Open PhD positions at the Institute of Molecular Genetics of the ASCR, v. v. i.

http://www.img.cas.cz/studium/phd-program/

Laboratory of Genome Integrity

http://www.img.cas.cz/research/jiri-bartek/

PhD position – cell/molecular biology

Project title: Molecular mechanisms for maintaining the integrity of human genome under conditions of replication stress

Supervisor: Jana Dobrovolná (jana.dobrovolna@img.cas.cz)
Co-suprevisor: Pavel Janščák (pavel.janscak@img.cas.cz)

Project description: The project will focus on molecular mechanisms involved in processing of highly genotoxic RNA:DNA hybrids, called R-loops, that are suspected to play role in cancer development. The candidate will identify the proteins associated with R-loops under conditions of chemically- and oncogene-induced replication stress and study their role in maintenance of genome stability. The project offers training in a broad range of molecular, cell biological and biochemical techniques. The student will also undergo short-term trainings at the Institute of Molecular Cancer Research of the University of Zurich where he/she will be exposed to front-line research in the field of DNA repair and cancer.

Candidate's profile (requirements): M.Sc. or equivalent in biochemistry or molecular/cellular biology, good English, independent thinking, strong interest in basic research and experimental work.

Laboratory of Cell Differentiation

http://www.img.cas.cz/research/petr-bartunek/

Project 1
Project title: Modeling human diseases using zebrafish
Supervisor: Petr Bartůněk (bartunek@img.cas.cz)

Candidate profile: Students with MSc or equivalent in molecular and developmental biology

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Project 2
Project title: Nuclear receptors in normal and cancer cells: Identification of new ligands

Supervisor: Petr Bartůněk (bartunek@img.cas.cz)

Candidate profile: Students with MSc or equivalent in molecular and developmental biology

Laboratory of Molecular Pharmacology

http://www.img.cas.cz/research/jaroslav-blahos/

Project description: For studies of Cannabinoid Receptor 1 regulation by novel molecular partners, namely SGIP+ that was discovered in our lab as an interactin partner of the receptor we plan to open positions for two Ph.D. students.
The techniques combine DNA recombination, protein chemistry, pharmacological functional tests of various intracellular signaling pathways, cell biology tools including fluorescence microscopy, TIRF, BRET and FRET.

Suprevisor: Jaroslav Blahoš (jaroslav.blahos@img.cas.cz)

Laboratory of Leukocyte Signalling

http://www.img.cas.cz/research/tomas-brdicka/

PhD position – imunology

Project title: Regulation of leukocyte signaling by membrane adaptor proteins

Supervisor: Tomas Brdicka (tomas.brdicka@img.cas.cz)

Project description: The project will focus on the regulation of signaling by chemokine receptor CXCR4. This receptor governs retention and homing of hematopoietic stem and progenitor cells and other leukocytes in the bone marrow. It is also involved in tumor metastasis and HIV infection and it is targeted in a number of disease therapies under clinical testing. The candidate will explore the role of a novel adaptor protein OPAL1 in the regulation of signaling by CXCR4 in leukocytes. The project will include analysis of leukocyte development, migration, immune response and signaling using genetically modified mouse models and cell lines. The candidate will also be involved in projects exploring function of other adaptor proteins involved in the regulation of leukocyte signaling and inflammation.

Candidate profile: The candidate must hold a Master degree (or be close to its completion) in immunology, molecular/cell biology, biochemistry or in a related field of life sciences. The applicant must be highly motivated, with strong interest in immunology and related biomedical sciences. Good communication skills (including communication in English) are required. Previous experience with mouse models or with analysis of signal transduction pathways is an advantage.

Laboratory of Mouse Molecular Genetics

http://www.img.cas.cz/research/jiri-forejt/

Supervisor: Petr Jansa (petr.jansa@img.cas.cz)
Co-supervisor: Jiří Forejt (jiri.forejt@img.cas.cz)

Project description: Positional cloning of a gene participating in infertility of hybrids between closely related species using genetic crosses, gene expression profiling and knockouts, and immunocytochemistry of proteins involved in recognition and pairing of homologous chromosomes during meiosis in infertile hybrids.

Candidate profile: M.Sc. or equivalent in genetics or cell or developmental biology. The candidate should have a solid knowledge of molecular biology and genetics and basic skills in methods of mouse genetics and DNA and RNA isolation and analysis.

