distribution to worldwide trends and variations in raised blood pressure: a pooled analysis of 1018 population-based measurement studies with 88.6 million participants. Int J Epidemiol. Epub 2018 Mar 19	9,804	PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH	5/176	1
2	2018	Neto F, Klaus-Bergmann A, Ong YT, Alt S, Vion AC, Szymborska A, Carvalho JR, Hollfinger I, Bartels-Klein E, Franco CA, **Potente M**, Gerhardt H. YAP and TAZ regulate adherens junction dynamics and endothelial cell distribution during vascular development. Elife. 2018; pii: e31037	8,385	BIOLOGY	4/85	1
3	2018	Bennabi I, Quéguiner I, **Kolano A**, Boudier T, Mailly P, Verlhac MH, Terret ME. Shifting meiotic to mitotic spindle assembly in oocytes disrupts chromosome alignment. EMBO Rep. 2018; 19(2):368-381	7,977	BIOCHEMISTRY & MOLECULAR BIOLOGY	22/290	1
4	2018	Herz K, Becker A, Shi C, Ema M, Takahashi S, **Potente M**, Hesse M, Fleischmann BK, Wenzel D. Visualization of endothelial cell cycle dynamics in mouse using the Flt-1/eGFP-anillin system. Angiogenesis. 2018; 21(2):349-361	4,649	PERIPHERAL VASCULAR DISEASE	9/63	1
5	2018	Balaji V, **Pokrzywa W**, Hoppe T. Ubiquitylation Pathways In Insulin Signaling and Organismal Homeostasis. Bioessays. 2018 Apr 3:e1700223	4,597	BIOCHEMISTRY & MOLECULAR BIOLOGY	63/290	1
6	2018	Saus E, Willis JR, **Pryszcz LP**, Hafez A, Llorens C, Himmelbauer H, Gabaldón T. nextPARS: parallel probing of RNA structures in Illumina. RNA. 2018; 24(4):609-619	4,392	BIOCHEMISTRY & MOLECULAR BIOLOGY	58/290	1
7	2018	Sulicka J, Pac A, Puzianowska-Kuźnicka M, Zdrojewski T, Chudek J, Tobiasz-Adamczyk B, **Mossakowska M**, Skalska A, Więcek A, Grodzicki T. Health status of older cancer survivors—results of the PolSenior study. J Cancer Surviv. Epub 2018 Jan 9	3,875	SOCIAL ISSUES	3/41	1
8	2018	Kiryukhin MV, Lau HH, Goh SH, Teh C, **Korzh V**, Sadovoy A. A membrane film sensor with encapsulated fluorescent dyes towards express freshness monitoring of packaged food. Talanta. 2018; 182:187-192	3,841	CHEMISTRY, ANALYTICAL	9/76	1
9	2018	Gogler-Pigłowska A, Klarzyńska K, Sojka DR, Habryka A, Głowala-Kosińska M, Herok M, Kryj M, **Halczok M**, Krawczyk Z, Scieglinska D. Novel role for the testis-enriched HSPA2 protein in regulating epidermal keratinocyte differentiation. J Cell Physiol. 2018; 233(3):2629-2644	3,689	PHYSIOLOGY	16/84	1
10	2018	Mróz TL, Eves-van den Akker S, Bernat A, Skarzyńska A, **Pryszcz L,** Olberg M, Havey MJ, Bartoszewski G. Transcriptome Analyses of Mosaic (MSC) Mitochondrial Mutants of Cucumber in a Highly Inbred Nuclear Background. G3: Genes, Genomes, Genetics. 2018; 8(3):953-965	3,356	GENETICS & HEREDITY	71/167	2
11	2018	Wyskida M, Owczarek A, **Szybalska A**, Brzozowska A, Szczerbowska I, Wieczorowska-Tobis K, Puzianowska-Kuźnicka M, Franek E, **Mossakowska M**, Grodzicki T, Więcek A, Olszanecka-Glinianowicz M, Chudek J. Socio-economic determinants of vitamin D deficiency in the older Polish population: results from the PolSenior study. Public Health Nutr. 2018; 1-9	2,824	PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH	59/176	2
12	2017	Mazur M, Bartoszewicz A, Dymek B, Salamon M, Andryianau G, Kowalski M, Olejniczak S, Matyszewski K, Pluta E, Borek B, **Stefaniak F**, Zagozdzon A, Mazurkiewicz M, Koralewski R, Czestkowski W, Piotrowicz M, Niedziejko P, Gruza MM, Dzwonek K, Golebiowski A, Golab J, Olczak J. Discovery of selective, orally bioavailable inhibitor of mouse chitotriosidase. Bioorg Med Chem Lett. 2018; 28(3): 310-314	2,286	CHEMISTRY, ORGANIC	24/59	2
13	2018	Holko P, Kawalec P, **Mossakowska M**. Quality of life related to oral, subcutaneous, and intravenous biologic treatment of inflammatory bowel disease: a time trade-off study. Eur J Gastroenterol Hepatol. 2018; 30(2):174-180	2,129	GASTROENTEROLOGY & HEPATOLOGY	60/79	4
14	2018	Majerczyk M, Kocełak P, Choręza P, Arabzada H, Owczarek A, Bożentowicz-Wikarek M, Brzozowska A, **Szybalska A**, Puzianowska-Kuźnicka M, Grodzicki T, Więcek A, Olszanecka-Glinianowicz M, Chudek J. Components of metabolic syndrome in relation to plasma levels of retinol binding protein 4 (RBP4) in a cohort of people aged 65 years and older. J Endocrinol Invest. Epub 2018 Mar 9	1,895	ENDOCRINOLOGY & METABOLISM	79/138	3

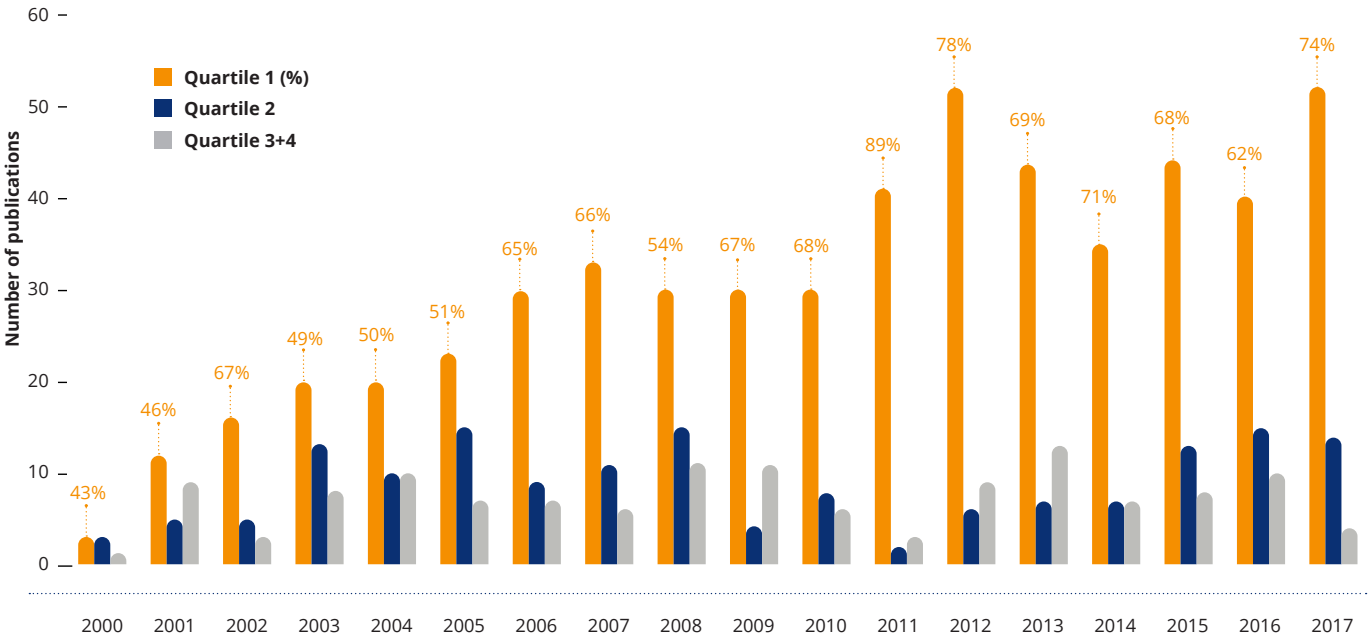
Cumulative citations (without self-citations) Hirsch index = 74



Number and average IF of journals with IIMCB's publications 2000-2017



Number of publications in Quartiles in Journals Category and % of Quartile 1



Grants

EU Horizon 2020

Number of projects 3

COST

- EPITRAN "European Epitranscriptomics Network" (CA16120); 2017-2021; J.M. Bujnicki, E. Purta
- MOBIEU "Between Atom and Cell: Integrating Molecular Biophysics Approaches for Biology and Healthcare" (OC-2015-1-19651); 2016-2020; **K. Skowronek, R. Szczepanowski**
- IONCHAN-IMMUNRESPON "Ion Channels and Immune Response toward a global understanding of immune cell physiology and for new therapeutic approaches" (BM1406); 2015-2019; **J. Kuźnicki**, **Ł. Majewski**

EU 7th Framework Programme

Number of projects 3

Funding 16 297 668 PLN

ERC StG

- NERCOMP "Structural studies of Nucleotide Excision Repair complexes" (281500); 1 498 000 EUR; 2012-2017; **M. Nowotny**
- MorphoCorDiv "The inherent morphological potential of the actin cortex and the mechanics of shape control during cell division" (311637); 1 500 000 EUR; 2013-2018; **E. Paluch** (grant implemented at University College London, UK)

Collaborative Project

- EPISTOP "Long-term, prospective study evaluating clinical and molecular biomarkers of epileptogenesis in a genetic model of epilepsy – tuberous sclerosis complex" (602391); 774 818 EUR; matching funds 829 113 PLN; 2013-2018; **J. Jaworski**

International Funds

Number of projects 3

Funding 5 860 919 PLN

- **Wellcome Trust International Senior Research Fellowship** "Structural and Biochemical studies of Holliday junction resolution" (0988022); 3 369 854 PLN; 2013-2018; **M. Nowotny**
- **Visegrad Fund** "Summer school in Bioinformatics & NGO data analysis" (21710381); 14 650 EUR; 2017; **L. Pryszcz**
- **Howard Hughes Medical Institute, International Early Career Award** "Structural and Mechanistic Studies of Nucleic Acid Processing" (55007428); 715 000 USD; 2012-2017; **M. Nowotny**

Foundation for Polish Science

Number of projects 8

Funding 17 501 525 PLN

EU Structural Funds

- SG OP 4.4. TEAM "Structural and biochemical studies of the mechanism of LINE-1 retrotransposition and hepadnaviral replication" (TEAM/2016-2/16); 3 690 834 PLN; 2017-2020; **M. Nowotny**
- SG OP 4.4. TEAM "Cellular consequences of endosomal dysfunction for proteostasis, metabolism and cancer biology" (TEAM/2016-2/15); 3 497 520 PLN; 2017-2020; **M. Miączyńska**
- SG OP 4.4. TEAM "Modeling of dynamic interactions between RNA and small molecules and its practical applications" (TEAM/2016-2/15); 3 449 541 PLN; 2017-2020; **J.M. Bujnicki**
- SG OP 4.4. TEAM-TECH "INFECTLESS New generation of antibacterial wound dressing" (TEAM TECH/2016-3/19); 3 463 780 PLN; 2017-2020; **I. Sabała**
- SG OP 4.4. FIRST TEAM "Genomics dissection of the heart pacemaker in zebrafish" (First TEAM/2016-1/8); 1 999 880 PLN; 2017-2019; **C.L. Winata**
- SG OP 4.4. HOMING "Role of ESCRT-I protein complex in amino acid and lipid metabolism in the context of erythropoiesis" (Homing/2016-1/1); 799 970 PLN; 2017-2018; **J. Cendrowski**

