

## Open PhD positions at the Institute of Molecular Genetics of the ASCR, v. v. i. for Academic Year 2018/2019

<http://www.img.cas.cz/education/phd-programme/>

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### Laboratory of Genome Integrity

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

#### Project 1

**Project title:** The role of Promyelocytic leukemia protein in ribosomal stress

**Group leader:** Jiri Bartek

**Supervisor:** Pavla Vasicova ([pavla.vasicova@img.cas.cz](mailto:pavla.vasicova@img.cas.cz))

**Project description:** A dysbalance in ribosomal biogenesis (ribosomal stress) is converted to inhibition of the cell cycle with p53 playing the key regulatory role. Upon several treatments known to cause the ribosomal stress following by the stabilization of p53 is promyelocytic leukemia protein (PML) relocalizes on the surface of the nucleolus [1, 2]. PML is considered a tumour suppressor partly by its participation in effector stages of DNA damage response and repair. Besides "interstitial" DNA damage, PML is involved in telomere maintenance, damage sensing and repair and alternative telomere lengthening but its role in ribosomal stress has not yet been described.

The aim of the project is to decipher the functional role of PML in ribosomal stress employing normal and cancer cell cultures as experimental model. The specific aims include to unravel the mechanism of regulation of PML localization to nucleolar surface, to identify PML interaction partners on nucleolar surface, to analyze posttranslational modifications of PML and its partners and to compare the PML wild type and PML knock-out cells in several functional tests. The molecular and cell biology methods and techniques such a cloning, site-directed mutagenesis, transfections, RNA interference, indirect immunofluorescence, immunoblottings, immunoprecipitation, and mass spectrometry will be used.

1. Condemine W, Takahashi Y, Le Bras M and de The H. A nucleolar targeting signal in PML-I addresses PML to nucleolar caps in stressed or senescent cells. *J Cell Sci.* 2007; 120(Pt 18):3219-3227.
2. Janderova-Rossmeslova L, Novakova Z, Vlasakova J, Philimonenko V, Hozak P and Hodny Z. PML protein association with specific nucleolar structures differs in normal, tumor and senescent human cells. *J Struct Biol.* 2007; 159(1):56-70.

#### Project 2

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

**Group leader:** Jiri Bartek

**Supervisor:** Pavel Janscak ([pavel.janscak@img.cas.cz](mailto:pavel.janscak@img.cas.cz))

**Co-supervisor:** Jana Dobrovolna ([jana.dobrovolna@img.cas.cz](mailto:jana.dobrovolna@img.cas.cz))

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**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.

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## Laboratory of Molecular Pharmacology

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

**Project title:** Novel mechanism of Cannabinoid Receptor 1 regulation by SGIP1

**Group leader:** Jaroslav Blahos

**Supervisor:** Jaroslav Blahos ([jaroslav.blahos@img.cas.cz](mailto:jaroslav.blahos@img.cas.cz))

**Project description:** Cannabinoid receptor 1 (CB1R) is central molecule of endocannabinoid signaling in brain. CB1R is also a target for marijuana, and prospectively for novel medicaments for treatment of pain, energy balance disorders, or certain mental conditions. Precise description of the receptor function, and its regulation is required for further progress in drug design. Recently, we discovered that CB1R function is influenced by interaction with SGIP1 (Hajkova et al. 2016). Molecular mechanism of the effect that SGIP1 exerts on CB1R, and other neurotransmitter systems, namely opioid signaling, will be explored using molecular biology, mice models, protein chemistry, and tools including fluorescent energy transfer, high resolution microscopy.

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## Laboratory of Leukocyte Signalling

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

**PhD position – immunology**

**Project title:** Regulation of inflammatory response by membrane adaptor proteins

**Group leader:** Tomas Brdicka

**Supervisor:** Tomas Brdicka ([tomas.brdicka@img.cas.cz](mailto:tomas.brdicka@img.cas.cz))

**Project description:** The project will focus on explaining the mechanisms contributing to the development of autoinflammatory disease in animals carrying mutations in adaptor protein PSTPIP2. The candidate will explore the molecular mechanisms of how PSTPIP2 suppresses inflammatory signalling in neutrophils and other leukocytes of myeloid lineage and how the disease develops when this protein is mutated or absent. The project will include analysis of leukocyte development, migration, immune response and signalling pathways using genetically modified mouse models and

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cell lines. The disease closely resembles several human autoinflammatory bone disorders and the relevance of the results obtained within this project for human autoinflammatory disease will also be studied. In addition, the candidate will be involved in projects exploring function of other adaptor proteins involved in the regulation of leukocyte signalling 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 related field of life sciences. The applicant must have a strong interest in immunology and related biomedical sciences. Ability to communicate in English is required.