Laboratory of Integrative Biology

http://www.img.cas.cz/research/martin-gregor/

Project title: The role of junctional and desmosomal constituents on architecture and barrier function of the intestinal epithelia

Supervisor: Martin Gregor (martin.gregor@img.cas.cz)

Project description: Dysfunction of intestinal epithelial barrier is a hallmark of many pathological processes. Recently, tight junctions (TJ) and desmosomes (DS) were proposed to play crucial role in disease pathogenesis. The major objective of this project is to study the role of model constituents of TJ (claudin 8 and 13) and DS (plectin) in protection of intestinal simple epithelia from inflammation and tumorigenesis.

Applications are invited for Ph.D. student positions in the Department of Integrative Biology, at the Institute of Molecular Genetics of the ASCR, v. v. i. (IMG, Prague, Czech Republic). The positions (up to five years) are fully funded by several grants.

The successful candidates will learn and utilize advanced cell-biology, molecular-biology, physiology and imaging techniques, while developing and analyzing various mouse models.

Candidate profile: We are seeking outstanding self-motivated candidates with master's degree in molecular biology, physiology, general biology, biochemistry or related fields. We are offering research at a state-of-the-art equipped institute with experienced colleagues, international working environment and international collaborations.

For background information see:
https://www.researchgate.net/profile/Martin_Gregor
Applications in English including structured CV containing research experience and a letter of interest should be sent to the email address above.

Laboratory of Biology of the Cell Nucleus

http://www.img.cas.cz/research/pavel-hozak/

Project 1
Project title: Contribution of (pre)lamin A – phosphoinositides complexes to intranuclear order

Supervisor: Pavel Hozák (pavel.hozak@img.cas.cz)

Project description: Lamins are intermediate filament proteins present in nuclear lamina and, to less extent, in the nuclear interior. They are involved in a variety of nuclear functions, such as regulation of gene expression, DNA replication, DNA repair, chromatin organization, and cellular ignalling. Mutations in lamins cause severe disease – laminopathies. While interactions and functions of lamins in lamina are extensively addressed, much less is known, about the lamin pool in the nuclear interior. Our preliminary data demonstrate that lamin A forms a complex with nuclear myosin I and a phosphoinositide phosphatidylinositol 4,5-bisphosphate. This project focuses on detailed characterization of these complexes by biochemical, structural and advanced microscopy methods using various experimental models. The project will implement molecular biology and biochemistry methods as well as the state-of-the-art imaging techniques including fluorescence, confocal and super-resolution (SIM, STED, STORM) microscopy. The project is supported by recently awarded funding from the Grant Agency of the Czech Republic.

Candidate profile: M.Sc. (Mgr.) degree or equivalent in molecular/cellular biology or biochemistry, good English, independent thinking, strong interest in basic research and experimental work, dedication to learn and develop new techniques.

Project 2
Project title: Phosphoinositides compartments in the cell nucleus – their structure and functions

Supervisor: Pavel Hozák (pavel.hozak@img.cas.cz)

Project description: Phosphoinositides are phosphorylated species of phosphatidylinositol. They are present at all membranous structures within a cell (plasma membrane, ER, GA, endosomes and various vesicles) where they direct membrane trafficking and serve as signalling molecules. Surprisingly, phosphoinositides localize also to the cell nucleus, which is internally absent of membrane. We have previously demonstrated that phosphatidyl inositol-4,5-bisphosphate (PIP2) is present in the nucleolus as well as carbon-rich patches which we termed the lipid islets. We have shown that nucleolar PIP2 stimulates activity of RNA polymerase I and other transcription factors such as UBF and fibrillarin and thus modulates transcription of rDNA genes. In the nucleoplasm, lipid islets associate with RNA polymerase II and their absence negatively affects transcription of protein-

coding genes. The exact mechanism, however, remains largely unknown. This project focuses on finding (i) the detailed composition of lipid islets as well as (ii) defining a cross-talk between various phosphoinositides within the nucleus, (iii) defining direct protein interacting partners of phosphoinositides, and (iv) elucidating the mechanism by which the phosphoinositides modify nuclear processes, e. g. RNA polymerase II transcription.

The PhD project will implement molecular biology and biochemistry methods as well as the state-of-the-art imaging techniques including fluorescence, confocal and super-resolution (SIM, STED) microscopy. The project is supported by funding from the Grant Agency of the Czech Republic.

