

Registration form for Polish scientific institution

1. Scientific institution data (name and address):

International Institute of Molecular and Cell Biology in Warsaw (IIMCB)
Ks. Trojdena 4 Street, 02-109 Warsaw
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www.iimcb.gov.pl
NIP: 526-22-78-704, REGON: 013082798

2. Type of scientific institution¹ (select one out of 7 listed options):

4) international scientific institute

3. Head of the institution

Prof. Jacek Kuźnicki, PhD, Acting Director
Prof Marta Międzyńska since January 1, 2019

4. Contact information of designated person(s) for applicants and NCN: first and last name, position, e-mail address, phone number, correspondence address):

Scientific contact: Jacek Jaworski, PhD, Deputy Director for Science, jaworski@iimcb.gov.pl,
+48 22 5970755

Operational contact: Dorota Libiszowska, Head of Grants Office, dlibiszowska@iimcb.gov.pl,
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Postal address for both persons: indicated in Item 1

5. Science discipline in which strong international position of the institution ensures establishing a Dioscuri Centre (select one out of 25 listed disciplines):

Life Sciences

Molecular biology, structural biology, biotechnology

6. Description of important research achievements from the selected discipline from the last 5 years including list of the most important publications, patents, other (up to one page in A4 format):

Founded in 1999, IIMCB is a modern research institute, ranked with the highest score (category A+) by the Polish Ministry of Science and Higher Education. We have nine independent research groups that conduct studies in the fields of molecular cell biology, biochemistry, neuroscience, structural biology, bioinformatics, and developmental genomics.

Publications: Between 2000-mid 2018, IIMCB researchers published over 830 papers in leading journals. The most important publications from the last 5 years are the following (names of IIMCB lab leaders in bold):

- Razew M, [...], **Nowotny M.** Structural analysis of mtEXO mitochondrial RNA degradosome reveals tight coupling of nuclease and helicase components, *Nat. Commun.* 2018.
- **Winata CL.**, [...], Mathavan S. Cytoplasmic polyadenylation mediated translational control of maternal mRNAs direct zebrafish maternal to zygotic transition. *Development.* 2018.
- Jastrzebski K, [...], **Międzyńska M.** Multiple routes of endocytic internalization of PDGFR β contribute to PDGF-induced STAT3 signaling. *J Cell Sci.* 2017.

¹ As specified in „Adresaci ogłoszenia”

- **Mleczo-Sanecka K**, [...], Muckenthaler MU. Imatinib and spironolactone suppress hepcidin expression *Haematologica*. 2017.
- Szewczyk LM, [...], **Kuznicki J**. ST8SIA2 promotes oligodendrocyte differentiation and the integrity of myelin and axons. *Glia*. 2017.
- Majewski Ł, [...], **Kuznicki J**. Overexpression of STIM1 in neurons in mouse brain improves contextual learning and impairs long-term depression. *BBA-MCR*. 2017.
- Maminska A, [...], **Miaczynska M**. ESCRT proteins restrict constitutive NF-κB signaling by trafficking cytokine receptors. *Sci Signal*. 2016.
- Wrobel L, [...], **Chacinska A**. Mistargeted mitochondrial proteins activate a proteostatic response in the cytosol. *Nature*. 2015.
- Bragoszewski P, [...], **Chacinska A**. Retro-translocation of mitochondrial intermembrane space proteins. *Proc Natl Acad Sci U S A*. 2015.
- Malik AR., [...], **Jaworski J**. Tuberous sclerosis complex neuropathology requires glutamate-cysteine ligase. *Acta Neuropathol. Commun*. 2015.
- Glow D, [...], **Bujnicki JM**. Sequence-specific cleavage of dsRNA by Mini-III RNase. *Nucleic Acids Res*. 2015. (distinguished as a "Breakthrough Article")
- Mierzejewska K, [...], **Bujnicki JM**, [...], **Bochtler M**. Structural basis of the methylation specificity of R.DpnI. *Nucleic Acids Res*. 2014.
- Nowak E, [...], Le Grice SFJ, **Nowotny M**. Ty3 reverse transcriptase complexed with an RNA-DNA hybrid shows structural and functional asymmetry. *Nat Struct Mol Biol*. 2014.
- Wojciechowski M, [...], **Bochtler M**. CpG underrepresentation and the bacterial CpG specific DNA methyltransferase M.Mpel. *Proc Natl Acad Sci U S A*. 2013.