FNP's subventions

- Master "Functional studies on human and viral methyltransferases involved in RNA cap biosynthesis: from in silico docking and in vitro validation, to RNA methylation inhibition in human cells" (1./2014); 300 000 PLN; 2015-2017; **J.M. Bujnicki**
- Master "mTOR kinase and protein sorting by retromer and trans-Golgi network" (5./2014); 300 000 PLN; 2015-2017; **J. Jaworski**

National Centre for Research and Development

Number of projects 3

Funding 6 899 620 PLN

- **STRATEGMED** "Application of novel diagnostic and therapeutical methods in epilepsy and neurodevelopmental abnormalities in children based on the clinical and cellular model of mTOR dependent epilepsy (acronim EPIMARKER)" (306306); 3 088 120 PLN (total grant budget: 16 847 247 PLN); 2017-2020; **J. Jaworski** (partner); Coordinator: Medical University of Warsaw
- **STRATEGMED** "Development of new cancer therapies based on selective antitumor immunomodulators (acronim DIMUNO)" (265503); 982 500 PLN (total grant budget: 31 929 500 PLN); 2015-2018; **M. Nowotny** (partner); Coordinator: OncoArendi Therapeutics
- **Applied Research Programme (PBS)** "Development of new biotechnology products based on innovative technique of ribonucleic acid cleavage" (245550); 2 829 000 PLN (total grant budget: 3 316 441 PLN); 2015-2018, coordinator: **J.M. Bujnicki**

National Science Centre

Number of projects 47

Funding 49 638 416 PLN

MAESTRO

- "Cross-talk between the transport of mitochondrial proteins and cellular protein homeostasis" (2015/18/A/NZ1/00025); 4 271 581 PLN; 2016-2021; **A. Chacińska**
- "Molecular mechanisms of pro-survival processes in breast cancer" (2012/06/A/NZ1/00089); 3 000 000 PLN; 2013-2019; **M. Żylicz**
- "Structural RNomics" (2012/04/A/NZ2/00455); 3 000 000 PLN; 2012-2018; J.M. Bujnicki
- "Transgenic mice with elevated basal level of calcium ions in neurons as a model of aged-induced neurodegeneration of sporadic Alzheimer's disease" (2011/02/A/NZ3/00144); 2 989 800 PLN; 2012-2018; **J. Kuźnicki**
- "New functions of endocytic proteins in transcriptional regulation" 2 875 000 PLN; 2012-2018; **M. Miączyńska**

POLONEZ

- "The link between mitochondria and the protein quality control system" (2016/21/P/NZ3/03891); 872 088 PLN; 2017-2019; **M. Turek**
- "Deciphering BMP6 regulatory mechanisms using CRISPR/Cas9-based screening approach" (2015/19/P/NZ2/03278); 893 104 PLN; 2017-2018; K. Mleczko-Sanecka
- "Deciphering the role of RNA editing in zebrafish development" (2015/19/P/NZ2/03655); 921 064 PLN; 2017-2018; **L. Pryszcz**
- "Genomic profiling of zebrafish cardiac pacemaker cells" (2015/19/P/NZ3/03613); 921 064 PLN; 2016-2018; **R. Minhas**
- "Regulation of genome activity in plastids" (2015/19/P/NZ1/03619); 402 932 PLN; 2016-2017; **A.T. Wierzbicki**

SYMFONIA

- "Mitochondrial RNA decay and surveillance – comprehensive interdisciplinary studies" (2014/12/W/NZ1/00463); 2 953 248 PLN (total grant budget: 6 879 968 PLN); 2014-2019; **M. Nowotny**

SONATA BIS

- "Role of Rap proteins in regulation of mTOR function" (2012/07/E/NZ3/00503); 1 500 000 PLN; 2013-2018; **J. Jaworski**

HARMONIA

- "Structural biology of mixed lineage leukemia (MLL) proteins" (2014/14/M/NZ5/00558); 1 255 000 PLN; 2015-2018; **M. Bochtler**

OPUS

- "Exploring Baltic Sea cyanobacteria for small-molecule inhibitors of microRNA function" (2017/25/B/NZ9/00202); 27 000 PLN (total grant budget: 1 410 100 PLN); 2018-2021; **F. Stefaniak** (partner); coordinator: University of Warmia and Mazury in Olsztyn
- "mTOR kinase impact on cellular functions of selected molecular motors" (2016/21/B/NZ3/03639); 1 336 250 PLN; 2017-2020; **J. Jaworski**
- "Finding novel determinants of the brain ventricular system" (2016/21/B/NZ3/00354); 1 294 885 PLN; 2017-2020; **V. Korzh**
- "Biochemical and structural studies of retroviral reverse transcriptases evolution" (2016/21/B/NZ1/02757); 1 145 000 PLN; 2017-2020; **E. Nowak**
- "The impact of intracellular distribution and endocytic transport of lymphotoxin beta receptor (LTbetaR) on its signalling" (2016/21/B/NZ3/03637); 996 125 PLN; 2017-2020; **M. Banach-Orłowska**
- "The role of E3 ligase complexes in integration of protein homeostasis and aging" (2016/23/B/NZ3/00753); 1 116 875 PLN; 2017-2020; **W. Pokrzywa**
- "A coarse-grained method for RNA 3D structure modeling, with emphasis on noncanonical base pairing" (2016/23/B/ST6/03433); 741 250 PLN; 2017-2020; **M. Boniecki**
- "Role of STIM2 isoforms in regulation of neuronal calcium channels in *Danio rerio*" (2016/23/B/NZ3/03142); 2 085 031 PLN; 2017-2020; **J. Kuźnicki**
- "Identification of genes controlling brain development through genomic analysis of patients" (2015/19/B/NZ2/01824); 162 960 PLN (total grant budget: 1 539 596 PLN); 2016-2019; **C.L. Winata** (partner); coordinator: Institute of Mother and Child
- "Characterization of the TIM23 pathway of protein import into mitochondria in mammalian cells" (2015/19/B/NZ3/03272); 1 198 600 PLN; 2016-2019; **M. Wasilewski**
- "Mechanisms protecting from oxidative damage during aging" (2015/19/B/NZ1/03444); 1 200 800 PLN; 2016-2019; **U. Topf**
- "New 5-hydroxymethylcytosine binding proteins" (2014/13/B/NZ1/03991); 1 283 750 PLN; 2015-2019; **M. Bochtler**
- "Elucidating the gene regulatory network of zebrafish heart development using genomics" (2014/13/B/NZ2/03863); 955 500 PLN; 2015-2018; **C.L. Winata**
- "Coupling of synthesis and transport for proteins targeted to the mitochondria" (2013/11/B/NZ3/00974); 1 165 520 PLN; 2014-2018; **A. Chacińska**

SONATA

- "Characterizing the functions and molecular mechanisms of VPS4B action in biology of colorectal cancer (CRC) cells and in CRC pathogenesis" (2016/21/D/NZ3/00637); 791 850 PLN; 2017-2020; **E. Szymańska**
- "Uncovering the molecular mechanisms of heart regeneration in zebrafish through profiling of contributing genomic factors" (2016/21/D/NZ2/03843); 556 708 PLN; 2017-2020; **K. Nieścierowicz**
- "Role of Tollip protein in embryonic development and protein homeostasis in the model of zebrafish (*Danio rerio*)" (2016/21/D/NZ4/00494); 583 750 PLN; 2017-2020; **L. Wolińska-Nizioł**
- "Endocytosis of AXL receptor and its role in AXL-mediated signaling" (2015/19/B/NZ3/03270); 762 929 PLN; 2016-2019; **D.P. Zdżalik-Bielecka**
- "Modeling 3D structures and dynamics of RNA complexes with metal ions, with particular emphasis on the formation of non-canonical base pairs: extension of the SimRNA coarse-grained model towards hish-resolution" (2015/17/D/NZ1/01560); 465 400 PLN; 2016-2019; **D. Niedziałek**
- "The role of Zebrafish mTOR in neuronal development in vivo as a key regulator of neuronal circuit formation" (2015/17/D/NZ3/03735); 689 000 PLN; 2016-2019; **J. Zmorzyńska**
- "Modulation of mitochondrial calcium traffic in pink1 mutant Zebrafish model of Parkinson's disease" (2014/15/D/NZ3/05176); 583 437 PLN; 2015-2018; **S. Soman**
- "Role of CacyBP/SIP in the dysregulation of beta-catenin ubiquitination in YAC128 mouse model of Huntington's disease" (2014/15/D/NZ3/05181); 650 000 PLN; 2015-2018; **M. Czeredys**
- "Functional Characterization of Non-Collagenous Extracellular Matrix Proteins as a Potential Molecular Target and Novel Biomarker of Liver Fibrosis" (2014/15/D/NZ5/03421); 541 875 PLN; 2015-2018; **M. Pawlak**
- "Extramitochondrial factors regulating turnover of mitochondrial intermembrane space proteins" (2013/11/D/NZ3/02294); 796 100 PLN; 2014-2017; **P. Brągoszewski**
- "Patient-specific iPS cells as a novel approach to study pathophysiology of mTOR related neurodevelopmental disorders" (2013/11/D/NZ3/01079); 700 000 PLN; 2014-2018; **E. Liszewska**
- "The contribution of STIM proteins and the role of Store Operated Calcium Entry (SOCE) in calcium homeostasis of neurons" (2011/01/D/NZ3/02051); 684 000 PLN; 2011-2018; **J. Gruszczyńska-Biegała**

PRELUDIUM

- "The role of mu2-adaptin serine 45 and serine 309 phosphorylation in clathrin mediated endocytosis" (2017/25/N/NZ3/01280); 120 000 PLN; 2018-2020; **A. Tempes**
- "Is endocytosis disrupted in tuberous sclerosis complex? Novel studies on human neural stem cells" (2016/23/N/NZ3/00108); 100 000 PLN; 2017-2019; **A. Kościelny**
- "Regulation of the human cap methyltransferase CMTr1 by an RNA helicase" (2015/19/B/NZ1/03449); 49 800 PLN; 2016-2017; **M. Zielińska**
- "RNA structure prediction based on modeling the target sequence and homologous sequences" (2015/17/N/NZ2/03360); 49 400 PLN; 2016-2017; **M. Magnus**
- "Genome wide high throughput analysis of 5-hydroxymethyl cytosine in *Danio rerio*" (2012/05/N/NZ2/02233); 150 000 PLN; 2013-2017; **K. Mierzejewska**
- "Regulation of mTOR kinase signaling pathway by ESCRT-II complex in dendritogenesis" (2012/07/N/NZ3/01661); 140 000 PLN; 2013-2017; **M. Pieprzyk**

FUGA

- "Analysis of the mitochondrial proteins translocase TIM22 in human cells" (2016/20/S/NZ1/00423); 612 000 PLN; 2016-2019; **K. Chojnacka**

MINIATURA

- "The influence of surface net charge on the activity of new peptidoglycan hydrolases from Staphylococcus pettenkoferi" (2017/01/X/NZ1/00512); 47 740 PLN; 2017-2018; **E. Jagielska**

Ministry of Science and Higher Education

Number of projects **2**

Funding **3 355 980 PLN**

- **Diamond Grant** "Elucidating the mechanism of translational control of maternal transcripts through cytoplasmic polyadenylation" (DI2014 008644); 199 980 PLN; 2015-2019; **M. Łapiński**
- **Ideas Plus** "Coupling of synthesis and transport for proteins targeted to the mitochondria" (000263); 3 156 000 PLN; 2014-2017; **A. Chacińska**

Selected projects

Interdisciplinary Innovative Projects

NERCOMP, ERC Starting Grant, FP7

The overall objective of the ERC project of **Dr. Marcin Nowotny** entitled, "Structural studies of nucleotide excision repair complexes", is to expand the knowledge of DNA repair mechanisms. Specifically, Dr. Nowotny focuses on the structural and biochemical characterization of protein complexes that are involved in nucleotide excision repair pathways in bacteria and eukaryotes. This is a key process to gain a basic understanding of genome stability. Disturbances in these mechanisms can result in tumorigenesis in humans.