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## Laboratory of Signal Transduction

<http://www.img.cas.cz/research/petr-draber/>

**Two projects** will be opened and focused on the role of ORMDL proteins in cell physiology

**Group leader:** Petr Draber

**Supervisor:** Petr Draber ([petr.draber@img.cas.cz](mailto:petr.draber@img.cas.cz))

Two highly motivated PhD students will solve interconnected projects on the role of ORMDL proteins in cell physiology.

The **1<sup>st</sup> project** will focus on analysis of mice, which were recently prepared in our laboratory and which are deficient in ORMDL-3. Various methods, including passive systemic anaphylaxis, histopathology, histochemistry, and mast cell activation assays will be used to determine functions of ORMDL-3 under *in vivo* and *in vitro* conditions.

The **2<sup>nd</sup> project** will focus on interaction partners of ORMDL-3 proteins, namely those, which are associated with endoplasmic reticulum signalosomes in nonactivated and activated cells. Cultured bone marrow-derived mast cells and distinct mast cells populations will be isolated from wild-type or ORMDL-3 knock-out mice and examined in various tests to determine the role ORMDL-3 protein and its partners in immunoreceptor signaling. Interaction partners of ORMDL-3 protein will be identified by mass spectrometry after pull-down of ORMDL proteins from cell lysates. Emphasis will be also put on gene expression profiling in wild type and ORMDL-deficient cells.

**Background.** A family of widely expressed ORM-like (ORMDL) proteins has been recently linked to asthma and some other inflammatory diseases in genome-wide association studies in humans. ORMDL isoforms (ORMDL-1, -2, and -3) are small (17.5 kDa) endoplasmic reticulum membrane proteins that are highly conserved from yeasts to mammals. They play roles as negative regulators of sphingolipid biosynthesis, in unfolded protein response, and in homeostasis of calcium signaling (reviewed in Paulenda and Draber, *Allergy*, 71: 918-930, 2016). Recently, we found that ORMDL-3 protein in mast cells is a negative regulator of the high-affinity IgE receptor signaling (Bugajev et al., *Cell. Mol. Life Sci*, 73: 1265-1285, 2016).

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## Laboratory of Mouse Molecular Genetics

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

**PhD position – focused on meiosis and germ cells**

**Group leader:** Jiri Forejt

**Supervisor:** Jiri Forejt ([jjiri.forejt@img.cas.cz](mailto:jjiri.forejt@img.cas.cz))

**Location :** BIOCEV, Institute of Molecular Genetics, Vestec , Czech Republic

Student will be working in the team of Professor Jiří Forejt investigating the mechanism of infertility of hybrids between closely related species.

### We expect

- A background in molecular genetics.
- A Master's degree in relevant field.
- Good English communication and interpersonal skills.
- Enthusiasm and creativity.

### We welcome

Qualification in cell biology and genomics, such as immunofluorescence, genetic transformation, immunoprecipitation, two -hybrid systems, cultivation techniques, genomics including data assembly, genome annotation, methods of comparative genomics.

### We offer

- An international and vibrant working environment.
- Part-time (0.7) position since September 2018.
- Good quality start into your next scientific carrier (see the publications bellow).

The following selected publications of the group show the quality of research and participation of PhD students in the projects (bold font):

**Mihola, O.**, Trachtulec, Z., Vlcek, C., Schimenti, J.C., Forejt, J.: A mouse speciation gene encodes a meiotic Histone H3 methyltransferase. *Science*, 323:373—375, 2009.

**Dzur-Gejdošová, M., Simecek, P.**, Gregorova, S., Bhattacharyya, T., Forejt, J.: Genetic architecture of hybrid sterility in the house mouse. *Evolution*, 66: 3321–3335. 2012.

**Bhattacharyya, T.**, Gregorova, S., Mihola, O., Anger, M., Sebestova, J., Denny, P., Simecek, P., Forejt, J.: Mechanistic Basis of male infertility in Mouse Interspecific Hybrids. *Proc Natl Acad Sci U S A*. Feb 5;110(6):E468-77, 2013.

**Bhattacharyya, T.**, Reifova, R, Gregorova, S., Simecek P., Gergelits V., Mistrik, M., Martincova, I., Pialek, J., Forejt, J.: X Chromosome Control of Meiotic Chromosome Synapsis in Mouse Inter-Subspecific Hybrids. *PLoS Genetics* 10(2):e1004088, 2014.