Candidate profile: M.Sc. (Mgr.) degree or equivalent in molecular/cellular biology or biochemistry, good English, independent thinking, strong interest in basic research and experimental work, dedication to learn and develop new techniques.

Laboratory of Cancer Biology

http://www.img.cas.cz/research/vladimir-korinek-biocev/

Ph.D. in Cancer Biology Lab

Project Title: Regulated protein degradation in cancer development and therapy.

Supervisor: Lukáš Čermák (lukas.cermak@img.cas.cz)

Project description: The aim of the study is to characterize novel substrates of Cullin-dependent ubiquitin ligases and the significance of their degradation in the context of cancer biology and physiology. The intended methodology will include classical biochemical and molecular biology approaches in combination with proteome and genome scale studies, using modern mass-spectrometry analysis and screening methods utilizing CRISPR-mediated genome editing.

Candidate profile: M.Sc. or equivalent in molecular, cell and developmental biology or biochemistry; fluent in English

Suggested reading: Skaar JR, Pagan JK, Pagano M.: Mechanisms and function of substrate recruitment by F-box proteins. Nature Rev Mol Cell Biol. 2013

Cermak L, Pagano et al.: FBXO11 targets BCL6 for degradation and is inactivated in diffuse large B-cell lymphomas. Nature. 2012

Laboratory of Cancer Cell Biology

http://www.img.cas.cz/research/libor-macurek/

PhD position: cell/molecular biology

Project title: New regulators of the G2/M transition in mammalian cells

Supervisor: Libor Macurek (libor.macurek@img.cas.cz)

Project description: Proliferation is essential for life and therefore transition between individual phases of the cell cycle is tightly regulated. This project will focus on functional characterization of newly identified proteins expressed during the G2 phase. The candidate will use molecular biology, microscopic and biochemical techniques to address the function of these proteins in normal G2/M transition and in response to genotoxic stress.

Candidate profile: Eligible candidates should have M.Sc. degree or equivalent in cell/molecular biology or biochemistry and show a deep interest in experimental work. Previous experience with cell culture and basic molecular biology techniques is advantage. Language of the lab is English.

Laboratory of Structural Biology

http://www.img.cas.cz/research/pavlina-rezacova/

Project title: Extending the LEDGF/p75 interactome

Supervisor: Pavlína Řezáčová (pavlina.rezacova@img.cas.cz)

Project description: LEDGF/p75 is an epigenetic reader and an attractive therapeutic target involved in HIV integration and the development of mixed lineage leukemia (MLL) fusion-driven leukemia. Although highly relevant in the light of ongoing LEDGF/p75 drug development, its physiological function is not completely understood. We are seeking highly motivated PhD students that would investigate various aspects linked with both LEDGF/p75 physiological and pathological roles using protein biochemistry, biophysics and structural biology.

Čermáková, K., et al., *Validation and structural characterization of the LEDGF/p75-MLL interface as a new target for the treatment of MLL-dependent leukemia.* Cancer Research, 2014. **74** (18): 5139

Těšina, P., et al., *Multiple cellular proteins interact with LEDGF/p75 through a conserved unstructured consensus motif.* Nature Communications, 2015. **6**: 7968

Laboratory of Transgenic Models of Diseases

http://www.img.cas.cz/research/radislav-sedlacek/

Project title: The role of Cullin-RING ubiquitin ligases (CRL) in tissue regeneration and homeostasis

Supervisor: Jan Prochazka PhD jan.prochazka@img.cas.cz
Co-supervisor: Doc Radislav Sedlacek PhD radislav.sedlacek@img.cas.cz

Aim: The study will be focused on evaluation of the role of Cullin-RING ubiquitin ligase complexes in process of regeneration of epithelial tissues in gastrointestinal tract. The role of CRL complexes in molecular signaling pathways by will be accessed by use of *in-vivo* reporter systems, biochemistry and with the state of art mouse molecular genetics with employing conditional knock out

approaches, lineage tracing experiments and clonal analysis (confetti reporter). Gene ablation with CRISPR/Cas9 technology and organoid culture experiments, transcriptome profiling and advanced non-invasive *in-vivo* imaging have been established in the lab. They will be used for comprehensive study of physiology of epithelial organs in Cullin compromised conditions *in vitro* and *in vivo*.