A complete list of publications is available at www.iimcb.gov.pl/en/research/publications.

Recent patents:

1. Sabała I and **Bochtler M**: "A method of proteolysis, a peptidase, a composition for use as a bacteriostatic or bactericidal agent, a kit and the uses of the active form of LytM of *S. aureus* or a derivative thereof" (EP 2699254). Patent granted in the USA, Canada, and Japan, one **licensing agreement** signed for the use of the LytM enzyme.
2. **Bujnicki JM**, Sulej A and Skowronek K: "dsRNA endoribonucleases" (EP 2718431)
3. **Bujnicki JM**, Sulej A, Skowronek K and **Nowotny M**: "Sequence-specific engineered ribonuclease H and the method for determining the sequence preference of DNA-RNA hybrid binding proteins" (EP 2718430)
4. **Dastych J**: "Tools and methods useful in characterising the immunotoxic activity of xenobiotic substances" (US 8361711 B2)

7. List of no more than 3 important research projects from the selected discipline awarded in national and international calls to the institution in the last 5 years (title, name of PI, source of funding, amount of funding):

The majority of IIMCB funding is provided by external competitive sources, both Polish and international. Between 2000 and mid-2018, IIMCB scientists received 297 grants, constituting approximately 70% of the total institutional budget. Among these, 60 were awarded by foreign funding institutions, such as the European Commission within the Framework Programmes and Horizon 2020 (37 projects with 3 ERC grants), EMBO (5), HHMI (3), Wellcome Trust (3), Polish-Norwegian Research Fund and Polish-Swiss Research Programme (3), Max Planck Society, National Institutes of Health (4), and Deutsche Forschungsgemeinschaft, among others. In the same period, 237 projects were granted by Polish domestic agencies, mainly the National Science Centre (NCN), Foundation for Polish Science, National Centre for Research and Development, and Polish Ministry for Science and Higher Education. Notably, in the last official NCN Report², IIMCB is highlighted as one of best performing Polish Host Institutions.

² <https://www.ncn.gov.pl/aktualnosci/2018-07-10-wnioskodawcy-w-konkursach-2013-2017>

In years 2013-2017, IIMCB had the highest success rate among all NCN calls (62%) and received 50 311 060 PLN (ca. 12 578 000 EUR) in total and 632 844 PLN (ca. 158 000 EUR) per researcher, the latter amount being the highest funding in the area of Life Sciences.

The three most important research projects that were awarded to IIMCB in the past 5 years are the following:

1. ERC, Starting Grant

Title: "Structural studies of Nucleotide Excision Repair Complexes" (agreement no. 281500)

Principal Investigator: Marcin **Nowotny**

Period: 01.01.2012 - 31.12.2017

Source of Funding: European Commission, 7th Framework Programme

Amount of funding: 1 498 000 EUR

2. EMBO, EMBO Installation Grant

Title: "Identification of signals coordinating the proteolytic quality control networks." (project no. 3913)

Principal Investigator: Wojciech **Pokrzywa**

Period: 01.05.2018 - 30.04.2021

Source of Funding: EMBO

Amount of funding: 150 000 EUR

3. National Science Centre, MAESTRO

Title: "Structural RNomics" (agreement no. UMO-2012/04/A/NZ2/00455)

Principal Investigator: Janusz M. **Bujnicki**

Period: 08.10.2012-07.10.2017

Source of Funding: National Science Centre

Amount of Funding: 3 000 000 PLN (ca. 750 000 EUR)

8. Description of the available laboratory and office space for Dioscuri Centre (*up to one page in A4 format*):

The Dioscuri Centre holder will be provided the best conditions to conduct their research. The new leader will be offered laboratory space and neighboring furnished office space that are ready to be equipped according to Centre needs and specifications. The size of the space will be adjusted to the number of new Centre team members, which will increase with time if needed. The new PI will have at their disposal a laboratory space, an equipment room and a culture room. The Dioscuri holder will also have office space, for themselves and for the team members. In addition to IIMCB Core Facilities (see point 9), the Centre will benefit from full and unlimited access to common infrastructure, such as -80°C freezers, centrifuges, incubators, isotopes, cell cultures, autoclaves, and washing devices, and will be supplied with common standard services, such as the Mili-Q ultrapure water system. The Dioscuri holder will have full access to zebrafish and *C. elegans* facilities while access to mouse/rat facilities can be arranged at the Ochota Campus. Lastly, the Dioscuri Centre will benefit from the space of a meeting room, small conference rooms, a seminar room, a quiet work room, and a social room.