**Balcova M, Faltusova B, Gergelits V**, Bhattacharyya T, Mihola O, Trachtulec Z, Knopf C, Fotopulosova V, Chvatalova I, Gregorova S, Forejt J. Hybrid Sterility Locus on Chromosome X Controls Meiotic Recombination Rate in Mouse. *PLoS Genet*. Apr 22;12(4):e1005906. 2016

Forejt J. Genetic: Asymmetric breaks in DNA cause sterility. *Nature* 530:167-8. 2016.

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## Laboratory of Integrative Biology

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

### Project 1

**Project title:** The role of extracellular matrix stiffness and composition in development of liver fibrosis

**Group leader:** Martin Gregor

**Supervisor:** Markéta Jirouskova ([marketa.jirouskova@img.cas.cz](mailto:marketa.jirouskova@img.cas.cz))

**Co-supervisor:** Martin Gregor ([martin.gregor@img.cas.cz](mailto:martin.gregor@img.cas.cz))

**Project description:** Liver fibrosis is excessive scarring process resulting from chronic insults of heterogenous etiology. The major hallmark of liver fibrosis is deposition of fibrous extracellular matrix (ECM) synthesized mainly by hepatic stellate cells (HSCs). The major goal of this project is analysis of interplay between HSCs and altering ECM niche, using newly developed mouse model harboring HSCs with compromised ECM-receptor signaling. This phenomena will be then studied in vitro, using human HSC line and mouse primary HSCs to better understand the processes regulating deposition and composition of ECM in liver fibrosis.

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

**Candidate profile:** We are seeking outstanding self-motivated candidates with master's degree in molecular biology, physiology, 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.

### Project 2

**Project title:** Cytoskeleton-dependent regulation of liver stem cells

**Group leader:** Martin Gregor

**Supervisor:** Martin Gregor ([martin.gregor@img.cas.cz](mailto:martin.gregor@img.cas.cz))

**Project description:** Quiescent liver stem cells are activated upon liver injury to restore damaged liver tissue. The ongoing project is focused on understanding how cytoskeletal cytoarchitecture regulates liver stem cells in biliary tract. Successful candidate will analyze established mouse models and CRISPR/Cas9 knockout cell lines. This project will use standard as well as advanced microscopy techniques, cell biology methods and biochemical analysis of signaling pathways.

**Candidate profile:** We are seeking outstanding self-motivated candidates with master's degree in molecular biology, physiology, 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.

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## Laboratory of Viral and Cellular Genetics

<https://www.img.cas.cz/research/jiri-hejnar/>

**Project title:**

**Group leader:** Jiri Hejnar

**Supervisor:** Jiri Hejnar ([jiri.hejnar@img.cas.cz](mailto:jiri.hejnar@img.cas.cz))

**Project description:** It will be added soon.

**Candidate profile:**

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## Laboratory of Biology of the Cell Nucleus

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

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

**Group leader:** Pavel Hozak

**Supervisor:** Pavel Hozak ([pavel.hozak@img.cas.cz](mailto: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 signaling. 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.

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## IMG – Laboratory of Cancer Biology (BIOCEV)

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

**Project title:** Regulated protein degradation in cancer development and therapy.

**Group leader:** Vladimir Korinek

**Supervisor:** Lukas Cermak ([lukas.cermak@img.cas.cz](mailto: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

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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. The project will be supported by recently awarded funding from the Grant Agency of the Czech Republic.

**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

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## Laboratory of Cell and Developmental Biology

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

**Project title:** Adult somatic stem cell niche: a crossroad between tissue renewal and cancer

**Group leader:** Vladimir Korinek

**Supervisor:** Tomas Valenta ([tomas.valenta@imls.uzh.ch](mailto:tomas.valenta@imls.uzh.ch))

**Project description:** The crucial feature of stem cells is their ability to self-renew and develop into the cell types constituting tissues. Intestinal epithelial stem cells (IESCs) represent the paradigm of somatic stem cells that maintain tissue homeostasis throughout life to fulfil proper functions of the intestine. Wnt signaling plays a pivotal role in the homeostasis of the intestinal epithelium by promoting renewal of stem cells. Encompassed by the term “Wnt signaling” is a diverse collection of signal branches differing in the network of their downstream signaling cascades. The  $\beta$ -catenin-dependent branch is well known to be essential for the maintenance of undifferentiated IESCs. Importantly, deregulated Wnt/ $\beta$ -catenin signaling is implicated in intestinal cancer. Despite more than two decades of research, the cells that secrete Wnt ligands and thus trigger Wnt signaling in IESCs have been determined just recently and are only partially characterized. We showed that these cells are essential for the proper intestinal homeostasis by constituting stem cell niche-supporting IESCs. Interestingly, besides Wnt ligands activating Wnt/ $\beta$ -catenin outputs, these niche cells also secrete Wnts connected to  $\beta$ -catenin-independent roles.