International Senior Research Fellowship (ISRF), Wellcome Trust

The project, "Structural and biochemical studies of Holliday junction resolution", is an extension and completion of the first ISRF grant that was awarded to **Dr. Marcin Nowotny.** It seeks to determine the structural basis of the recognition of four-way DNA structures by proteins. This is important for such processes as DNA repair.

TEAM Programme, FNP

Prof. Marta Miączyńska was awarded the grant, "Cellular consequences of endosomal dysfunction for proteostasis, metabolism and cancer biology". The first objective is to characterize the ways in which endosomal stress impacts cellular proteostasis and lipid metabolism. The second objective is to study whether the lower expression of ESCRT-I subunits (observed in colorectal cancer) may result in the endosomal stress response and whether this response can be modulated pharmacologically.

TEAM Programme, FNP

Prof. Janusz M. Bujnicki received funding for the project, "Modeling of dynamic interactions between RNA and small molecules and its practical applications". It focuses on the development of new computational methods for modeling RNA interactions with small-molecule ligands and its application to study and regulate the mechanism of action of viral and bacterial RNA molecules.

TEAM Programme, FNP

The aim of the project, "Structural and biochemical studies of the mechanism of LINE-1 retrotransposition and hepadnaviral replication", led by **Dr. Marcin Nowotny**, is to determine the structure and mechanism of RTs from non-LTR retrotransposons and HBV. This will expand the understanding of RTs and enable the design of novel inhibitors of their activity. We also plan to elucidate the structural basis of retrotransposon silencing by the KRAB-KAP1 system.

First Team Programme, FNP

Dr. Cecilia L. Winata received funding for the project, "Genomics dissection of the heart pacemaker in zebrafish", with the aim of elucidating the gene regulatory network in heart pacemaker development using zebrafish as a model organism. The project seeks to uncover the ways in which the underlying molecular mechanism translates into the proper functioning of pacemakers and the consequences of their dysregulation in zebrafish.

SYMFONIA grant, NCN

Dr. Marcin Nowotny is a leader of the multi-partner project, "Mitochondrial RNA decay and surveillance: comprehensive interdisciplinary studies". The consortium partners are the Institute of Biochemistry and Biophysics (Dr. R. Szczęsny), Faculty of Biology of the University of Warsaw (Prof. P. Golik), and Faculty of Mathematics, Informatics and Mechanics of the University of Warsaw (Dr. B. Wilczyński). SYMFONIA is a prestigious funding opportunity that is intended for exceptional established researchers who perform interdisciplinary or cross-domain research in collaboration with teams from different research areas.

Application-oriented Projects

EPISTOP, Collaborative project, FP7

The aim of the EPISTOP project, "Long-term, prospective study evaluating clinical and molecular biomarkers of epileptogenesis in a genetic model of epilepsy – tuberous sclerosis complex", is to better understand the mechanisms of epilepsy in patients with tuberous sclerosis complex (TSC). This multicenter study comprises 14 hospitals and laboratories from Europe and the United States, including **Prof. Jacek Jaworski's** group. The project seeks to identify the risk factors and biomarkers of epileptogenesis, including the development of clinical seizures and course of the disease. Another important goal of the project is to identify targets and the means by which to prevent epilepsy and modify development of the disease. In the long term, we plan to prepare new directions and guidelines regarding the treatment of patients with TSC and epilepsy that can improve patients' quality of life.

EPIMARKER, STRATEGMED Program, NCBR

Prof. Jacek Jaworski is a partner on the project, "Application of novel diagnostic and therapeutical methods in epilepsy and neurodevelopmental abnormalities in children based on the clinical and cellular model of mTOR dependent epilepsy (acronym EPIMARKER)", led by the Medical University of Warsaw. EPIMARKER is the first project that is being carried out in humans that prospectively examines clinical, electroencephalographic, and molecular biomarkers to produce an integrative tool that is useful for the routine diagnosis and treatment of epilepsy in children to prevent the development of drug-resistant epilepsy and its behavioral comorbidities, such as mental retardation and autism.

eRNAza, project within Applied Research Program, NCBR

A consortium of the applied research project, "Development of new biotechnology products based on innovative technique of ribonucleic acid cleavage", led by **Prof. Janusz M. Bujnicki**, won the competition of the National Centre for Research and Development (NCBR). The research is conducted in a consortium with A&A Biotechnology S.C., a Polish company in Gdynia (Group Leader: Dr. S. Dabrowski).

TEAM TECH Programme, FNP

Dr. Izabela Sabała is involved in the project, "INFECTLESS New generation of antibacterial wound dressing". It seeks to develop a new generation of wound dressing that is functionalized with patented bacteriolytic enzymes and based on modern biomaterials, such as hydrogels and nanofibers. This project, performed in collaboration with scientific and commercial partners, will be a tremendous opportunity to introduce young researchers to various scientific areas and train them in commercial aspects of the implementation of project results.


SCIENTIFIC
EVENTS

Scientific Meetings and Lectures

25-27/3/2018

IIMCB organized the **2nd International FishMed Conference on Zebrafish Research (FishMed2018)** to share the most recent knowledge and developments in zebrafish research. The program included keynote lectures by **Wiebke Herzog** (Germany) and **Randall Peterson** (USA), plenary talks by invited speakers, short oral presentations that were given by PhD students and postdocs, poster sessions, and extensive time for discussions. The special focus of the conference was on early-stage researchers for whom dedicated competitive "Young FishMed" sessions were designed. Thus, 14 early-stage researchers who submitted the best abstracts according to the Scientific Committee had been invited to give talks to present their research. Of the 93 posters that were presented, two were distinguished by Poster Awards: **Elisa Lidron** (Italy) and **Gloria Casas Gemeno** (The Netherlands). The conference gathered more than 200 participants from 22 countries, including a number of Polish scientists who are increasingly more interested in using zebrafish as a research model in various aspects of their work. The conference was also a good occasion to promote the "Be Healthy as a Fish" educational campaign with the help of enthusiastic primary school children. More information, including the Abstract Book, can be found at http://fishmed2018.pl/.

19-21/3/2018

"**Talking molecules: the networks that shape the living world**" – The 2nd COST - sponsored plenary meeting of the Association of Resources for Biophysical Research in Europe - Molecular BioPhysics in Europe (ARBRE-MOBIEU) was held at IIMCB. The meeting was attended by 140 participants, representing resource laboratories, infrastructures, and facilities from 25 different European countries. Keynote lectures were presented by **Toshio Yanagida**, **Malgorzata Lekka**, **Jonathan B. Chaires**, and **Sandro Keller**. The scientific program included four scientific sessions and two poster sessions that focused on:

- Nanomechanics, from Virus to Cell-based Diagnosis
- Combining Biophysical Methods
- Intrinsically Disordered Proteins
- Macromolecular Structure and Interactions.

28-30/9/2017

Matthias Bochtler, Marcin Nowotny, Małgorzata Figiel, and Anna Piasecka organized the **20th Heart of Europe Bio-Crystallography Meeting** at Wojanów Castle in southwest Poland. The event was attended by 113 participants. It is the most prominent meeting of crystallographers and structural biologists from central Europe, with an opportunity for young scientists to present their results.

26/9/2017

IIMCB organized two **"Be Healthy as a Fish" workshops** as one of the **festival lessons at the 21st Science Festival in Warsaw**. The objective of the IIMCB educational program is to teach children basic knowledge about the life of fish and possibilities of their use in studies of certain human diseases.

10-17/9/2017

IIMCB supported the Summer School in Bioinformatics and Next Generation Sequencing Data Analysis (NGSchool2017: Single-cell sequencing) in Jachranka, Poland, organized by Leszek Pryszcz, Laboratory of Zebrafish Developmental Genomics. In the 1-week course, 66 participants from 19 countries attended the series of lectures and workshops, covering various aspects of computational biology, with a focus on state-of-the-art techniques that are related to next generation sequencing and its application in research, healthcare, and industry. The event was mainly geared toward students and researchers in the early stage of their careers.

10-15/9/2017

Marta Miączyńska was the Chair and main organizer of the **EMBO Conference "Endocytic Trafficking and Signalling in Health and Disease"** in Serock. More than 170 participants from all over the world discussed recent advances in the field of endocytosis, which now extends beyond cell biology and is integrated into physiology, developmental biology, molecular medicine, physics of biological processes, and systems biology. The opening lecture was given by Prof. Margaret Robinson and discussed how endocytic coats evolved from yeast to humans. Prof. Rob Parton in the closing lecture shed light on caveolae as mechanosensor organelles of the cell.

10-14/7/2017
24-27/9/2017

IIMCB, in cooperation with BioCEN, organized **summer workshops for talented youth from Ukraine**, chosen by the Minor Academy of Sciences of Ukraine. Children (10-14 years old) were taught how to examine their own DNA and how DNA can be analyzed in forensic science. They also learned about the inner life of cells, cellular superstructures, and enzymes. Younger children (9-11 years old) attended the "Be Healthy as a Fish" workshop. At the workshop that was organized by BioCEN, the children learned that fluorescence naturally occurs in nature and is widely used by humans in industry, research, and medicine. They were also taught about photosynthesis and why plants can be called "green sweet factories."

12-13/6/2017

IIMCB supported the CRISPR Workshop, organized by Katarzyna Mleczko-Sanecka, Laboratory of Iron Homeostasis. During this 2-day event, approximately 50 participants from different Polish institutions attended lectures and an interactive task-driven session to learn various aspects of CRISPR-mediated gene editing in cells and living organisms, with a strong focus on applying this innovative technique in practice.

9/6/2017

Annual Report Session, Białobrzegi, where IIMCB scientists gave 11 lectures.

27/3/2017

Marcin Nowotny delivered the lecture, "How to understand the operation of an organism at the level of individual atoms? Example from research on the repair mechanisms of the genetic material," at the **"Polish Scientists – World-Class Science"** event organized by the National Contact Point for Research Programs of the European Union.

27/2/2017

IIMCB participated in organizing the conference, "**CePT - a development platform for innovative medicine**." The purpose of the event, conceived by the Center for Preclinical Research and Technology (CePT), was to initiate a substantive discussion on the cooperation of science, business, and government in the area of bioinnovation. Over 300 representatives of science, business, and government attended the event.