Candidate profile: Successful candidate should have Master degree in molecular, cell or developmental biology. The person should be experienced in cell cultures, basic microscopy techniques and work with mouse.

Laboratory of RNA Biology

http://www.img.cas.cz/research/david-stanek/

Project title: Formation of nuclear structures

Supervisor: David Staněk (david.stanek@img.cas.cz)

Topic: The main goal is to understand how diverse cellular structures are formed and maintained. The proposed project aims to describe molecular and biophysical mechanisms that underlie formation of membrane-less nuclear structures. This includes studies using advanced microscopy techniques including super-resolution microscopy, biophysical and biochemical analysis of scaffolding proteins and mathematical modeling.

Candidate profile: M.Sc. in molecular, cellular or developmental biology, biochemistry or biophysics

Laboratory of Epigenetic Regulations

http://www.img.cas.cz/research/petr-svoboda/

PhD position - developmental/molecular biology

Project title: Functions of small RNAs in the female germline in mammals

Supervisor: Petr Svoboda (petr.svoboda@img.cas.cz)

Project description: The project will focus on functional analysis of small RNA pathways in the mammalian female germline. The candidate will explore function of small RNAs in oocytes of different mammals, analyze phenotypes of genetically modified mouse models, and will participate in development of a genetically modified hamster model.

Candidate profile: M.Sc. or equivalent in molecular, cell or developmental biology. The minimal requirement is knowledge of basic molecular biology (at least molecular cloning, nucleic acid isolation & RT-PCR), a solid knowledge base in biology, curiosity, and endurance. Previous experience with mice, cell culture (especially oocytes and early embryos), confocal microscopy, genomics or high throughput expression analysis is a major advantage.

Laboratory of Adaptive Immunity

http://www.img.cas.cz/research/ondrej-stepanek/

Project 1
PhD position – Immunological Tolerance

Project title: How Antigens Shape the Action of Regulatory T Cells?

Supervisor: Ondřej Štěpánek (ondrej.stepanek@img.cas.cz)

Project description: After initial training, the student will accomplish an ongoing project concerning the mechanisms of regulatory T cells in preventing type I diabetes in an experimental animal model. In the meantime, the student will initialize a new project focusing on the role of antigenic specificity in the development, homeostasis, and function of regulatory T cells. This project will use a variety of approaches including extensive in vivo experiments, multicolor flow cytometry, DNA cloning, expression analysis, and single cell techniques.

Offer: We can offer enthusiastic environment of a newly established research lab with strong international connections and sufficient funding. The research focuses on solving emerging questions in current adaptive immunology.

Candidate profile: M.Sc. or equivalent in immunology, cell biology, or human/veterinary medicine or related fields. We are looking for an enthusiastic student with a strong commitment to science, some wet lab experience (e.g. MSc. project), good laboratory practice and ethics. Previous experience with animal models, flow cytometry, and/or methods of molecular biology and biochemistry is an advantage.

Project 2
PhD position – Immune Cell Signaling

Project title: From T cell Signaling to Self-tolerance and Immunocompetence

Supervisor: Ondřej Štěpánek (ondrej.stepanek@img.cas.cz)

Project description: After initial training, the student will accomplish an ongoing project concerning the role of coreceptor-Lck in regulating self-reactivity of CD4 and CD8 populations. In addition, the student will be involved in a new project focusing on T cell receptor triggering, search for chemical modulators of Lck-coreceptor binding, and developing a cell-line based system for modulating the Lck-coreceptor interaction.

Offer: We can offer enthusiastic environment of a newly established research lab with strong international connections and sufficient funding. The research focuses on solving emerging questions in current adaptive immunology.

Candidate profile: M.Sc. or equivalent in immunology, cell biology, biochemistry or related fields. We are looking for an enthusiastic student with a strong dedication to science, good laboratory practice and ethics. Previous experience with flow cytometry, cell culture, and/or animal experiments signaling is an advantage. Candidates experienced in immunology or cell signaling will be given preference.

Project 3
PhD position – Structural Determinants of Adaptive Immunity

Project title: From Receptor Structure to T Cell Fate Decisions

Supervisor: Ondřej Štěpánek (ondrej.stepanek@img.cas.cz)

Project description: After initial training, the student will accomplish an ongoing project concerning the origin of 'virtual' memory T cells. In the mean time, the student will initialize a multidisciplinary project focused on how TCR structure determines antigen recognition. This project will use a variety of approaches including TCR cloning, deep sequencing, single cell methods, structural studies, and bioinformatics.