9. List of the available scientific equipment for Dioscuri Centre:

In compliance with IIMCB rules, the Dioscuri holder and his group will benefit from unlimited, free-of-charge access to a broad range of cutting-edge research technology platforms at IIMCB that are available at its Core Facilities and Zebrafish Core Facility. The new group will also benefit from the infrastructure and facilities at neighboring institutes of the Ochota Campus where IIMCB is located. Experienced scientists will provide Dioscuri Centre's staff with initial training on methodological principles, experimental design, procedures that are needed for specific experiments, data analysis, and final data interpretation. Finally, the Dioscuri Centre

team members will be able to use the equipment of other laboratories. Free equipment sharing is one of core principles of IIMCB operations.

The majority of IIMCB equipment is concentrated in the **Core Facilities**. The equipment is available to all staff at no cost and is maintained by scientific staff members with substantial expertise. There are over 50 pieces of equipment that are grouped into several units based on leading technologies and applications:

The Macromolecule Crystallography Unit is one of the most advanced in Poland and is equipped with Oryx 4 (Douglas Instruments) and Crystal Phoenix (Art Robbins Instruments) crystallographic robots, X8 Proteum X-ray generator (Bruker) with 135 Platinum CCD detector (Bruker), Cryosystem series 700 cryostream cooler (Oxford Cryosystems), and two Minstrel Crystallographic Hotels (Rigaku).

IIMCB also has a **cryo-EM setup** that consists of a **120 kV TECNAI Spirit microscope (FEI)** equipped with a TVIPS CMOS 4K'4K camera and all additional equipment that is required for cryo-EM work, such as a Vitrobot cryo-holder (FEI). This equipment is suitable for tissue/cell imaging and single-particle EM sample preparation and characterization.

The Biochemical and Biophysical Analysis of Proteins and Nucleic Acids Unit comprises analytical instruments for in-depth analyses of proteins and nucleic acids using different methods: VP-ITC Isothermal Titration Calorimeter (MicroCal/Malvern), VP-DSC Differential Scanning Calorimeter (MicroCal/Malvern), ProteomeLab XL-I Analytical Ultracentrifuge (Beckman), Biacore S200 surface plasmon resonance (SPR) device (GE), HELEOSII and Optilab T-rEX SEC-MALS equipment (Wyatt), J-810 Spectropolarimeter CD (Jasco), TENSOR Series FT-IR Spectrometer (Bruker), Nano Drop 8000 spectrophotometer (Thermo), FP-8300 Spectrofluorometer (Jasco), DMA 5000 M density meter, and Lovis 2000 M rolling-ball viscometer (Anton Paar).

The Mass Spectrometry of Proteins and Nucleic Acids Unit has two mass spectrometers: MALDI-TOF-TOF ultrafleXtreem and LC-ESI-Ion Trap amaZon speed ETD (both from Bruker).

The Microscopy Bioimaging Unit has fluorescence-based imaging systems that are suited for cell biology applications: confocal microscope LSM800 (Zeiss), LSM710 NLO dual confocal/multiphoton microscope for live imaging (Zeiss), a system for real-time spinning-disk confocal microscopy and TIRF imaging Revolutions XD (Andor), Lightsheet Z.1 single-plane illumination microscope (Zeiss), CellIR/ScanR imaging station for intracellular calcium measurements (Olympus), 80i Eclipse microscope (Nikon), FACS Aria II a high-speed benchtop cell sorter and FACSCalibur for the quantitative analysis of fluorescence signals in suspension cells (BD) and high-content screening system Opera Phenix (Perkin Elmer) equipped with robotic arm for automatic sample loading. Additionally two electrophysiological rigs equipped with Zeiss and Scientifica microscopes are available to the IIMCB researchers.

The Next Generation Sequencing 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, and systems for nucleic acid quality and quantity measurements -TapeStation, NanoDrop 3300 Fluorospectrometer and Quantus.