Regular IIMCB seminars

Dr. Orsolya Barabas (EMBL, Heidelberg, Germany) *How genes jump: structural insights into the mechanisms of DNA transposition.* 12.01.2017

Dr. Nuno Morais (Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Portugal) *Profiling alternative splicing in evolution and disease.* 19.01.2017

Prof. Blanche Schwappach (University Medical Center Göttingen, Germany) *Targeting proteins to the ER - dissection of COPI-cargo interactions.* 26.01.2017

Dr. Zbiginiew Warkocki (Institute for Biochemistry and Biophysics PAS, Warsaw, Poland) *Role of terminal uridyltransferases (TUTs) in RNA expression and function in humans.* 02.02.2017

Dr. Radosław Pluta (IIMCB, Poland) *MobM relaxase of the HUH nucleases family: a novel histidine/metal-dependent DNA nicking/joining mechanism for gene transfer and antibiotic resistance spread.* 09.02.2017

Dr. Rafal Mostowy (School of Public Health, Imperial College London, UK) *How evolution shapes diversity of polysaccharide capsules in gram-positive and gram-negative bacteria.* 16.02.2017

Prof. Paweł Brzuzan (The University of Warmia and Mazury in Olsztyn, Poland) *MicroRNAs in microcystin induced liver injury (hepatotoxicity) in fish: from pathways to functions to therapies.* 23.02.2017

Dr. Szymon Świeżewski (Institute of Biochemistry and Biophysics PAS, Warsaw, Poland) *Making sense of antisense.* 02.03.2017

Dr. Anna Sarnowska (Stem Cell Bioengineering Unit, Mossakowski Medical Research Centre PAS, Warsaw, Poland) *Clinical application of freshly isolated adipose derived regenerative cells (ADRC).* 09.03.2017

Dr. Rafał Czajkowski (Nencki Institute of Experimental Biology PAS, Warsaw, Poland) *Neural correlates of socially transferred emotions.* 16.03.2017

Dr. Habil. Ewelina Knapska (Nencki Institute of Experimental Biology, PAS, Warsaw, Poland) *Neural correlates of socially transferred emotions*. 23.03.2017

Dr. Bartek Wilczynski (Institute of Informatics, University of Warsaw, Poland) *Finding regulatory domains and their contacts in Hi-C data.* 30.03.2017

Dr. Jan Kosinski (EMBL, Heidelberg, Germany) *Structure of the human nuclear pore complex by integrative structure determination.* 06.04.2017

Dr. Frédéric Pontvianne (CNRS, Laboratoire Génome et Développement des Plantes, Perpignan, France) *Role of the nucleolus in A. thaliana genome organization.* 07.04.2017

Dr. Joanna Sulkowska (Centre of New Technology CENT I, Warsaw, Poland), Interdisciplinary Laboratory of Biological Systems Modelling) *New type of entanglement in proteins and possible role of knotted topology: Methyl Transfer by Substrate Signaling from a Knotted Protein Fold.* 13.04.2017

Professor Javier F. Caceres (Institute of Genetics and Molecular Medicine IGMM, University of Edinburgh, Western General Hospital, Edinburgh, UK) *Biogenesis and turnover of small RNAs in health and disease.* 20.04.2017

Dr. Stephanie Kermorgant (Barts Cancer Institute - a CR-UK Centre of Excellence, Queen Mary University of London, UK) *How and why a membrane receptor signals inside cancer cells: example of c-Met.* 27.04.2017

Prof. Magda Konarska (Centre for New Technologies, Warsaw University, Poland) *Spliceosome function in the age of cryo-EM structures.* 11.05.2017

Prof. Israel Sekler (Ben-Gurion University of the Negev, Beer Sheva, Israel) *Control and regulation of mitochondrial metabolism and Ca2+ signaling.* 18.05.2017

Prof. Karin Krupinska (Botanisches Institut, Christian-Albrechts-Universität zu Kiel, Kiel, Germany) *Functional implications of WHIRLY1-dependent chromatin modelling in monocot chloroplasts.* 19.05.2017

Prof. Katarzyna Turnau (Institute of Environmental Sciences, Malopolska Centre of Biotechnology, Jagiellonian University, Cracow, Poland) *Intimate relationships between plants, fungi and animals.* 25.05.2017

Prof. Magdalena Król (Warsaw University of Life Sciences, Warsaw, Poland) *MDC: Macrophage-Drug Conjugate as a Trojan horse approach against cancer.* 31.05.2017

Prof. Kathrin Thedieck (University Medical Center Groningen, AV Groningen, The Netherlands & Carl von Ossietzky University Oldenburg, Oldenburg, Germany) *Systems approaches to the mTOR network.* 05.06.2017

Dr. Kristian M. Rother (Academis, Berlin, Germany) *Best Practices for Debugging, Testing and Maintaining Software.* 28.07.2017

Dr. Lucyna Budźko (Institute of Bioorganic Chemistry, PAS, Poznań, Poland) *Activation-induced cytidine deaminase: structural determinants of its activity on modified and non-modified substrates.* 28.08.2017

Dr. Stanislaw K. Jozwiakowski (University of Zurich, Institute of Molecular Cancer Research, Zurich, Switzerland) *PrimPol – Ancient Guardian of the Genome.* 04.09.2017

Prof. Jonathan Heddle (Malopolska Centre of Biotechnology, Jagiellonian University, Cracow, Poland) *Caged Biology: Building nanometric containers with biological molecules.* 07.09.2017

Dr. Lukasz Kielpinski (Roche Pharma Research and Early Development, Copenhagen, Denmark) *RNase H sequence preferences influence antisense oligonucleotide efficiency and have shaped the HIV-1 genome.* 10.09.2017

Prof. Eric Westhof (University of Strasbourg, Strasbourg, France) *The Third Genetic Code.* 05.10.2017

Alessandro Costa (The Francis Crick Institute, London, UK) *Cryo-EM approaches to understanding the eukaryotic replisome.* 05.10.2017

Dr. Kris Kobielak (Centre of New Technologies University of Warsaw, Poland) *Coexistence of Variety of Skin Stem Cells in Tissue Specific Homeostasis and Regeneration.* 12.10.2017

Prof. Ichiro Yamashita (Graduate School of Engineering Osaka University, Ibaraki, Japan) *Biological Path to Nanodevices.* 19.10.2017

Prof. Matthias Bochtler (IIMCB & Institute of Biochemistry and Biophysics, Warsaw, Poland) *The Q-rule for posttranslational modification.* 26.10.2017

Dr. Punit Seth (Ionis Pharmaceuticals, Carlsbad, USA) *Engineering selectivity into therapeutic oligonucleotides through chemical design.* 09.11.2017

Dr. Tomasz Rzymski (Head of Targeted Therapeutics Platform Selvita S.A., Cracow, Poland) *Novel therapeutic strategies based on the concept of synthetic lethality.* 16.11.2017

Dr. Francesca Vinchi (University of Heidelberg and EMBL, Germany LFKRI, New York Blood Centre, New York, USA) *Iron restriction strategies ameliorate iron-aggravated atherosclerosis.* 23.11.2017

Dr. Devrim Kilinc (Institut Pasteur de Lille, France) *Microfluidic Neuron Culture Devices to Study Neural Development and Disease.* 29.11.2017

Dr. Małgorzata Zakrzewska (Faculty of Biotechnology, University of Wrocław, Poland) *The double life of FGF1.* 30.11.2017

Prof. Vladimir Korzh (IIMCB, Poland) *The empty-headed guide into hollow brains.* 14.12.2017

Patrick Shaw Stewart (Douglas Instruments Ltd, Hungerford, UK) *How new strategies can improve productivity in crystallization and cryoEM.* 21.12.2017

Dr. Aleksandra Walczak (Laboratoire de Physique Théorique Ecole Normale Supérieure Paris, France) *Diversity and predictability in immune repertoires.* 22.12.2017

Annual Report Session, June 9, 2017, Białobrzegi, Poland

Jan Brezovsky, Laboratory of Biomolecular Interactions and Transport UAM/IIMCB ***Ligand-transport pathways in proteins: Molecular functions & pathologies***
Magdalena Banach- Orłowska, Laboratory of Cell Biology ***Crosstalk between endocytosis and signaling: biology of lymphotoxin β receptor***
Karolina Górecka, Laboratory of Protein Structure ***RuvC resolvase: from structure to mechanism of action***
Elżbieta Jagielska, Aurezyna Project ***Auresine, new antistaphylococcal agent - from structure to product***
Filip Maciąg, Laboratory of Neurodegeneration ***Exploring new roles of SOCE proteins in neurons by electrophysiology***
Marcin Magnus, Laboratory of Bioinformatics and Protein Engineering ***RNA 3D Structure Prediction Using Multiple Sequence Alignment Information***
Michał Pawlak, Laboratory of Zebrafish Developmental Genomics ***Genomic approaches to understanding heart development in zebrafish***
Anna Piasecka, Laboratory of Structural Biology ***The Y. bercovieri Anbu crystal structure sheds light on the evolution of highly (pseudo)symmetric multimers***
Maria Śladowska, Laboratory of Mitochondrial Biogenesis ***Disruption of mitochondrial import machinery and its beneficial effects in Caenorhabditis elegans***
Aleksandra Tempes, Laboratory of Molecular and Cellular Neurobiology ***Regulation of molecular motor – adaptor interaction: a new role for mTOR kinase***
Katarzyna Mleczko-Sanecka, Laboratory of Iron Homeostasis ***Insights into iron sensing and iron uptake***
Jacek Kuźnicki, Conclusions, Institute's matters, discussion


SUPPORTING
YOUNG
SCIENTISTS

Supporting Young Scientists

IIMCB has continued its **doctoral program** in partnership with other institutions of the Ochota Campus. Currently, 40 PhD students are enrolled in the doctoral programs of the three Warsaw research institutes: Institute of Biochemistry and Biophysics PAS (25), Nencki Institute of Experimental Biology PAS (11), and Medical University of Warsaw (4).

PhD students at IIMCB self-organize a **PhD Students Council**, with **Małgorzata Maksymowicz** and **Gabriela Jędruszewska** as representatives. The Council functions as a bridge of communication between PhD students, Laboratory Leaders, and Directors. Moreover, it organizes meetings and integration events within the institute and with other scientific institutions. During the last year, three PhD sessions were held at IIMCB. Each session comprised 10 presentations from PhD students, representing different laboratories.

Postdocs similarly self-organize a **Postdoctoral Council**, with **Joanna Krwawicz** and **Małgorzata Figiel** as representatives. Their meetings are devoted to presenting the personal experiences of young scientists.

In January 2017, the PhD Student and Postdoctoral Councils organized **Career Path Day**. More than 80 young researchers participated in the event, the goal of which was to foster the personal development of scientists and support them in shaping their career development. They had an opportunity to listen and talk to professionals from academia, pharma, clinical trials, start-up companies, consulting firms, patent attorney offices, and scientific support institutions.

At the turn of March and April 2017, both Councils and the Institute of Pharmacology PAS from Cracow organized the "**Interdisciplinary Junior Scientific Workshop on Neuropharmacology and Molecular Biology**" in Białka Tatrzańska, Poland. During this 3-day meeting, young scientists and students presented and discussed their data in four oral sessions and a poster session. Opening lectures were given by Prof. Władysław Lasoń (Institute of Pharmacology) and Michał Pawlak (IIMCB).