What is the role of such  $\beta$ -catenin-independent outputs for intestinal homeostasis, regeneration, and intestinal cancer is the focus of the proposed PhD project. An important part of the research will be directed to studying the complex interactions between the stem cell niche and IESCs, not only in the light of Wnt signaling. The curiosity and effort of the PhD candidate will be directed to uncovering how the fate of adult stem cells is controlled, either intrinsically or by interactions with surrounding niche cells, and what are the molecular mechanisms changing healthy stem cells to cancer-initiated cells or whether such a change can be reverted.

The research will combine working with mouse models, tissue organoids, and primary cell lines with utilization of the CRISPR/Cas9, immunohistochemistry, flow cytometry and next generation sequencing techniques.

This is a dynamic and exciting research area, and we welcome motivated researchers to join us in this important quest.

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**Further reading:**

Valenta, T. *et al.* Wnt ligands secreted by subepithelial mesenchymal cells are essential for the survival of intestinal stem cells and gut homeostasis. *Cell Rep* 15, 911-918, (2016).

Krausova, M., Korinek, V. Wnt signaling in adult intestinal stem cells and cancer. *Cell Signal.* 26(3), 570-9, (2014).

Valenta T., *et al.* The many faces and functions of  $\beta$ -catenin. *EMBO J.* 31(12),2714-36, (2012).

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## Laboratory of Transcriptional regulation

<http://www.img.cas.cz/research/zbynek-kozmic/>

### Project 1

**Project title:** Evolution of eyes and photoreceptors

**Group leader:** Zbynek Kozmik

**Supervisor:** Zbynek Kozmik ([kozmic@img.cas.cz](mailto:kozmic@img.cas.cz))

**Project description:** Position is available in the area of evolutionary developmental biology (evo-devo). Project will focus on molecular mechanisms underlying the evolution of animal photoreceptors and eyes. Functional role of genes and gene regulatory networks will be studied in selected animal models currently available in the laboratory such as the zebrafish, medaka fish and marine invertebrates amphioxus and annelid worm *Platynereis* ('a living fossil'). The methods used will include bioinformatics, gene isolation, gene knockouts using Crispr/Cas9 system, transgenesis, gene expression studies by whole-mount in situ hybridization and immunohistochemistry. Next generation sequencing based transcriptome data will be collected and analysed in order to provide insight into evolution of specific cell types of animal eyes.

We offer full-time employee position in the enthusiastic team, well equipped research environment, open possibilities for international collaborations and sufficient funding.

**Candidate profile:** Eligible candidates should have M.Sc. or equivalent in molecular, cell, developmental, evolutionary biology or biochemistry. We seek self-motivated candidates with an interest in evolutionary developmental biology and with a strong commitment to experimental work. The most important assets of suitable candidates are the willingness to learn and to work hard.

### Project 2

**Project title:** Analysis of enhancer function and enhancer evolution

**Group leader:** Zbynek Kozmik

**Supervisor:** Zbynek Kozmik ([kozmic@img.cas.cz](mailto:kozmic@img.cas.cz))

**Project description:** Position is available in the area of gene regulation, developmental biology and evolutionary developmental biology. Project will focus on function of enhancers in gene regulation, molecular dissection of enhancer activity and enhancer evolution. Special attention will be paid to the question of how regulatory information encoded in invertebrate (amphioxus) enhancers becomes interpreted in the context of heterologous vertebrate species (fish). The methods used will include bioinformatics, enhancer identification and isolation, reporter gene transgenesis, site-

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directed mutagenesis of enhancers coupled to transgenic reporter gene assays and enhancer knockouts in the context of the entire organism using Crispr/Cas9 system.

We offer full-time employee position in the enthusiastic team, well equipped research environment, open possibilities for international collaborations and sufficient funding.