Other pieces of IIMCB equipment include 14 FPLC Chromatography systems, a Sally Sue system for automated Western blot analysis (ProteinSimple), two Techforce-S bioreactors (Infors), HPLC 2996 detector and HPLC pumps (Waters), Odyssey Infrared Imaging System (LI-COR), Odyssey FC Imaging System (LI-COR), Optima LE-90K, Optima LE-80K, and Optima MAX XP Ultracentrifuges (Beckman Coulter), 7900HT Real Time PCR (Life Technologies), Typhoon Trio Variable Mode Imager (GE Healthcare), Imager ImageQuant

LAS 4010 (GE), Centro XS3 LB 960 Microplate Luminometer (Berthold Technologies), Infinite M1000 Plate Fluorimeter (TECAN), Sunrise Plate Reader (TECAN), STERIVAP Steam Sterilizers (BMT), Acquity UPLC (Waters), B Series Cell Disruption System (Constant Systems) and OPS-201 Oligonucleotide Purification System.

The new leader will also have full and free access to the Zebrafish Core Facility, a licensed breeding and research facility with a zebrafish stock collection of more than 16,000 fish. The ZCF is equipped with incubators, microscopes, injectors, and a thermocycler. Zebrafish Core Facility users have at their disposal a behavioral room that is equipped with a housing system for acclimatization and two automated systems that allow observations and the tracking of larval and adult zebrafish behavior.

A more comprehensive list of equipment is available at www.iimcb.gov.pl/en/equipment-facilities/equipment.

10. List of the additional benefits that the Institution declares to provide for Dioscuri Centre (i.e.: additional funds, personal benefits, other) (up to one in page A4 format):

IIMCB follows organizational standards of the best European research centers. It fosters an international work environment and positive workplace culture with a “team spirit” that stimulates creativity. IIMCB holds the “HR Excellence in Research Award,” a prestigious accreditation that is awarded by the European Commission, recognizing IIMCB as a quality employer that offers its researchers a favorable working environment. Altogether, the supportive environment at IIMCB allows the academic staff to devote their time primarily to scientific tasks. The Dioscuri Centre will be fully integrated in this environment and carefully supported at both the scientific and administrative levels:

Employment. The Dioscuri holder will be employed with a professorial position and full-time contract. The salary will be specified by the Dioscuri program, and the Dioscuri holder will have no teaching obligations. The new leader will receive a benefits package according to national legislation, IIMCB bonuses, and private medical care. These will also apply to other Centre members, depending on their type of employment.

Additional funds. In agreement with the Dioscuri program rules, IIMCB will support the Centre with 25,000 EUR annually and additionally with 75,000 EUR of start-up funds. Further support will be negotiated, depending on specific research needs of the Dioscuri Centre.

Research Freedom. The Dioscuri holder will be offered an independent lab leader position, with full freedom in scientific and organizational management of the research group. The new leader will also be responsible for the Centre and its research achievements.

PhD Schools. PhD students who are recruited by the Dioscuri Centre will be enrolled in one of the PhD Schools of the Ochota Campus.

English-speaking administrative personnel. IIMCB will provide an administrative manager who is employed full-time and dedicated to support the Dioscuri Centre. The new team will receive professional and comprehensive assistance from English-speaking highly professional and friendly administrative personnel.

Support with grant applications. To ensure the Dioscuri Centre’s sustainability, the new PI is expected to apply for external funding. Currently, numerous grant schemes are available, especially from Polish sources. During the application process, the Dioscuri holder will receive thorough internal support and mentoring, both scientific (from other PIs) and administrative (from the dedicated Grants Office).

Laboratory technical support. Dedicated technicians who are employed by IIMCB will provide basic laboratory support to the Dioscuri Centre, including glass cleaning, media preparation, and material sterilization.

Access to certification courses and training. If needed, IIMCB will offer the Centre’s researchers free participation in required certification courses on the usage of laboratory

animals (in English). New staff will also be offered professional in-house training (e.g., on the use of equipment) and will be fully supported to participate in specialized, external training.

Robust networking possibilities. Dioscuri Centre staff will be integrated in IIMCB's research community. They will participate in weekly open seminars that are held in English (a forum to share experiences and network with in-house researchers and outstanding invited scientists). They will also be invited to networking events that are organized at IIMCB and neighboring institutes of the Ochota Campus. These are tremendous opportunities for the Centre to broaden its scientific horizons and develop inspiring contacts.

