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 hemato-oncology

http://www.img.cas.cz/research/meritxell-alberich-jorda/

Project title: Mechanisms regulating leukemic stem cells: role of the β-catenin/Tcf signaling pathway
Supervisor: Meritxell Alberich-Jorda (alberich@img.cas.cz)

Project description: The project will focus on the role of the β-catenin/Tcf signaling pathway in maintenance and self-renewal of leukemic stem cells (LSC). LSC possess limitless self-renewal and are responsible for maintenance of leukemia. Understanding the mechanisms that control LSC in disease is critical for the design of novel therapeutic strategies in cancer. In the present proposal the Ph.D candidate will employ murine leukemic models to determine the role of the β-catenin/Tcf signaling pathway in disease initiation and progression. The project will include assays such as in vitro clture of LSC, in vivo bone marrow transplantation assays, lentiviral production, primary cell transductions, flow cytometry analysis and sorting, and drug treatment *in vitro* and *in vivo*.

Candidate profile: The candidate should hold a master degree in genetics, molecular biology, cell biology, or in a related field. The candidate should be highly motivated and enthusiastic, and willing to work with murine models. Excellent English is required. We offer a friendly and supporting environment in a state-of-the-art institution with international collaborations.

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: Zebrafish models for normal and malignant hematopoiesis
Supervisor: Petr Bartůněk (bartunek@img.cas.cz)

Project description: This project aims at understanding the molecular mechanisms underlying cell fate determination and differentiation of blood cell progenitors as well as studying processes involved in cell transformation of leukemic cells. The candidate will further develop ex vivo and in vivo techniques and employ already established methods like hematopoietic cell transplantation, embryo microinjection, in situ hybridization, immunohistochemistry, flow cytometry, RNAseq, ChIPseq and advanced live animal imaging including light-sheet microscopy.

References: Svoboda et al. Blood. 2014; 124(2):220-8, Svoboda et al. Nat Protocols. 2016; 11(5):1007-20.

Candidate's profile (requirements): MSc or equivalent in cell and/or developmental biology.

Project 2

Project title: Zebrafish models of human cancer
Supervisor: Petr Bartůněk (bartunek@img.cas.cz)

Project description: This project will focus on establishment of new models of human cancer and will aim at understanding the process of tumor initiation, propagation and spreading in vivo. This knowledge will be used to design therapeutical strategies that will be further tested in zebrafish. The candidate will employ established methods and techniques like

embryo microinjection, tumor cell transplantation, drug treatment, high-throughput microscopy, whole body and MALDI imaging.

Candidate's profile (requirements): MSc or equivalent in cell and/or developmental biology.

Laboratory of Molecular Pharmacology
http://www.img.cas.cz/research/jaroslav-blahos/

Project title: Novel mechanism of Cannabinoid Receptor 1 regulation by SGIP1
Suprevisor: Jaroslav Blahoš (jaroslav.blahos@img.cas.cz)

Project description: We plan to open position for Ph.D. students in a project of Cannabinoid Receptor 1 regulation by molecular partner SGIP1. This molecule was discovered in our lab as an interacting partner of the receptor. This interaction has profound effect on the receptor signaling. The techniques planned will combine DNA recombination, protein chemistry, pharmacological functional tests of various intracellular signaling pathways, cell biology tools including fluorescence microscopy, TIRF, BRET and FRET.

Laboratory of Leukocyte Signalling
http://www.img.cas.cz/research/tomas-brdicka/

PhD position – immunology

Project title: Regulation of leukocyte signalling by membrane adaptor proteins
Supervisor: Tomas Brdicka (tomas.brdicka@img.cas.cz)

Project description: The project will focus on the regulation of myeloid cell signalling by adaptor protein PSTPIP2. This protein is a known suppressor of neutrophil inflammatory response and its absence in mice results in autoinflammatory disease similar to several human disorders. The candidate will explore the molecular mechanism of how this protein suppresses inflammatory signalling in neutrophils and other leukocytes of myeloid lineage and how it prevents the development of autoinflammatory disorder. The project will include analysis of leukocyte development, migration, immune response and signalling pathways 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 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.

