REGISTRATION FORM FOR CZECH SCIENTIFIC INSTITUTION

1. Research institution data (name and address):

Institute of Molecular Genetics of the Czech Academy of Sciences
Vídeňská 1083
142 20 Prague 4, Czech Republic

2. Type of research institution:

Public research institution – Czech Academy of Sciences (veřejná výzkumná instituce – Akademie věd České republiky)

3. Head of the institution: Petr Dráber, DSc, petr.draber@img.cas.cz

4. Contact information of designated person(s) for applicants:

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5. Research discipline in which the strong international position of the institution ensures establishing a Dioscuri Centre:

Life Sciences: *Human and animal immunology and infection* - immunity, immune disorders, immunotherapy, infectious and invasive diseases, microbiology, transplantology, allergology

6. Description of important research achievements from the selected discipline from the last 5 years including a list of the most important publications, patents, or other results:

Formation of spermatogonia and fertile oocytes in golden hamsters requires piRNAs. piRNAs are small RNAs that contribute to the genome defence in animal germ cells. The piRNA pathway recognizes and silences endogenous retroviruses and other parasitic mobile DNA sequences. Studies of piRNAs in mouse mutants suggested that mammalian piRNAs are not essential for oocytes. However, analysis of hamsters, whose piRNA pathway is similar to other mammals including humans, showed that mammalian piRNAs are also essential for oocytes, while in the mouse model they evolved in a different way (1).

Meis homeobox genes control progenitor competence in the retina. Vision is a crucial sense of vertebrates. Genetic manipulation in mice allows addressing the role of individual genes in eye development, and given the conserved role of genes, implicate their function in humans as well. The authors show that in the developing mouse embryo, Meis transcription factors control complex gene regulatory networks responsible for the maintenance of progenitor cells and retina differentiation (2).

β-Catenin and TCF/LEF signalling induces resting and standby granulopoiesis through an increase in G-CSF receptor expression. The study describes a previously unknown role of the canonical Wnt signalling pathway in blood cell development. In this publication, the authors show that this signalling pathway is necessary for production of sufficient numbers of neutrophils–special cells of the innate immune system that are responsible for the inflammatory response and defence against microorganisms. Since insufficient numbers of neutrophils are associated with reduced immunity, this study reveals a new mechanism involved in the regulation of innate immunity (3).

Signalling by Toll family receptors in thymic epithelial cells leads to accumulation of monocytic dendritic cells and formation of T regulatory cells. Using mouse models, it has been shown that thymic epithelial cells, which "train" maturing T cells in the thymus, have Toll family receptors on their surface. Targeted removal of these receptors made them susceptible to the development of autoimmune intestinal inflammation and type 1 diabetes. Stimulation of these receptors, in turn, led to enhanced defences against autoimmune diseases. Thus, the discovery of these novel mechanisms holds promising therapeutic potential with respect to the prevention of autoimmune diseases (4).

Resistance to poultry leukosis induced by genome editing. Enveloped viruses enter host cells through specific surface proteins, called receptors. Alteration of the receptors can prevent the virus from entering, indicating resistance to a given viral disease. Using the molecular tools of CRISPR/Cas9, we genetically altered chicken ion exchanger chNHE1, which uses the dangerous avian leukosis virus as its receptor. The resulting chicken line is completely resistant to the disease. This is the world's first genome editing and the first artificially induced resistance in poultry (5).

References

1. Loubalova, Z., H. Fulka, F. Horvat, J. Pasulka, R. Malik, M. Hirose, A. Ogura, and P. Svoboda. 2021. Formation of spermatogonia and fertile oocytes in golden hamsters requires piRNAs. *Nat. Cell Biol.* 23: 992-1001.
2. Dupacova, N., B. Antosova, J. Paces, and Z. Kozmik. 2021. Meis homeobox genes control progenitor competence in the retina. *Proc. Natl. Acad. Sci. U. S. A* 118, e2013136118.
3. Danek, P., M. Kardosova, L. Janeckova, E. Karkoulia, K. Vanickova, M. Fabisik, C. Lozano-Asencio, T. Benoukraf, R. Tirado-Magallanes, Q. Zhou, M. Burocziova, S. Rahmatova, R. Pytlik, T. Brdicka, D. G. Tenen, V. Korinek, and M. Alberich-Jorda. 2020. β-Catenin-TCF/LEF signaling promotes

steady-state and emergency granulopoiesis via G-CSF receptor upregulation. *Blood* 136: 2574-2587.