**Candidate profile:** Eligible candidates should have M.Sc. or equivalent in molecular, cell, developmental, evolutionary biology or biochemistry. We seek self-motivated candidates with an interest in gene regulation and with a strong commitment to experimental work. The most important assets of suitable candidates are the willingness to learn and to work hard.

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## IMG - Laboratory of Eye Biology (BIOCEV)

<http://www.img.cas.cz/research/zbynek-kozmic-biocev/>

### Project 1

**Project title:** The role of transcription factors in normal mouse eye development

**Group leader:** Zbynek Kozmik

**Supervisor:** Zbynek Kozmik ([kozmic@img.cas.cz](mailto:kozmic@img.cas.cz))

**Project description:** Position is available in the area of developmental biology. Project will focus on the role of transcription factors in vertebrate eye development using laboratory mouse as a model system. The methods used will include gene knockouts using Cre/loxP and Crispr/Cas9 technologies, gene expression studies of mutant mice by in situ hybridization, immunohistochemistry and RNA-seq. Gene regulatory networks will be interrogated using a combination of transcriptomics, chromatin immunoprecipitation and reporter gene assays in cell lines and transgenic mice.

**Candidate profile:** Eligible candidates should have M.Sc. or equivalent in molecular, cell and developmental biology or biochemistry. We seek candidates with strong interest in experimental work using laboratory mice as a model. The most important assets of suitable candidates are the willingness to learn and to work hard.

### Project 2

**Project title:** Genetically modified mice as models of inherited human eye diseases

**Group leader:** Zbynek Kozmik

**Supervisor:** Zbynek Kozmik ([kozmic@img.cas.cz](mailto:kozmic@img.cas.cz))

**Project description:** Positions is available in the area of developmental biology and biomedicine. Project will focus on the role of transcription factors in human eye development using laboratory mouse as a model system. To get insight into the role of specific transcription factors in humans, genetically modified mice will be generated in order to produce animal models of inherited human eye diseases. The methods used will include a highly specific gene modification of mouse genome by Crispr/Cas9 technology followed by phenotypic and molecular analysis.

**Candidate profile:** Eligible candidates should have M.Sc. or equivalent in molecular, cell and developmental biology or biochemistry. We seek candidates with strong interest in experimental

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work using laboratory mice as a model. The most important assets of suitable candidates are the willingness to learn and to work hard.

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## Laboratory of Cancer Cell Biology

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

**Two projects will be opened**

**Group leader:** Libor Macurek

**Supervisor:** Libor Macurek ([libor.macurek@img.cas.cz](mailto:libor.macurek@img.cas.cz))

**Team description:** In Laboratory of Cancer Cell Biology at Institute of Molecular Genetics in Prague, we use human cells and mouse models to study cellular responses to DNA damage. We strive to understand how genome integrity is protected in healthy cells and how defects in these pathways contribute to cancer development.

### Project 1

**Project title:** The role of Wip1 phosphatase in DNA damage response

**Project description:** Protein phosphatase PPM1D/WIP1 is a negative regulator of the tumour-suppressor p53 and controls termination of the DNA damage response. Amplification of the PPM1D locus or C-terminal truncation of PPM1D promotes breast and ovarian cancer. This project will focus on investigation of molecular mechanisms that control Wip1 function as well as unrevealing new modes of Wip1 action.

### Project 2

**Project title:** The role of PLK3 kinase in cell proliferation and response to genotoxic stress

**Project description:** Protein kinases of the Polo-like family are involved in many events of nuclear and cell division. The project will focus on the least explored member of this kinase family, PLK3 that is involved in other cellular functions including DNA repair. Role of PLK3 will be studied using CRISPR/Cas9 mediated gene editing and ATP-analogue sensitive mutants allowing selective inhibition of PLK3.

**Candidate profile:** We seek two new PhD students to join our young international team located in Prague, Czech Republic. We are especially interested in candidates with strong background in biochemistry, molecular biology and/or cancer biology and with enthusiasm for basic science. For Project 2, previous experience with protein kinases will be considered as advantage.

**Suggested reading:**

Jaiswal et al., ATM/Wip1 activities at chromatin control Plk1 re-activation to determine G2 checkpoint duration. *EMBO J.* 2017; 36:2161-2176.

Kleiblova et al., Gain-of-function mutations of PPM1D/Wip1 impair the p53-dependent G1 checkpoint. *J Cell Biol.* 2013; 201:511-21.

Pechackova et al., Inhibition of WIP1 phosphatase sensitizes breast cancer cells to genotoxic stress and to MDM2 antagonist nutlin-3. *Oncotarget.* 2016; 7:14458-75.