Laboratory of Mouse Molecular Genetics

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

PhD position – cell/molecular biology

Project title: The role of PRDM9 allelic variation and activity for hybrid sterility in mice
Supervisor: Emil Parvanov (emil.parvanov@img.cas.cz)
Co-suprevisor: Jiří Forejt (jiri.forejt@img.cas.cz)

Project description: Explore the role of the zinc finger array of PRDM9 protein for mouse hybrid steriliy and determine the state of the PRDM9-dependent histone modifications and their relation to hotspot formation and distribution. The study will include the combination of classical genetic crosses, cytological observations, ChIP-seq experiments and so on.

Candidate's profile (requirements): M. Sc. or equivalent in genetics or cell biology. The candidate should have solid background in molecular biology and genetics and basic skills in methods of mouse genetics.

Laboratory of Integrative Biology

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

Project 1
Project title: Intestinal barrier dysfunction and epithelial-immune cell interactions in plectinopathy
Supervisor: Martin Gregor (martin.gregor@img.cas.cz)
Co-supervisor: Alžběta Kalendová (alzbeta.kalendova@img.cas.cz)

Project description: Inflammatory bowel disease (IBD) is characterized by compromised intestinal barrier function in association with excessive activation of the mucosal immune system. Using mouse model of plectinopathy we show that absence of plectin, a highly versatile cytolinker, in intestinal epithelium aggravates experimentally induced colitis and potentiates associated carcinogenesis. The major goal of this project is detailed analysis of molecular mechanism underlying governing role of plectin in intestinal barrier maintenance. In addition, we will study the impact of plectin deficiency on initiation and progression of colorectal cancer. We will further develop mouse model with tissue-specific plectin ablation in myeloid cell lineage and characterize it with respect to plectin-controlled epithelial-immune cell interactions. Understanding the mechanisms involved in the plectin-deficiency-mediated pathogenesis of IBD

and colorectal cancer is necessary to define new targets for disease screening and strategies for its prevention and treatment. 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, 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 cell-cell contacts in simple epithelia
Supervisor: Martin Gregor (martin.gregor@img.cas.cz)

Project description: The ongoing project is focused on understanding how cytoskeletal cytoarchitecture regulates cell-cell contacts (such as tight and adherens junctions, or desmosomes) in simple epithelia of GIT and biliary tracts. Successful candidate will analyze established CRISPR/Cas9 knockout cell lines in 2D and 3D (organoid) cultures. This project will use advanced microscopy techniques (including 3D time-lapse and super-resolution microscopy), biophysical methods and biochemical analysis of signaling pathways. The part of the project is in collaboration with Center for Medical Physics and Technology, Erlangen (traction force microscopy and magnetic tweezers experiments). The project is supported by recently awarded funding.

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

Laboratory of Cellular and Viral Genetics

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

Project title: Functional characterization of avian sarcoma and leukosis virus receptors¨
Supervisor: Daniel Elleder (**elleder@img.cas.cz**)

Topic: Avian sarcoma and leukosis virus (ASLV) served historically as a key model in both virus and cancer research. Our laboratory has long tradition with this model. More recently, we have identified and further characterized some of the cellular receptor molecules employed by the virus for entry into host cells. The current project will aim at elucidating the function that these receptor molecules play in the biology of the chicken cell, and how it impacts the cytopathic effects of the virus infection. The work will be mostly using molecular biology and virology techniques, but will also involve bioinformatic methods (their prior knowledge is not required). We will try to identify selection

pressures exerted during avian evolution on the receptor molecules. We will also try to identify endogenous receptor ligands. Lastly, we will try to identify how new virus subgroups are formed by recombination with chicken endogenous retroviruses. Further reading: 1. J Virol, 2005, 79:10408; 2. J Virol, 2004, 78:13489; 3. Virology, 2006, 344:25; 4. J Virol, 2016, PMID: 27881654; 5. Genome Biology, 2015, 16:164.

Candidate profile: M.Sc. or similar degree in molecular genetics or related field. Highly motivated.

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.