IIMCB PhD students also attended the ceremony of the **Opening of the Academic Year 2017/2018**, which was organized by the Mossakowski Medical Research Center PAS. The official opening ceremony was followed by a poster session for all PhD students from Biocentrum Ochota. Because the Council wanted to integrate students from the Institute, various informal meetings were also organized, which allowed the Council to address students' concerns.

Scholarships for outstanding young scientists from the Ministry of Science and Higher Education

Scholarships for remarkably talented young scientists are granted by the Minister each year, based on a competitive application submission process. The scholarships are awarded to scientists who are younger than 35, conduct high-quality research, and have impressive scientific achievements in different disciplines. The areas that are evaluated include scientific achievements of the candidate, the level of research, awards, and participation in international projects. Young scientists themselves decide how to allocate funds that are awarded in the scholarship. In 2017, three postdoctoral fellows from the Institute were laureates for this prestigious competition:

- **Jarosław Cendrowski** (Laboratory of Cell Biology): 194 040 PLN
- **Leszek Pryszcz** (Laboratory of Zebrafish Developmental Genomics): 194 040 PLN
- **Katarzyna Chojnacka** (Laboratory of Mitochondrial Biogenesis, relocated to CeNT): 194 040 PLN

Theses defended in 2017

- **Magdalena Machnicka, *Characterization of post-transcriptional RNA modification pathways*,** advisor: **J.M. Bujnicki**, 17.01.2017
- **Mirosław Śmietański, *Structural characteristics of human CMTr1 methyltransferase acting on the 5' end of RNA polymerase II synthesis products*,** advisor: **M. Nowotny**, 11.04.2017
- **Anna Jaworska, *Investigation of cellular processes involved in Alzheimer's disease: gamma- secretase activity and calcium homeostasis maintenance*,** advisor: **J. Kuźnicki**, 30.05.2017
- **Marcin Magnus, *Development of computational tools for RNA tertiary structure prediction*,** advisor: **J.M. Bujnicki**, 24.10.2017
- **Magdalena Pruszko, *Oncogenic activities of mutated TP53 in alternative splicing of vascular endothelial growth factor A*,** advisor: **A. Żylicz**, 12.12.2017
- **Krzysztof Szczepaniak, *Sequence design as a tool for studying proteins and nucleic acids*,** advisor: **J.M. Bujnicki**, 14.12.2017

All PhD dissertations were held at the Institute of Biochemistry and Biophysics PAS.

Training for Talented Youth

On March 6-10, 2017, IIMCB co-organized with the Polish Children's Fund special training in molecular biology for talented youth. On the first day, 30 young people had the opportunity to learn and see how the work at the Institute looks like. During the following days, four talented teenagers participated in the following activities:

- *Purification of Cas9 nuclease and its use for genomic engineering: genotyping using enzymatic and physicochemical techniques*, Laboratory of Structural Biology, Małgorzata Perycz, Joanna Krwawicz, and Marlena Kisiała
- *Purification and testing of the activity of selected proteases*, Laboratory of Protein Structure, Elżbieta Nowak and Mariusz Czarnocki-Cieciura
- *Basic techniques of molecular biology*, Laboratory of Cell Biology, Agata Poświata and Lidia Wolińska-Nizioł
- *How gene editing can discover new mechanisms that regulate iron levels in the body*, Laboratory of Iron Homeostasis, Katarzyna Mleczko-Sanecka and Gabriela Jędruszewska

Internship program at IIMCB

In 2017, within the innovative MatchBeta career planning platform, IIMCB as the only scientific institution in Poland funded six paid internships at the institute:

- 3 internships, Laboratory of Zebrafish Developmental Genomics Max Planck/IIMCB Research Group
- 2 internships, Laboratory of Protein Structure
- 1 internship, Auresine Project

Do Science!

(http://doscience.iimcb.gov.pl/) is an informal science club that was formed by PhD students and postdocs from IIMCB and is maintained by young scientists of the Biocentrum Ochota Campus. The Do Science! team seeks to create an opportunity for young scientists to meet, discuss, and learn from the most successful scientists from Poland and abroad in an informal atmosphere where lectures are followed by a short career advice session and a long discussion in a relaxed setting.

In 2017 Do Science! organized the following meetings

31/1/2018

Duncan Smith, New York University, USA

From a reductionist analysis of the spliceosome to a global view of DNA replication

Duncan Smith is a former PhD student of Prof. Magda Konarska and now an Assistant Professor of Biology at NYU. His areas of research include mechanisms and regulation of DNA replication, epigenetics, and RNA processing. Duncan was extremely successful in pursuing his PhD with Prof. Konarska at The Rockefeller University and had an outstanding postdoctoral fellowship on DNA replication in the Iestyn Whitehouse laboratory. During the last 4 years, Duncan has been a Principal Investigator at NYU, expanding his postdoctoral research. He has already made important discoveries with regard to lagging strand synthesis during eukaryotic DNA replication.

26/11/2017

Bogumił Kaczkowski, RIKEN, Yokohama Institute, Japan

Integrative Analyses of Transcriptomic and Epigenomic Data in Cancer Research

Bogumił is a postdoc in Piero Carninci's Genome Information Analysis Team at RIKEN, Yokohama. During our Do Science! Club, he gave a talk on transcriptome profiling in cancer research.

28/09/2017

Dominika Nowis, Centre of New Technologies, University of Warsaw, Poland

The role of arginase-1 in antitumor immune response

Dominika Nowis graduated from medicine at the Medical University of Warsaw and defended her PhD thesis 2 years later. She did her postdoc in the Laboratory of Cell Biology, Indiana University School of Medicine, Evansville, and was an Associate Professor in the Department of Immunology, Medical University of Warsaw. Her main focus is immunotherapy, specifically the role of arginase-1 in the antitumor immune response. Her group also identifies and validates other novel molecular targets for anti-cancer therapies, such as stimulator of interferon genes (STING), glutamine metabolism in plasma cell myeloma, and MLK4 amplification in breast cancer.

20/06/2017

Andrzej Wierzbicki, University of Michigan, USA

Gene regulation by long non-coding RNA

Andrzej Wierzbicki is interested in determining the molecular mechanisms of RNA-mediated transcriptional silencing, which in plants is known as RNA-directed DNA methylation. The long-term objective of Prof Wierzbicki's laboratory is to understand the molecular mechanisms of genome control, especially the roles of ncRNAs and the ways in which they affect the organization of DNA into chromatin. They use plant model systems and an array of genetic, biochemical, and genomic tools to investigate the ways in which ncRNAs

01/06/2017

Jordan Ramilowski, RIKEN, Yokohama Institute, Japan

Functional characterizations of long non-coding RNAs: turning "junk" into a treasure trove

Jordan Ramilowski's research focuses on cell-cell communication, mammalian transcriptional networks, and functional annotations of long non-coding RNAs (lncRNAs). In his talk, he mainly focused on the importance of lncRNA research and presented exciting developments and challenges in the field. He also briefly mentioned current efforts of the FANTOM consortium to further functionally characterize lncRNAs. Jordan also shared some of his perspectives on the ways in which biological sciences differ from physical sciences and the ways in which science in general is approached in particular countries, such as Japan and the United States.

01/05/2017

Walter Chazin, Vanderbilt University, USA

Mechanisms for counting and handoff by human DNA primase: a role for the 4Fe-4S

Walter Chazin is a Chancellor Professor of Biochemistry and Chemistry and Ingram Professor of Cancer Research in the Department of Chemistry at Vanderbilt University, Nashville, Tennessee, USA. His group uses a wide range of techniques, including NMR spectroscopy, X-ray crystallography, calorimetry, fluorescence spectroscopy, and X-ray scattering. He has very broad scientific interests, including DNA replication, Ca2+ metabolism, and protein homeostasis. In his talk, he presented a unique signaling mechanism during DNA replication, in which a change in oxidation state of the [4Fe4S] cluster acts as a switch for the DNA binding of human DNA primase.

06/04/2017

Jan Kosiński, EMBL Heidelberg, Germany

Solving 3D puzzles in nuclear transport, translation, and transcription

Jan is a structural biologist in the European Molecular Biology Laboratory (EMBL), Heidelberg. He studied at the University of Warsaw and did his PhD at IIMCB. He then moved abroad for his postdoc, first in Italy at Sapienza University in Rome and then in Germany at the EMBL in Heidelberg. In September 2017, he started his own research group at the EMBL and CSSB institutes in Hamburg. In his recent research, he made significant contributions to developing and applying methods for integrative structural modeling. His work has been published in such journals as Nature, Science, and Nature Methods. He built a near-atomic model of one of the largest complexes in the cell: the human nuclear pore complex. His visit to IIMCB was a sentimental trip to a place where his passion for science was sparked.

06/03/2017

Bartek Wilczyński, University of Warsaw, Poland

Computation as a tool for studying chromosomes

Bartek Wilczyński is a Group Leader at the Institute of Informatics, University of Warsaw. He did his PhD in Mathematics at the Institute of Mathematics of the Polish Academy of Sciences. After his PhD, he became a postdoc in Eileen's Furlong laboratory at the EMBL in Heidelberg where he studied gene regulatory networks during Drosophila development. He then returned to Poland where he became an Assistant Professor at the University of Warsaw. Bartek and his group apply computational methods to study chromatin state dynamics in transcription regulation, model gene regulatory networks, and analyze regulatory sequences.

06/03/2017

Tamara Hendrickson, Wayne State University, USA

Non-canonical mechanisms to aminoacylate t-RNA

Tamara Hendrickson is an Associate Professor at Wayne State University. Her research focuses on two main projects: (1) glycosylphosphatidylinositol membrane anchoring of proteins and (2) indirect tRNA aminoacylation pathways, particularly in Helicobacter pylori. During her talk, she focused on the second project where she and her group investigate the indirect biosynthesis of Gln-tRNAGln and Asn-tRNAAsn in the pathogenic bacterium H. pylori. They are interested in understanding the evolution of direct vs. indirect tRNA aminoacylation pathways and the mechanisms that are used by H. pylori to prevent misacylated tRNAs from entering the ribosome prior to conversion to their accurately aminoacylated counterparts.

26/01/2017

Paweł Grzesiowski, Centre of Preventive Medicine and Rehabilitation, Warsaw, Poland

Protective vaccination

Paweł Grzesiowski, MD, is the initiator of the introduction of methods for the transplantation of intestinal microbiota. Along with Dr. Adam Hermann and a team of colleagues, he developed transplantation methodology and performed the first clinical procedures in Poland. Dr. Grzesiowski is a founder of the Centre for Research and Transplantation of Intestinal Microbiota at the Centre of Preventive Medicine and Rehabilitation in Warsaw. Dr. Grzesiowski's lecture mainly focused on the current state of protective vaccinations and new developments in the field.

In previous years, Do Science! organized meetings with the following individuals:

- **Three Nobel Prize laureates:** V. Ramakrishnan, B. Kobilka, and R. Huber
- **International scientists:** G. Schatz, I. Braakman, F. Perez, V. Šiksnys, A. Tramontano, B. Stoddard, X. Cheng, V. Nagaraja, N.D. Rao, J. Sponer, S. McKenna, G. Bussi, W. Galej, P. Sicinski, J. Nelson, B. Marzluff, T. Gabaldon
- **Polish scientists:** M. Konarska, S. Swieżewski, L. Kaczmarek, M. Żylicz, M. Nowotny, A. Udalski, J. Kufel, J. Trylska, A. Dziembowski, W. Bogdanowicz, M. Komorowski, T. Prószyński, P. Niewiadomski, M. Górna, E. Knapska, P. Golik

Our initiatives have been supported by IIMCB, EMBO, Biocentrum Ochota, RNA Society, Eppendorf, VitaInSilica, and Sigma-Aldrich.