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Macůrek et al., Wip1 phosphatase is associated with chromatin and dephosphorylates gammaH2AX to promote checkpoint inhibition. *Oncogene*. 2010; 29:2281-91.

Benada et al., Polo-like kinase 1 inhibits DNA damage response during mitosis. *Cell Cycle*. 2015; 14:219-31.

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## Laboratory of Structural Biology

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

**Project title:** Extending the LEDGF/p75 interactome

**Group leader:** Pavlina Maloy Rezacova

**Supervisor:** Pavlina Maloy Rezacova ([pavlina.rezacova@img.cas.cz](mailto: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. The aim of the master thesis will be investigation of various aspects linked with both LEDGF/p75 physiological and pathological roles using protein biochemistry, biophysics and structural biology.

**Keywords:** epigenetics, leukemia, protein complexes, biophysics, 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

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## Laboratory of Adaptive Immunity

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

**Project title:** Molecular mechanisms of the assembly and function of BBSome

**Group leader:** Ondrej Stepanek ([ondrej.stepanek@img.cas.cz](mailto:ondrej.stepanek@img.cas.cz))

**Supervisor:** Martina Huranova ([martina.huranova@img.cas.cz](mailto:martina.huranova@img.cas.cz))

**Project description:** BBSome is a protein complex which facilitates transport of various signaling receptors into and from a primary cilium. BBSome consists of eight subunits and loss-of-function mutations of any of these subunits leads to a multi-organ disease, Bardet-Biedl Syndrome.

We are studying mechanisms of BBSome function as well as its potential role in the immune system. We established a set of research tools including: a genetic mouse model of Bardet-Biedl Syndrome, BBSome-deficient cell lines, stable cell lines with BBSome subunits and BBSome cargoes tagged with fluorescent proteins, tools for detection of BBS gene products on protein and RNA level, assays for the analysis of signaling pathways regulated by the BBSome, and a database of diagnostic data of Bardet-Biedl Syndrome patients.

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We are currently looking for a motivated PhD candidate who will uncover the mechanisms of BBSome assembly and function. The candidate will use CRISPR-Cas9 and retroviral techniques to genetically manipulate model cell lines and analyze them by biochemical methods and advanced microscopy techniques.

We can offer enthusiastic, well-equipped research environment and sufficient funding. The research focuses on solving emerging questions in cell and developmental biology.

**Candidate profile:** M.Sc. or equivalent in cell biology, molecular biology or related fields. We are looking for a highly motivated and enthusiastic student with a strong commitment to science, wet lab experience (e.g. MSc. project), good laboratory practice and ethics. Previous experience with cell cultures, animal models, fluorescence microscopy, and/or methods in molecular/cell biology and biochemistry is an advantage.

We encourage candidates to contact us directly prior to the PhD Interviews.

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## Laboratory of Developmental Biology

<http://www.iem.cas.cz/en/research/departments/developmental-biology/index.html>

**Project title:** Transcriptional regulation during differentiation of the neural crest cells

**Group leader:** Ondrej Machon

**Supervisor:** Ondrej Machon ([ondrej.machon@img.cas.cz](mailto:ondrej.machon@img.cas.cz))

**Project description:** Our team studies developmental processes in the mouse embryo. The project will focus on transcriptional regulation during differentiation of the neural crest cells that generate a wide variety of cell types spanning from the bone and cartilage, pigment cells, neurons or smooth muscles. Such a broad differentiation potential is ensured by a precise control of transcription of cell type specifying genes. The project will study phenotypic changes in mouse embryos in which transcription factors of Meis family are inactivated in the neural crest cells by conditional knock-out technology Cre-loxP. These mouse mutants have been recently produced in our lab and they display numerous severe defects in derivatives of the neural crest including craniofacial defects, cranial nerves and muscles. However, a detailed mechanism of gene regulatory network underlying these phenotypic changes is still to be uncovered. The student will analyze changes in gene expression by genome-scale expression analysis (Illumina, RNA seq, ChIP seq) and verify target genes of transcription factors Meis in mouse or zebrafish embryos. This project will surely be attractive to students who are interested in developmental biology.

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*In case, you might have still some doubts concerning the PhD programme at IMG, please, do not hesitate to contact me, Katerina Solcova ([katerina.solcova@img.cas.cz](mailto:katerina.solcova@img.cas.cz)), a PhD Administrator at IMG, Prague.*

OR you will find more information here: <https://www.img.cas.cz/education/phd-programme/>

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