Project 3

Project title: Identifying the interactions of chromatin and the nuclear periphery

Supervisor: Jindřiška Fišerová (jindriska.fiserova@img.cas.cz)

Co-supervisor: Pavel Hozák (hozak@img.cas.cz)

A nuclear periphery involves a nuclear envelope with a lamina tightly attached to the inner nuclear membrane and nuclear pore complexes facilitating nucleocytoplasmic transport. The nuclear periphery plays a crucial role in chromatin organisation, regulation of gene transcription, gene silencing or in mediating the communication between the nucleus and the cytoplasm. The importance of the nuclear periphery is also demonstrated by number of diseases (called envelopathies) resulting from a mutation in genes encoding for one of the peripheral protein such as lamin or emerin. The structure of the nuclear periphery as well as the role of proteins associated with the periphery in the above mentioned processes is fragmentary. This project focuses on those topics and aims to further uncover the biochemical interactions at the nuclear periphery. The PhD project will implement the state-of-the-art imaging techniques including super-resolution (SIM, STED) as well as molecular biology and biochemistry methods for in-depth studies of the role of periphery associated proteins in chromatin organisation.

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

Laboratory of Eye Biology

http://www.img.cas.cz/research/zbynek-kozmik-biocev/

Project title: The role of transcription factors and enhancers in mouse embryonic development

Supervisor: Zbynek Kozmik (kozmik@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 ChIP-seq and reporter gene assays in cell lines and transgenic animals. In addition, genetically modified mice will be generated using CRISPR/Cas9 approach in order to investigate enhancer redundancy (shadow enhancers).

Candidate profile: Eligible candidates should have M.Sc. or equivalent in molecular, cell and developmental biology or biochemistry. We seek candidates with interest in experimental work using laboratory mice as a model.

Laboratory of Transcriptional Regulation

www.img.cas.cz/research-groups/zbynek-kozmik

Project title: Evolution of developmental control mechanisms
Supervisor: Zbynek Kozmik (**kozmik@img.cas.cz**)
Project description: Position is available in the area of evolutionary-developmental biology (evo-devo). Project will focus on animal eye evolution. Evolution of genes and gene regulatory networks will be studied using selected animal models available in the laboratory (zebrafish, amphioxus, annelid worm, cnidaria). The methods used will include bioinformatics, gene isolation, gene expression studies by in situ hybridization, transgenesis and gene knockouts using Crispr/Cas9 system.

Candidate profile: Eligible candidates should have M.Sc. or equivalent in molecular, cell, developmental, evolutionary biology or biochemistry. We seek candidates with independent thinking, strong interest in basic research who are willing to allocate significant amount of their time for experimental work in the wet lab.

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 1
Project title: Elucidation of the biological role of Tiki, Wnt-specific Metalloproteases
Supervisor: Radislav Sedláček (radislav.sedlacek@img.cas.cz)

Project description: The project focuses on TIKI1 and especially TIKI2 (TRABD2A and TRABD2B genes) whose biological role in mammals is still purely understood. TIKIs function as negative regulators of the Wnt signaling pathway, mediating cleavages of N-terminal residues of a subset of Wnt proteins. Phylogenetic analysis shows that Tiki1 and Tiki2 orthologues are highly conserved among vertebrate and mammalian species although the Tiki1 is missing in rodents. The role of Tiki proteases will be studied in mouse and human systems and the work will start with the analysis of our TIKI2 –deficient mice. The aim of this study is to describe the pathophysiologic roles of TIKI2 (TIKI1).

Candidate's profile: M.Sc. (Mgr.) degree or equivalent in molecular/cellular biology or biochemistry, a good command of English, independent thinking but also team player, strong interest in basic research and experimental work, ability to work with animals (rodents – training will be provided).

Laboratory of RNA biology

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

Project title: Evolution of RNA splicing
Supervisor: David Staněk (stanek@img.cas.cz)

Project description: RNA splicing is a crucial step in gene expression during which non-coding introns are removed and exons are joined together. Introns have been found in all eukaryotic organisms but their function and origin remains mysterious. However, recently discovered unicellular marine predators contain new class of introns. This offers a unique opportunity to study a completely unexplored world in the RNA universe and reveal fundamental principles of intron evolution and function. This is a collaborative project with experts on unicellular organisms from the Institute of Parasitology and involves both bioinformatics as well as molecular biology approaches.