4. Vobořil, M., T. Brabec, J. Dobeš, I. Šplíchalová, J. Březina, A. Čepková, M. Dobešová, A. Aidarova, J. Kubovčiak, O. Tsyklauri, O. Štěpánek, V. Beneš, R. Sedláček, L. Klein, M. Kolář, and D. Filipp. 2020. Toll-like receptor signaling in thymic epithelium controls monocyte-derived dendritic cell recruitment and Treg generation. *Nat. Commun.* 11: 2361.
5. Koslová, A., P. Trefil, J. Mucksová, M. Reinišová, J. Plachý, J. Kalina, D. Kučerová, J. Geryk, V. Krchlíková, B. Lejčková, and J. Hejnar. 2020. Precise CRISPR/Cas9 editing of the NHE1 gene renders chickens resistant to the J subgroup of avian leukosis virus. *Proc. Natl. Acad. Sci. U. S. A* 117: 2108-2112.

7. List of no more than 3 important research projects in the selected discipline awarded in national and international calls to the institution in the last 5 years:

Title: **FunDiT - Functional Diversity of T Cells**

Name of PI: Ondřej Štěpánek, Ph.D.

Source of funding: European Research Council Executive Agency (ERCEA), ERC-2018-STG

Amount of funding: 1,725,000 EUR

Title: **Infrastructure Upgrade of CCP II**

Name of PI: PD. Dr. rer. nat. habil. Radislav Sedláček

Source of funding: MEYS - Operational Programme Research, Development and Education, 02_18_046 Research Infrastructures II

Amount of funding: 101,255,000 CZK

Title: **Modernization of the National Infrastructure for Biological and Medical Imaging Czech-BioImaging**

Name of PI: Prof. Pavel Hozák, Ph.D., DSc.

Source of funding: MEYS - Operational Programme Research, Development and Education, 02_18_046 Research Infrastructures II

Amount of funding: 281,824,400 CZK

8. Description of the available laboratory and office space for a Dioscuri Centre:

Laboratory space and equipment in the dedicated area of the main building of the BIOCEV Centre, Vestec, Průmyslová 595, near Prague (capital of the Czech Republic), airport and underground station, https://www.biocev.eu/en, Link to google maps.

- Laboratory (room H1.006; 57 m^2)
- Tissue culture (rooms H1.004 and 005; 27 m2) including a cell culture hood and a cell incubator
- Office (room H1.011; 20 m^2)
- Shared rooms including shared equipment:
    - Seminar room with kitchenette (room H1.014; 47 m^2)
    - Technical rooms and a cold room
    - The shared equipment includes the incubator (cooled), filter system for demi water, two refrigerated table centrifuges, a table centrifuge, an ice-maker, three shakers for cell/bacteria incubation, a UV box for mixing PCR reactions, two PCR machines (one gradient and one with three independent insets), gel documentation system, analytical balances, stereomicroscope DISCOVERY V12 S 1 O.

BIOCEV is the European Centre of Excellence in biomedicine and biotechnology established in a joint project of six institutes of the Academy of Sciences of the Czech Republic (Institute of Molecular Genetics, Institute of Biotechnology, Institute of Microbiology, Institute of Physiology, Institute of Experimental Medicine, and Institute of Macromolecular Chemistry) and two faculties of Charles University in Prague (Faculty of Science and First Faculty of Medicine).

Research infrastructures within the BIOCEV include the Czech Centre for Phenogenomics, (IMG) - Czech Infrastructure for Integrative Structural Biology, Imaging Methods, OMICS Proteomics, Centre of Molecular Structure, Gene Core – Quantitative and digital PCR, OMICS Genomics, Media preparation and washing units, and Cryobank (IMG). At the following web address, you can also find a list of key equipment of the core facilities: https://www.biocev.eu/en/services. All core facilities are open to users to provide them with research services.