Cooperation, technology transfer, and commercialization. The Dioscuri Centre will benefit from IIMCB contacts with pharmaceutical and biotechnology firms and will be supported by Biotech Innovation Ltd., an IIMCB company, in efficient technology transfer to industry and commercialization.

11. Other information about internationalization of the scientific institution, foreign scientists employed at the institution, availability of the English language seminars etc. (*up to one page in A4 format*):

The international character of IIMCB is strongly reflected by all aspects of its functioning. English is the official language of communication of IIMCB, which includes correspondence, seminars, and meetings. All positions are filled through open competitions, and lab leaders are selected by the International Advisory Board, a unique body in Poland that ensures full objectivity of the process. **This international and highly competitive character of the lab leader selection and IIMCB's reputation attract outstanding researchers from all over the world.** Of the nine principal investigators, seven are Poles who came back from abroad after extensive postdoctoral training in renowned research centers, and two are from foreign countries (Germany, Singapore). Additionally, IIMCB has two partnering labs: one led by a Czech researcher (Jan Brezovsky) at the Adam Mickiewicz University in Poznan and one led by a German researcher (Michael Potente) at the Max Planck Institute in Bad Nauheim. Furthermore, IIMCB alumni successfully develop their careers in both Polish and foreign research institutes and businesses.

The international recognition of IIMCB researchers is best expressed in their **publication record, ability to attract competitive funding from external sources** (see points 6 and 7), and **active participation in international conferences.** Senior scientists are invited to prestigious meetings as speakers, and young researchers give talks. **IIMCB is also an organizer of international conferences and workshops.** To name just a few from recent years: three meetings on zebrafish (Heart of Europe: Zebrafish Meeting in 2014, FishMed2016 and FishMed2018); Talking molecules: the networks that shape the living world - 2nd ARBRE-MOBIEU plenary meeting, 2018; EMBO Conference (Endocytic trafficking and signaling in health and disease) organized by Prof. Miaczynska in 2017; 20th Heart of Europe Biocrystallography Meeting, 2017; three editions of the Summer School in Bioinformatics & NGS Data Analysis (NGSchool2016 in Dolný Smokovec, Slovakia, NGSchool2017 in Warsaw, and NGSchool2018 in Lublin); Workshop for the hydrodynamic and thermodynamic analysis of biological macromolecules and their interactions with SEDFIT and SEDPHAT in 2016. The high level of IIMCB events is assured by renowned international invited speakers.

During several years of work, **IIMCB became visible as part of the European and international research network, reflected by long-term scientific cooperation with world-leading foreign research centers, such as the Max Planck Society.** Under this strategic partnership, four laboratories were established with double MPS and IIMCB affiliations: two laboratories at IIMCB (Prof. Bochtler's Lab of Structural Biology MPG/PAS [2001] and Dr. Winata's Lab of Developmental Zebrafish Genomics Max Planck/IIMCB [2014]) and two in MPS Institutes (Prof. Paluch's Lab of Cell Cortex Mechanics MPG/PAS located at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden [2006] and Dr. Potente's Angiogenesis and Metabolism Lab at the Max-Planck Institute for Heart and Lung Research in Bad Nauheim [2015]). **IIMCB research groups also develop individual international**

collaborations through common grants, regular contacts, exchange visits, and open seminars that are systematically organized with outstanding invited speakers from all over the world.

The international recognition of IIMCB is also visible in the **active participation of IIMCB researchers in prestigious European and international organizations:**

- EMBO members: J.M. Bujnicki, M. Miaczynska (2 of 12 Polish EMBO members)
- member of the Academia Europaea: J.M. Bujnicki
- member of the European Science Advisors Forum J.M. Bujnicki
- member of the seven-member Scientific Advice Mechanism High Level Group: J.M. Bujnicki
- evaluation panelists of ERC: M. Bochtler, M. Miaczynska, and J.M. Bujnicki
- member of Advisory Group for Health in FP7: J. Kuznicki
- evaluation panelists of MSCA: J. Kuznicki and I. Sabala

IIMCB's multinational and multicultural character is created by its people. A total of 31% of IIMCB research staff are foreigners, representing fourteen nationalities. **They are supported by professional English-speaking administrative personnel** whose specific task is to assist foreign employees with organizing their stay in Poland. This creates a multinational, vibrant environment and an attractive location to perform research at the highest level.