The Do Science! team also manages the **Do Science! SciEvents calendar** that aggregates all scientific events that are held on the campus and the newsletter that is sent every week.

RNA Club Warsaw

In 2016, a spin-off of Do Science! was born at IIMCB: the RNA Club Warsaw (http://rnaclub.iimcb.gov.pl/). The RNA Club Warsaw is modeled after other RNA Clubs around the world. The aim of the RNA Club Warsaw initiative for 2017/2018 is to make our meetings more frequent, more intense, and more dedicated to the needs of junior scientists. We want to continue to enhance scientific discussions and inspire future collaborations between groups and institutions. The RNA Club Warsaw seeks to connect various aspects of RNA research, foster collaborations, and guide junior researchers in their careers in the exciting world of RNA. This year, once again, the club was selected by the RNA Salon Selection Committee (RNA Society) to receive a $1,000 USD grant to support our activities.

We organized six meetings so far with the following presenters:

Academic year 2017/2018

- RNA Club meets #NGSchool (Workshop), 08.02.2018
  Maciej Łapiński (Introduction to Linux, IIMCB), Leszek Pryszcz (Introduction to Bioinformatics and NGS, IIMCB)
- RNA Club I 2017/2018, 22.01.2018
  Grzegorz Brzyżek (IBB), Zbigniew Pietras (IBB), Radosław Pluta (IIMCB), Marcin Równicki (CeNT), Adam Mamot (CeNT)
- Prof. Eric Westhof (RNA Club Warsaw Keynote 2017), 05.10.2017

Academic year 2016/2017

- **RNA Club II 2016/2017, 13.03.2017**
  Joanna Kufel (UW), Szymon Świeżewski (IBB), Andrzej Dziembowski (IBB), Maria Górna (UW), Sebastian Glatt (MCB)
- **RNA Club I 2016/2017, 29.11.2016**
  Janusz Bujnicki (IIMCB), Joanna Trylska (CeNT), Magdalena Boguta (IBB), Cecilia Winata (IIMCB), Marcin Nowotny (IIMCB)
- **RNA Club Warsaw Kickoff meeting, 17.06.2016**
  Paweł Piątkowski (Bujnicki Lab), Tomasz Kuliński (Dziembowski Lab), Halina Fedak (Świeżewski Lab), Aleksandra Kwaśnik (Kufel Lab), Marta Jarczewska (Malinowska Lab)


EDUCATION

Centre for Innovative Bioscience Education (BioCEN)

Head

Jacek Patryn (until April 2018)
Patrycja Dołowy, PhD (since April 2018)

Project Manager

Aleksandra Kot-Horodyńska

Laboratory Manager

Karolina Więcek (until September 2017)

Coordinators

Karolina Kurzela (maternity leave)
Zuzanna Sobańska

The Centre for Innovative Bioscience Education (BioCEN)—currently located at Grójecka 93 in the 21st Kołłątaj High School building - was established in 2002 by enthusiastic students and young scientists who recognized the importance of popularizing science among the broader community. Since that time, BioCEN has been continuously working to achieve this goal by organizing and carrying out educational activities, such as laboratory workshops for primary, junior high, and high school students, practical courses for school teachers, scientific training for businesses, open lectures for broader audiences, scientific shows, and picnics for kids, etc. BioCEN could not continue its mission without financial support from the International Institute of Molecular and Cell Biology, which has been BioCEN's Strategic Sponsor since 2015. In addition to IIMCB's generosity support, BioCEN is also subsidized by the Nencki Institute of Experimental Biology Polish Academy of Sciences, Institute of Biochemistry and Biophysics Polish Academy of Sciences, University of Warsaw Faculty of Biology, and BioEducation Foundation.

Workshops

BioCEN workshops appear to be a remedy for a weakness of the Polish education system, namely an insufficient focus on practical and experimental approaches in the area of life sciences. Therefore, our goal is to cover several scientifically and educationally important topics, such as molecular and cellular biology, histology, immunology, biochemistry, biotechnology, plant physiology, bionics/bioengineering, and medical sciences. We encourage participating students to take advantage of their creativity while working individually on real-life experiments. This is advantageous because workshops at BioCEN for most students are the only opportunity to perform laboratory work on their own. Notably, over the last 17 years, more than 34,000 students have had the chance to take advantage of the workshops that are offered by BioCEN.

According to ongoing reform of the education system in Poland, we began to modify our education to the new reality, in which junior high schools are being shut down while elementary schools are being extended to the 8th grade. We introduced four

new workshops for elementary schools that are related to fundamental biophysical phenomena (e.g., surface tension, material densities, non-Newtonian fluid, and vision with regard to basic optics). We also introduced one new class for the new elementary school 7th and 8th grades, with a main focus on plant physiology.

We also launched "Histology, Embryology, and Stem Cells" the most sophisticated, advanced, and manually demanding laboratory workshop for high school students offered by BioCEN to date. This class covers the latest achievements in cancer research, regenerative medicine, stem cells, and applied embryology. It is dedicated to select groups of students who seek to continue their education in medicine, medical sciences, and molecular biology.

Workshops at BioCEN are divided into three main categories, based on the age of the participating students.

High School

- Histology, embryology, and stem cells
- Sentenced in accordance with the law of DNA
- Cellular superstructures
- Synergy: the inner life of cells
- Miracles of biotechnology: purification of jellyfish protein from bacteria
- Explore your own DNA: examining DNA by PCR methods
- Protein fingerprints of different tissues
- Biotechnology of antibodies in clinical practice
- Protozoa as model organisms

Junior High / New Elementary School 7th and 8th Grades

- Yeast: a living micro-factory
- On the trail of DNA
- Do you know what you eat?
- Enzymes
- Secrets of photosynthesis

Elementary School

- Green sugar factories: how photosynthesis works
- What sticks and what floats?
- How colors are made
- The world of colors
- The world of substances
- See DNA
- Acidic or nonacidic?
- Secrets of food
- Secrets of fluorescence
- How much sugar do plants contain?

Because of the location of BioCEN, access is somewhat limited to students who live outside Warsaw. As such, the BioCEN team is ready to organize and implement laboratory workshops outside its headquarters. We believe this move will be an effective way to increase life sciences awareness and scientific skills among a wider population and thus will be an important component of our program.

International cooperation

Workshops for Minor Academy of Science of Ukraine and European Minor Academy of Sciences

BioCEN is available for various collaborations with both domestic and international partners. In July 2017, we co-organized, together with the Minor Academy of Science of Ukraine, European Minor Academy of Sciences, and International Institute of Molecular and Cell Biology in Warsaw, an international scientific summer school for young, talented students from Ukraine. We organized and held a series of six laboratory workshops for a group of 30 high school students and two laboratory workshops for a group of 28 elementary school students. All of the experimental lessons were held in the BioCEN laboratory at Grójecka 93.

Professional training for school teachers

Comprehensive laboratory course for teachers from the Dolnośląskie Voivodship

One of our main goals is to improve the teaching skills of science educators who work at all levels of education: primary school, junior high school, and high school. In 2017, BioCEN was involved in an extended educational project that was aimed at school teachers from three different counties (Kamiennogórski, Jaworski, and Wałbrzyski) of Dolnośląskie Vioivodship. The entire venture was conducted from February 2017 to the end of November 2017 and involved more than 20 teachers who had an exceptional opportunity to learn new experimental skills that can be applied in their regular teaching activities. Moreover, all of the participating teachers were shown how to perform relatively simple and inexpensive scientific experiments that can be performed under non-laboratory conditions. Finally, the BioCEN team demonstrated the educational effectiveness of the experimental approach by performing a series of scientific demonstration classes, which involved over 160 students from several schools from Kamieniogórski, Jaworski, and Wałbrzyski counties.

16th Educational Symposium for Biology Teachers

This symposium has become one of our most important events. The most recent symposium was held on Saturday, December 9, 2017. During this meeting, biology teachers from all over Poland had the opportunity to receive up-to-date information on frontline discoveries in neuroscience and become more familiar with cutting-edge studies, such as those that were related to the Nobel prizes in Chemistry and Medicine. Moreover, teachers have a unique opportunity to talk to academic researchers in person and create social networks, which has a positive impact on the quality of their teaching.

Professional training for business

In 2017, BioCEN continued its cooperation with Nutricia Polska by organizing, preparing, and carrying out new laboratory training that is dedicated to a group of Nutricia employees. The "Sugar" course was held in September 2017 and focused mostly on the role of carbohydrates in human metabolism and physiology. During the training, all of the participants could perform experimental tasks individually, analyze the results, and draw final conclusions.

Experimental kits and other scientific tools

For those who are unable to take advantage of our workshops, regardless of circumstances, we have alternative options. BioCEN produces laboratory kits that are commercially available through our website. All of the kits come with the necessary chemicals, dishes, tubes, theoretical summaries, instructions, and protocols that are needed by students to perform a particular experiment either at school or at home.

To date, the following experimental kits are available:

- We are studying DNA
- The sweet world of enzymes
- Photosynthetic dyes
- A necklace with your own DNA

We also emphasize the notion of "learning while playing." As such, we also produce high-quality, genuine BioCEN educational board games:

- By the trails of evolution
- Dare to assemble your cell

Events

21st Festival of Science

As in previous years, BioCEN participated in the 21st Festival of Science, but it was the first time that BioCEN co-organized scientific shows at the Physics Department, University of Warsaw. Thus, we prepared and held three 90-minute scientific shows entitled, "In the glow of life: the role of light and colors in living organisms."

4th Educational Picnic in Mikołajki

The 4th Educational Picnic in Mikołajki was co-organized by BioCEN and the Nencki Institute of Experimental Biology and took place at the Hydrobiology Research Station in Mikołajki. This event was an exceptional opportunity for students from local schools to perform laboratory experiments and exercises that normally cannot be performed as part of their daily education.

BioCEN animators and co-workers

Important members of the BioCEN team include animators and coworkers without whom the educational activities would not be possible. In 2017, the following individuals collaborated with BioCEN in this capacity: Kryspin Andrzejewski, Paulina Brodacka, Aleksandra Fesiuk, Maciej Grochowski, Andrzej Gruza, Piotr Horodyński, Weronika Iwaniuk, Joanna Jabłońska, Monika Jakubiak, Katarzyna Jędrzejowska, Agnieszka Kamińska, Magdalena Karpińska, Maciej Kotliński, Katarzyna Krzyczmonik, Maciej Lirski, Katarzyna Łepeta, Michał Niziołek, Michał Oziębło, Martyna Poprzeczko, Kamil Synoradzki, Barbara Świerczek and Michał Wielądek.