9. List of the available research equipment for a Dioscuri Centre:

The Genomics and Bioinformatics Core Facility operates instruments for functional genomics. It provides next-generation sequencing and single-cell transcriptomics services, including consultations on project considerations and experimental design. The facility also performs primary bioinformatical analyses. The core facility is equipped with an Illumina NextSeq 500 next-generation sequencer, two single-cell technologies (10x Genomics Chromium Controller and Bio-Rad ddSEQ), two real-time PCR cyclers (Roche LC480), two legacy microarray platforms (Affymetrix GeneChip System and Illumina BeadStation 500) and an EnVision Plate Reader (PerkinElmer). The laboratory also operates instruments for assessment of the quality and quantity of processed samples (Nanodrop spectrophotometer, Qubit fluorometer, capillary electrophoreses Agilent Bioanalyzer 2100, and Agilent Fragment Analyzer 5200). Two ultrasonicators (Covaris ME 220 and Bioruptor) are available as shared equipment.

The Light Microscopy Core Facility is a state-of-the-art research facility equipped with a wide range of high-end microscopy technologies and image-processing tools. Most of the instrumentation in the facility is available on the self-service basis, for trained users. User access to the facility is supported via the "Czech-BioImaging open access" programme both for in-house and external scientists. The available technologies range from simple wide-field and confocal fluorescence microscopes to more advanced systems such as light-sheet, confocal spinning disc and superresolution techniques SMLM, SIM and STED. In addition, the facility personnel provides expertise on final image processing and analysis, including image registration, routine deconvolution, tracking, image segmentation, analysis of photo-kinetic experiments, mathematical modelling and simulations of biological processes.

The Electron Microscopy Core Facility provides expertise and cutting-edge equipment for a broad range of biological sample preparation and ultrastructural imaging techniques. The sample preparation techniques include routine chemical fixation and resin embedding, cryofixation using the high-pressure freezing technique, freeze-substitution, plunge-freezing, cryosectioning, and immunolabelling, including simultaneous detection of multiple targets by our self-developed methods. High-pressure freezing machines, two automatic freeze-substitution machines, freeze-fracture and replica making device, cryo-ultramicrotomes, Leica EM GP2 for automated plunge-freezing, as well as additional wet lab equipment are available. The core facility is equipped with two transmission electron microscopes (TEM) installed in November 2019 – a standard instrument for routine observation and an advanced 200 kV instrument providing the possibility of high-resolution TEM, STEM, 3D electron tomography, cryo-electron microscopy and EDS elemental analysis and mapping. The facility provides open access to our technologies and expertise via Czech-BioImaging and Euro-BioImaging infrastructures.

The Flow Cytometry Core Facility provides methodological and instrumentation background for flow cytometry. The facility is equipped with two flow cytometers with a high-throughput automated sampler and two polychromatic high-speed cell sorters. The facility includes a magnetic separator for automatic rapid sorting of cells. Cytometers and magnetic separator are available for trained users on a self-service basis. Sorting in polychromatic high-speed cell sorters is performed by operators.

The Monoclonal Antibodies and Cryobank Core Facility provides generation of mouse monoclonal antibodies including immunization, ELISA testing, (sub)cloning of selected hybridomas, sample freezing, production of cell culture supernatants, and isotype determination of the produced antibody. Further services comprise testing of cell culture supernatants for the presence of mycoplasms. The cryobank serves for long-term storage of samples in liquid nitrogen. The current cryobank capacity is 320,000 samples, with further possible extension. The cryobank stores cell lines, hybridomas, mouse sperm, and mouse embryos. The storage containers (LABS40K – Taylor-Wharton and 24K) are connected to the exterior liquid nitrogen container and supplied automatically. The entire cryobank system is secured by a backup energy source in case of power failure. All operations, diagnostics and

monitoring of the level of liquid nitrogen in the storage containers are fully automated and controlled. Parameters (temperature, humidity, O2 concentration) and safety both in the cryobank and in the individual storage containers are followed by the monitoring system with GSM and web interface outputs.

The X-ray Irradiation Facility is equipped with an X-RAD 225XL Biological Irradiator for regulated radiation of cells and mice. The instrument is used by trained personnel as self-service.

The Histological Laboratory provides equipment for tissue dehydration, creation of paraffin blocks, tissue sectioning, deparaffination and antigen retrieval. The most important laboratory equipment consists of a set of four Leica devices – tissue processor, paraffin embedding station, and two microtomes. The facility is based on semi-self-service – tissue dehydration is collective and handled by the staff, all the other steps are carried out by each user individually independently and without time limitations.