Offer: We can offer enthusiastic environment of a newly established research lab with strong international connections and sufficient funding. The research focuses on solving emerging questions in current adaptive immunology.

Candidate profile: M.Sc. or equivalent in immunology, molecular biology, biochemistry, structural biology, biophysics, or related fields. We are looking for an enthusiastic student with a strong dedication to science, some research experience (e.g. MSc. project), good laboratory practice and ethics, good sense for numbers, and excellent analytical skills. An ideal candidate has a relatively strong background in quantitative approaches and at least limited experience with biological experiments or vice versa. Previous experience with flow cytometry, methods of molecular biology and biochemistry, structural biology, quantitative biology and/or analysis of large datasets is an advantage.

Laboratory of Cell Motility

http://www.img.cas.cz/research/vladimir-varga/

Project 1
PhD positions – cell biology/biochemistry

Project title: Identification and characterization of flagellar tip proteins in *Trypanosoma brucei*

Supervisor: Vladimir Varga (vladimir.varga@img.cas.cz)
Project description: The project will focus on identification of flagellar tip proteins in the parasitic protozoan *Trypanosoma brucei* using biochemical approaches. Functions of the identified proteins in

flagellum biology will be addressed using mutant cell lines allowing for inducible depletion of individual proteins. Resulting phenotypes will be studied by means of light and electron microscopy.

Candidate profile: M. Sc. or equivalent in cell biology, biochemistry or parasitology. Knowledge of basic molecular biology and biochemistry techniques (PCR, cloning, cell fractionations) and high motivation are required. Experience in handling microorganisms, mass spectrometry or electron microscopy would be advantageous.

Project 2
Project title: Identification and characterization of mammalian ciliary tip proteins

Supervisor: Vladimir Varga (vladimir.varga@img.cas.cz)

Project description: The project will focus on identification of proteins at tips of motile and primary cilia. The identified proteins will be further studied for their precise localization and cellular functions. For this purpose tissue culture cell lines depleted of the proteins will be created.

Candidate profile: M. Sc. or equivalent in cell biology or biochemistry. Knowledge of basic molecular biology and biochemistry techniques (PCR, cloning, cell fractionations) and high motivation are required. Experience in mammalian tissue cultures, immunoprecipitations or mass spectrometry would be highly advantageous.

Project 3
Project title: Expression, purification and biochemical characterization of flagellar proteins

Supervisor: Vladimir Varga (vladimir.varga@path.ox.ac.uk)

Project description: The project will focus on purification of flagellar and other cytoskeletal proteins from various expression systems. Subsequently, the proteins will be characterized using variety of biochemical approaches including cutting edge single-molecule microscope-based techniques.

Candidate profile: M. Sc. or equivalent in cell biology or biochemistry. Knowledge of basic molecular biology techniques (PCR, cloning), some experience with biochemical approaches for protein expression and purification and high motivation are required.

Laboratory of Germ Cell Development
http://www.img.cas.cz/research/zdenek-trachtulec/

Supervisor: Zdeněk Trachtulec (zdenek.trachtulec@img.cas.cz)

PhD project: Analysis of the relationship between the *Prdm9* gene alleles and low copy number repeat variation in fertile mice and rat, as well as in various models of reduced fertility. The applied methods will include: fertility phenotyping (dissections, sperm count and malformation assays,

fluorescent microscopy (cytology and histology of testes and ovaries)), genotyping, gene expression analyses.

Research Topic: The PRDM9 protein is an epigenetic factor important for both male and female fertility that determines the sites of meiotic recombination. PRDM9 variants contribute to non-allelic homologous recombination leading to genomic disorders and were found in sterile men. We identified mouse *Prdm9* as the first vertebrate hybrid sterility gene. *Prdm9* participates in our mouse models of complete sterility (azoospermia), time-dependent (semi)sterility (shortened reproductive age), reduced sperm count, and sperm malformations (oligoteratozoospermia), and mild meiotic arrest. Spermatogenesis of the semisterile mice might be affected by copy-number variation introduced by some transgenes due to non-allelic recombination.

Candidate profile: M.Sc. or equivalent in molecular genetics (molecular biology), active English