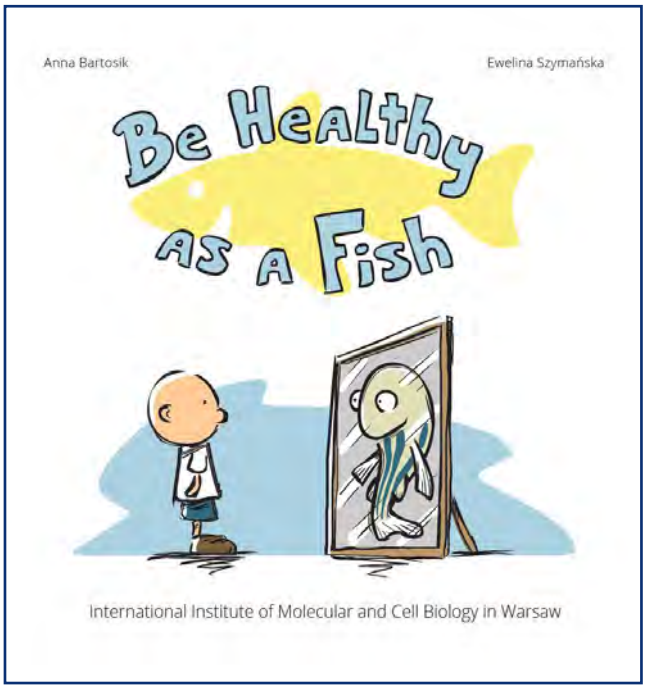
Be Healthy as a Fish educational campaign

Be Healthy as a Fish workshops

The purpose of the *Be Healthy as a Fish* educational program is to **educate children about how zebrafish can be used as a model organism** to help scientists understand the way the human body works. The ***Be Healthy as a Fish* workshops** are introduced to primary school students, together with two kinds of materials under the same title: a **book** and a short animated **movie**. The program focuses on the field of biology in a way that complements the children's classroom curriculum and encourages them to broaden their interest in biology in the future. To maximize accessibility of the learning resources, the *Be Healthy as a Fish* book and movie are available online (both in Polish and English).

Be Healthy as a Fish book

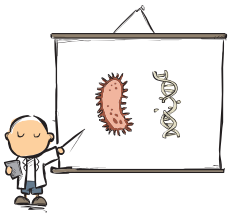
The book brings the complex world of science closer to young readers. Because the book is intended for primary school children with elementary knowledge of the life sciences, it is illustrated with cartoons to make the content more interesting for a young audience. Moreover, to help readers absorb the story's message, the book provides engaging assignments. A short glossary defines terms that are used in the book that may be difficult for some readers to understand. Importantly, the factual content was created in consultation with an educational biology expert to ensure that the message of the story is both understandable and inspiring for a young audience. The book is distributed to all of the participants of the *Be Healthy as a Fish* workshops as an invitation to broaden their knowledge beyond the issues that are discussed in their classes.



Be Healthy as a Fish movie

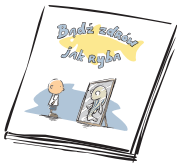
The aim of the movie is to familiarize viewers with IIMCB's facilities and scientific interests and show what scientists' everyday work lives look like. This 6-min movie is mostly animated. However, part of it shows real images of various locations within the institute (e.g., laboratories, fish facility, office of the Director of IIMCB, and a lecture hall where the workshops take place). The storyline of the animation consists of a humorous tour around the institute that is guided by two cartoon characters: the Professor and a zebrafish. During the tour, the children are told the reason why the zebrafish facility was established, and they can witness the formation of a new international team of scientists. The viewers are informed that science has no borders, and new discoveries result from the joint efforts of scientists around the word who exchange information during seminars and conferences. Both Polish and English versions of the movie are available on the IIMCB YouTube channel.

Be Healthy as a Fish in numbers



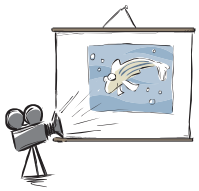
Workshops:
810 participants

+



Book:
2700 downloads

+



Movie: **4300 views and 1450 downloads**

Achievements

Presentation at the 9th European Zebrafish Meeting in Oslo, Norway	Poster prize at the 6th European Forum for Marketing of Scientific and Research Organizations in Warsaw, Poland	Publication in the Zebrafish journal (Goś et al., Zebrafish. 2016 Aug 1; 13[4]: 266-271)	Presentation at the 7th European Forum for Marketing of Scientific and Research Organizations in Warsaw, Poland
Publication in the Polish Journal of Environmental Sciences "Wszechświat" (No. 10-12, 2016)	Invitation for the co-author of the *Be Healthy as a Fish* educational program to chair the Education Session at the 10th European Zebrafish Meeting in Budapest, Hungary	Organization of the workshops for Ukrainian students as part of the International Biology School in cooperation with the Minor Academy of Sciences of Ukraine	Large interest at the Biologists' Night 2018 at the Faculty of Biology, University of Warsaw


RESEARCH
SUPPORT
UNITS & STAFF

Research Support Units
as of April 2018

Administration

Agnieszka Potęga Administration and Tenders Specialist
Jakub Komorowski Administration Specialist
Daria Goś Senior PR Specialist
Piotr Wiaksa Junior Administration Specialist
Anna Zolnik Deputy Director for Operations
Adam Kucharski Building Maintenance
Dominika Dubicka-Boroch Senior Administration and Organization Specialist
Andrzej Cudny Building Infrastructure Specialist

Grants Office

Agnieszka Faliszewska Project Specialist
Dorota Libiszowska Head
Marcin Ogonowski Vice Head
Agata Skaruz Project Specialist
Justyna Szopa Project Specialist

Scientific Coordination Unit

Agnieszka Kolano Specialist for Science Cooperation
Agnieszka Wagner-Ziemka Senior Expert

Animal Welfare

Piotr Korzeniowski Veterinarian

Financial Unit

Renata Knyziak Accounting Specialist
Monika Nowicka Payroll Specialist
Hanna Iwaniukowicz Deputy Director of Finance / Chief Accountant
Agnieszka Kuna Accounting Specialist
Małgorzata Bytner Accounting Specialist

Human Resources Unit

Monika Domańska-Paśko Junior Human Resources Specialist
Beata Tkacz Senior Human Resources Specialist
Marta Bargielska Human Resources Expert

Technical Support

Agnieszka Olszewska Technician
Alina Zielińska Technician
Iwona Ptasiewicz Technician
Monika Matuszczyk Technician
Wanda Gocal Technician

Staff at IIMCB
(as of March 31, 2018)

Directors

Jacek Kuźnicki	Acting Director	IIMCB
Marcin Nowotny	Deputy Director for Science	IIMCB
Urszula Białek-Wyrzykowska	Deputy Director for Development	IIMCB (3/4)
Anna Zolnik	Deputy Director for Operations	IIMCB
Hanna Iwaniukowicz	Deputy Director for Finance	IIMCB

Laboratory of Structural Biology

Matthias Bochtler	Head	IIMCB
Honorata Czapińska	Senior Scientist	NCN Opus
Humberto Fernandes	Postdoc	Volunteer (IBB PAS)
Anna Fricke	Postdoc	NCN Harmonia
Thomas Fricke	Postdoc	IIMCB
Joanna Krwawicz	Postdoc	NCN Opus
Małgorzata Perycz	Postdoc	IIMCB
Marlena Kisiała	PhD Student	Volunteer
Norbert Osiński	PhD Student	NCN Harmonia
Michał Pastor	PhD Student	Volunteer (IBB PAS)
Dominik Rafalski	PhD Student	IIMCB
Anton Slyvka	PhD Student	NCN Opus
Anna Stroynowska-Czerwińska	PhD Student	NCN Harmonia
Katarzyna Szafran	PhD Student	NCN Opus
Paulina Okafor	Laboratory-Administrative Partner	IIMCB (1/2)

Laboratory of Bioinformatics and Protein Engineering

Janusz M. Bujnicki	Head	IIMCB/FNP Team
Elżbieta Purta	Senior Scientist	IIMCB
Filip Stefaniak	Senior Scientist	FNP Team
Michał Boniecki	Postdoc	NCN Opus
Lucyna Budźko	Postdoc	NCBR PBS
Justyna Czarnecka	Postdoc	NCBR PBS (maternity leave)
Pritha Ghosh	Postdoc	FNP Team
Radosław Pluta	Postdoc	NCBR PBS
Tomasz Wirecki	Postdoc	NCN Opus
Nithin Chandran	Research Associate	IIMCB
Marcin Magnus	Research Associate	NCBR PBS
Astha	PhD Student	NCN Etiuda (fellowship abroad)
Błażej Bagiński	PhD Student	NCN Opus
Pietro Boccaletto	PhD Student	IIMCB
Magdalena Orłowska	PhD Student	FNP Team
Diana Toczydłowska-Socha	PhD Student	NCN Etiuda (fellowship abroad)
Adriana Żyła	PhD Student	NCN Maestro
Agata Bernat	Research Technician	J. Sulkowska's grant at UW
Małgorzata Kurkowska	Research Technician	NCBR PBS
Katarzyna Merdas	Research Technician	NCBR PBS
Ewa Skowronek	Research Technician	FNP Team
Magdalena Sroka	Research Technician	NCBR PBS
Joanna Broniarek	MSc Student	Volunteer
Dharm Skadh Jain	MSc Student	IIMCB

Laboratory of Molecular and Cellular Neurobiology

Jacek Jaworski	Head	IIMCB/NCBR Strategmed
Ewa Liszewska	Senior Scientist	NCBR Strategmed
Matylda Macias	Senior Scientist	IIMCB/EU Epistop (1/2)
Magdalena Błażejczyk	Postdoc	IIMCB/EU Epistop
Agnieszka Brzozowska	Postdoc	NCN Opus
Aleksandra Janusz-Kamińska	Postdoc	NCN Sonata Bis
Bartosz Tarkowski	Postdoc	IIMCB
Michalina Wężyk	Postdoc	NCBR Strategmed
Justyna Zmorzyńska	Postdoc	NCN Sonata
Marcelina Firkowska	Research Assistant & Laboratory-Administrative Partner	IIMCB
Kinga Kuchcińska	Research Assistant	NCBR Strategmed
Katarzyna Rydz	Research Assistant	NCBR Strategmed
Katarzyna Banasiak	Junior Researcher	NCN Sonata
Magdalena Kędra	PhD Student	IIMCB
Katarzyna Kisielewska (Świtoń)	PhD Student	FNP Master/NCN Sonata Bis
Alicja Kościelny	PhD Student	IIMCB
Hadi Mirzapourdelavar	PhD Student	NCN Opus
Aleksandra Tempes	PhD Student	EU Epistop
Jan Węsławski	PhD Student	NCN Opus

Laboratory of Neurodegeneration

Jacek Kuźnicki	Head	IIMCB
Łukasz Majewski	Senior Scientist, Vice Head	IIMCB/NCN Maestro
Magdalena Czeredys	Senior Scientist	IIMCB/NCN Sonata
Joanna Gruszczyńska-Biegała	Senior Scientist	IIMCB/NCN Sonata
Vladimir Korzh	Senior Scientist	IIMCB/NCN Opus
Smijin Karthully Soman	Senior Scientist	IIMCB/NCN Sonata
Małgorzata Wiweger	Senior Scientist	IIMCB
Tomasz Węgierski	Senior Staff Scientist	IIMCB (1/2)
Evgene Gasanov	Postdoc	NCN Opus
Oksana Palchevska	Postdoc	NCN Opus
Michał Bazała	Research Assistant	IIMCB (1/2)
Rishikesh Kumar Gupta	PhD Student	IIMCB
Justyna Jędrychowska	PhD Student	NCN Opus
Filip Maciąg	PhD Student	IIMCBzv
Iga Wasilewska	PhD Student	NCN Opus
Klaudia Strucińska	MSc Student	NCN Sonata