Other (specific) services are provided by large research infrastructures hosted by IMG:

Czech-BioImaging (https://www.czech-bioimaging.cz/) is a large national research infrastructure, consisting of 14 closely cooperating facilities, for biological and medical imaging. Its aim is to allow permanent access to cutting-edge imaging technologies and expertise in imaging to scientists who do not have them available at their own institutions.

The National Infrastructure for Chemical Biology CZ-OPENSCREEN (https://www.openscreen.cz/en) operates the most advanced research infrastructure for basic and applied research in the fields of chemical biology and genetics in the Czech Republic; the infrastructure provides open access to its external users. CZ-OPENSCREEN offers comprehensive services for biologists such as standard biological and biochemical assays, consultancy and development of new assays, high-throughput screening (HTS), profiling of chemical compounds on a panel of cell lines, and medicinal chemistry optimization of newly identified biologically active compounds. CZ-OPENSCREEN systematically builds a library of both commercial chemical compounds as well as compounds synthesized in the research Institutes. An integral part of the services is cheminformatics support, such as data analysis and storage, development of new analytical tools and database systems.

Czech Centre for Phenogenomics (CCP) (https://www.phenogenomics.cz/) is the largest biomedical research infrastructure and the main site in the Czech Republic with the expertise and capacity for large-scale generation of genetically modified mouse and rat models, and their advanced and standardized phenotyping. This expertise, together with high breeding capacity under specific pathogen-free (SPF) conditions and cryo-archiving and recovery services, provides open access to services and expertise at a level comparable to the leading research institutions in the Europe.

10. List of the additional benefits (other than listed in the conditions for hosting a DC, see invitation) that the Institution declares to provide for a Dioscuri Centre (i.e.: additional funds, personal benefits, dual career options, relocation support or other):

The Institute has a well-established classification system of professional ranks (including salaries). Excellent employees achieving outstanding results can be promoted to a higher rank. The promotion is based on the recommendation of the institutional Attestation Committee and signed by the Director. The Institute actively supports women in science and has pro-active family policy. Apart from flexible working hours, one of the important steps in this direction was foundation of an IMG day care/kindergarten. Additionally, IMG offers its own guesthouse located on the campus in Prague 4 Krc. The Institute also offers a canteen and cafeteria, gym and squash court, and subsidizes theatre tickets. IMG organizes a St. Nicholas party with games and theatre performance for children of the employees.

11. Other information about the internationalization of the research institution, international researchers employed at the institution, the availability of English language seminars etc.:

Support of foreign employees - IMG provides comprehensive assistance in the enrolment process, from sending the necessary documents for obtaining an entry visa to the arrival in the Czech Republic. In case of any uncertainties or difficulties with the embassy in their home country, professional support is provided to the foreigners. A member of the Building Maintenance department helps with the initial adaptation to IMG. In cooperation with EURAXESS Czech Republic, they arrange interviews at the Ministry of the Interior and check all the documents that the employee must take with him/her to the interview. A representative of the research group will then take over and help him/her to be introduced to the operation and functioning of the laboratory.

An International Employee Handbook is available to the new employees. The document can be found on the IMG intranet.

Accommodation - IMG has its own guesthouse and has available two other guesthouses located directly on the campus. They primarily serve for foreign employees and PhD students. Available are fully equipped units, with a washing machine and dryer in the common areas. The occupancy of the apartments is decided by the IMG Accommodation Committee. The accommodation contract is issued for one year with the possibility of renewal if capacity allows. A member of the Building Maintenance department goes over the contract in English with the new residents, explains the terms of accommodation and termination of the contract, what the handover of the apartment will look like, and explains the wage payment process – when they will receive their first salary and how it will be used to pay for accommodation. The accommodation contract is a very important document for the Ministry of the Interior. It is used to prove a secured stay in the Czech Republic.

Communications - Research and administrative issues are discussed at weekly meetings of group leaders. Additionally, each group presents its projects at regular Wednesday Institute seminars and annual conferences. The language of the IMG is English, which is used in official e-mail communications, binding documents for the staff and at seminars and conferences organized by the Institute. The content of the IMG website is the same in Czech and English. IMG actively supports international cooperation.

Courses - Every year in October, Czech language courses for foreigners start directly at the Institute.