Laboratory of Cell Biology

Marta Miączyńska	Head	IIMCB/FNP Team
Magdalena Banach-Orłowska	Senior Scientist	NCN Opus
Ewelina Szymańska	Senior Scientist	NCN Sonata
Daria Zdżalik-Bielecka	Senior Scientist	NCN Sonata
Jarosław Cendrowski	Postdoc	FNP Homing
Kamil Jastrzębski	Postdoc	FNP Team
Krzysztof Kolmus	Postdoc	FNP Team
Lidia Wolińska-Nizioł	Postdoc	NCN Sonata (maternity leave)
Marta Kaczmarek	PhD Student	FNP Team
Małgorzata Maksymowicz	PhD Student	NCN Opus
Agata Poświata	PhD Student	IIMCB
Karolina Wojciechowska	PhD Student	FNP Team
Michał Mazur	MSc Student	FNP Homing
Małgorzata Świątek	MSc Student	Volunteer/ FNP Homing
Kamila Kozik	BSc Student	NCN Sonata
Paulina Nowak	Internship Student	IIMCB
Patryk Ślusarczyk	Trainee	NCN Sonata
Renata Wyszyńska	Trainee	IIMCB
Paulina Okafor	Laboratory-Administrative Partner	IIMCB (1/2)

Laboratory of Iron Homeostasis

Katarzyna Mleczko-Sanecka	Head	NCN Polonez
Gabriela Jędruszewska	PhD Student	IIMCB
Ewa Mandziak	PhD Student	IIMCB
Dawid Mąkosa	MSc Student	NCN
Marta Niklewicz	Technician	IIMCB (1/2)
Aleksandra Szybińska	Laboratory-Administrative Partner	IIMCB (1/2)

Laboratory of Protein Structure

Marcin Nowotny	Head	IIMCB/ FNP Team
Elżbieta Nowak	Senior Scientist	FNP Team
Mariusz Czarnocki-Cieciura	Postdoc	NCN Symfonia
Małgorzata Figiel	Postdoc	FNP Team
Vineet Gaur	Postdoc	Wellcome Trust
Filip Gołębiowski	Postdoc	FNP Team
Karolina Górecka	Postdoc	Wellcome Trust
Zuzanna Kaczmarska	Postdoc	FNP Team
Zbigniew Pietras	Postdoc	NCN Symfonia
Sebastian Chamera	PhD Student	FNP Team
Marta Gapińska	PhD Student	FNP Team
Deepshikha Malik	PhD Student	IIMCB
Marzena Nowacka	PhD Student	NCN Opus
Michał Rażew	PhD Student	NCN Symfonia/ IIMCB
Justyna Studnicka	Research Technician	IIMCB/NCN Opus
Weronika Zajko	Research Technician	IIMCB
Małgorzata Krysiak	Internship	NCN Symfonia
Aleksandra Szlachcic	Internship	NCN Symfonia
Kinga Adamska	Laboratory-Administrative Partner	IIMCB

Laboratory of Protein Metabolism in Development and Aging

Wojciech Pokrzywa	Head	IIMCB/NCN Opus
Nilesh Shanmugam	Postdoc	NCN Opus
Selene Arno	PhD Student	IIMCB
Aniruddha Das	PhD Student	NCN Opus
Marta Kubań	Technician	IIMCB
Marta Niklewicz	Technician	IIMCB (1/2)
Aleksandra Szybińska	Laboratory-Administrative Partner	IIMCB (1/2)

Laboratory of Zebrafish Developmental Genomic Max Planck/IIMCB Research Group

Cecilia Winata	Head	FNP First Team/IIMCB
Rashid Minhas	Postdoc	NCN Polonez
Katarzyna Nieścierowicz	Postdoc	NCN Sonata
Michał Pawlak	Postdoc	NCN Sonata

Leszek Pryszcz	Postdoc	NCN Polonez
Agata Sulej	Postdoc	FNP First Team
Cristina Navarrete Hernandez	Research Assistant	NCN Polonez
Monika Kamińska	Research Assistant	NCN Polonez (CENTshared project)
Aleksandra Paterek	Research Assistant	NCN Polonez (1/2)
Witold Rybski	Research Assistant	IIMCB
Maciej Łapiński	PhD Student	MNISW Diamond Grant/IIMCB
Maciej Migdał	PhD Student	IIMCB
Karim Abu Nahia	PhD Student	FNP First Team
Sreedevi Sugunan	PhD Student	IIMCB
Angelika Brzozowska	Internship MSc Student	FNP First Team
Aleksandra Matrejek	Internship MSc Student	IIMCB
Eugeniusz Tralle	Internship MSc Student	NCN Opus
Tomasz Obrębski	Internship BSc Student	IIMCB
Alexia Danyłow	Laboratory-Administrative Partner	IIMCB (1/2)

Laboratory of Biomolecular Interactions and Transport AMU/IIMCB

Jan Brezovsky	Head	IIMCB (1/2)
Carlos Eduardo Sequeiros Borja	PhD Student	AMU
Bartłomiej Surpeta	PhD Student	AMU

Aurezyna Project

Izabela Sabała	Head, Senior Scientist	FNP Team Tech (4/5)
Elżbieta Jagielska	Senior Scientist	FNP Team Tech (9/10)
Piotr Małecki	Postdoc	FNP Team Tech
Paweł Mitkowski	PhD Student	FNP Team Tech
Alicja Wysocka	PhD Student	FNP Team Tech
Weronika Augustyniak	Technician	IIMCB

Study on Ageing and Longevity

Małgorzata Mossakowska	Head	IIMCB
Aleksandra Szybalska	Project Specialist	IIMCB

Maestro Project

Maciej Żylicz	Head	IIMCB (1/2)
Bartosz Wawrzynów	Postdoc	Volunteer
Marcin Herok	PhD Student	NCN Maestro
Marta Klimczak	PhD Student	SMM/NCN Maestro

Core Facility

Alicja Żylicz	Head	IIMCB
Roman Szczepanowski	Vice Head	IIMCB (3/4)
Matylda Macias	Senior Staff Scientist	IIMCB (1/2)
Katrzyna Misztal	Senior Staff Scientist	IIMCB
Krzysztof Skowronek	Senior Staff Scientist	IIMCB
Tomasz Węgierski	Senior Staff Scientist	IIMCB (1/2)

Biotech Innovations

Iwona Cymerman	Chief Executive Officer	IIMCB (1/2)

PRO Biostructures

Marcin Nowotny	Chief Scientific Officer	IIMCB/FNP Team
Paweł Kustosz	Chief Executive Officer	IIMCB
Aneta Bartłomiejczak	Research Assistant	IIMCB
Agnieszka Napiórkowska	Research Assistant	IIMCB
Malwina Hyjek	Internship PhD Student	IIMCB

Technical Support

Wanda Gocal	Technician	IIMCB (1/2) (CF)
Monika Matuszczyk	Technician	IIMCB (LCB/LN)
Agnieszka Olszewska	Technician	IIMCB (LBS/ZDGL/ZCF)
Iwona Ptasiewicz	Technician	IIMCB (LPS/LBPE/PRO Biostructures)
Alina Zielińska	Technician	IIMCB (LMCN)

IT Unit

Roman Szczepanowski	Head	IIMCB (1/4)
Łukasz Munio	IT Specialist	IIMCB (1/2)
Jakub Skaruz	IT Specialist	IIMCB
Michał Romiszewski	System Administrator	IIMCB
Tomasz Jarzynka	Computer Administrator	IIMCB (1/2)
Jan Kogut	Computer Administrator	IIMCB (1/2)

Administration

Dominika Dubicka-Boroch	Senior Administration and Organization Specialist	IIMCB
Agnieszka Potęga	Administration and Tenders Specialist	IIMCB
Jakub Komorowski	Administration Specialist	IIMCB
Piotr Wiaksa	Junior Administration Specialist	IIMCB
Andrzej Cudny	Building Infrastructure Specialist	IIMCB
Adam Kucharski	Building Maintenance	IIMCB
Izabela Kwiatkowska	Archive Specialist	IIMCB
Dudzin Magdalena	HS Specialist	IIMCB (1/4)

PR Unit

Daria Goś	Senior PR Specialist	IIMCB

Grants Office

Dorota Wasiak-Libiszowska	Head	IIMCB
Marcin Ogonowski	Vice Head	IIMCB
Agnieszka Faliszewska	Project Specialist	IIMCB
Katarzyna Nakielska	Project Specialist	IIMCB (maternity leave)
Agata Skaruz	Project Specialist	IIMCB
Justyna Szopa	Project Specialist	IIMCB

Scientific Coordination Unit

Agnieszka Wagner-Ziemka	Senior Expert	IIMCB
Agnieszka Kolano	Specialist for Science Cooperation	IIMCB

Financial Unit

Monika Nowicka	Payroll Specialist	IIMCB
Małgorzata Bytner	Accounting Specialist	IIMCB
Renata Knyziak	Accounting Specialist	IIMCB
Agnieszka Kuna	Accounting Specialist	IIMCB

Human Resources Unit

Beata Tkacz	Senior Human Resources Specialist	IIMCB
Marta Bargielska	Human Resources Expert	IIMCB (1/2)
Monika Domańska-Paśko	Junior Human Resources Specialist	IIMCB

Centre for Innovative Bioscience Education (BioCEN)

Jacek Patryn	Head	IIMCB (3/4)
Karolina Kurzela	Coordinator	IIMCB (3/4) (maternity leave)
Zuzanna Sobańska	Coordinator	IIMCB (3/4)
Aleksandra Kot-Horodyńska	Project Manager	Volunteer

Contents

The beginning of the Institute...

Paris, May 26, 1995: Prof. F. Mayor, Director General of UNESCO and **Prof. A. Luczak,** Deputy Prime Minister and Head of KBN signed the "***Agreement between the Government of the Republic of Poland and the United Nations Educational, Scientific and Cultural Organization concerning the Establishment and Operation of the International Institute of Molecular and Cell Biology in Warsaw***".

Warsaw, October 2-7, 1995: The International Conference on "New Frontiers in Cell and Molecular Biology" **inaugurated the scientific activities of the Institute.**

LET'S CELEBRATE!
20
YEARS OF IIMCB

ANNIVERSARY SYMPOSIUM

Thursday, May 17, 2018
IIMCB, Warsaw, Poland

15:00 **Angelo Azzi** Tufts University, USA
Opening

15:10 **Jacek Kuźnicki** IIMCB, Poland
Anniversary lecture

15:45 Coffee break

Scientific lectures
Chair: Angelo Azzi, Tufts University, USA

16:15 **Anne Spang** University of Basel, Switzerland
Compartmentation - modes of intracellular organization

16:45 **Walter Chazin** Vanderbilt University, USA
Pushing the Horizon of Structural Biology

17:15 Coffee break

17:45 **Lilianna Solnica-Krezel** Washington University, USA
Regulation of microtubule cytoskeleton by an atypical cadherin Dachsous

18:15 **Aaron Ciechanover** Technion-Israel Institute of Technology, Israel
The ubiquitin proteolytic system: from basic mechanisms through human diseases and into drug targeting

19:30 Let's celebrate: cocktail dinner

INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY IN WARSAW

Venue:

International Institute of Molecular and Cell Biology in Warsaw
4 Ks. Trojdena Street, Warsaw, Poland

Registration required. More information on www.iimcb.gov.pl

International Institute Molecular And Cell Biology in Warsaw
4 Ks. Trojdena Street, 02-109 Warsaw, Poland
www.iimcb.gov.pl