Candidate profile: M.Sc. in molecular, cellular or developmental biology, parasitology or bioinformatics.

Laboratory of Adaptive Immunity

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

PhD position in cell biology (with a taste of immunology)

Project 1

Project title: It is troublesome without BBSome
Supervisor: Martina Huranová (**martina.huranova@img.cas.cz**)

Project description: Primary cilium and immunological synapse are related structures. Both organelles concentrate sensory and signaling receptors of multiple signaling pathways. In addition, structural and functional establishment of these structures is dependent on polarized protein transport and remodeling of actin cytoskeleton. Bardet-Biedl syndrome (BBS) is a severe multiorgan disease (ciliopathy) caused by loss-of-function mutations in several BBS related proteins. BBSome is a complex of eight BBS proteins and regulates two key processes during ciliogenesis. First, BBSome transports multiple receptors to the ciliary membrane. Second, BBSome inhibits activity of RhoA GTPase, which regulates F-actin polymerization. The herein project aims to understand how BBSome regulates actin remodeling during ciliogenesis. Second part of the project will focus on the role of BBSome in the formation of the immunological synapse between T cells and antigen-presenting cells. The PhD candidate will analyze BBS4 deficient mice and generate and analyze BBS7 and BBS4 deficient cell lines. The experimental approaches will include fluorescence microscopy and superresolution microscopy, techniques of biochemistry and molecular biology and immunological assays.
Offer: 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.

Project 2

Project title: Track the Tregs
Supervisor: Ondřej Štěpánek (**ondrej.stepanek@img.cas.cz**)

Project description:
Regulatory T cells (Tregs) are crucial players in establishing self-tolerance. However, some aspects of Treg biology are still poorly understood. It is unclear how highly self-reactive T cells decide between

negative selection and Treg conversion in the thymus. The PhD candidate will address the role of Foxp3 transcription factor in this cell-fate decision checkpoint using transgenic animal models. Second part of the project will focus on the analysis of the role of pathogen specific Tregs during infection using monoclonal Tregs and Listeria monocytogenes infection. Third part of the project will analyze the heterogeneity of Treg population in the steady-state and during various disease conditions (infection, cancer, and autoimmunity).

Offer: We can offer enthusiastic environment of a young research team, well-equipped research environment and sufficient funding. The research focuses on solving emerging questions in immunology.

Candidate profile: M.Sc. or equivalent in immunology, cell biology, developmental 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 animal models and immunological research is an advantage.

Project 3

PhD position in cell biology
Project title: Molecular mechanisms of inflammation.
Supervisor: Peter Draber (Peter.Draber@img.cas.cz)

Project description: Inflammation is a principal mechanism of body defense against invading pathogens and its proper mounting is critical for clearing infection. At the same time, the hyper-activation of pro-inflammatory pathways might lead to severe autoimmune disorders and cancer. The initial activation of the immune system requires pro-inflammatory mediators, such as TNF, IL-1, and IL-17. The binding of these cytokines to their receptors on cell surface triggers formation of complicated signaling complexes. Very tight regulation of these complexes is required to ensure adequate activation and termination of inflammatory signaling. However, the precise molecular mechanisms guiding the assembly and activity of these signaling complexes are still largely enigmatic.

At first, the candidate will identify novel components of several pro-inflammatory signaling complexes (including IL-17 receptor signaling complex) using mass-spectrometry analysis. Subsequently, roles of the newly identified components will be studied *in vitro* by analyzing knock-out cell lines generated by Crispr-Cas9 technology. Finally, the candidate will focus on the role of these molecules *in vivo* using animal models. Altogether, the successful candidate should finish her/his PhD study with deep theoretical knowledge in the field of inflammation and be highly skilled to perform up-to-date molecular biology methods and analysis of mouse models.

Candidate profile: M.Sc. or equivalent in cell biology, biochemistry, molecular biology, or a related field. We are looking for a highly motivated and enthusiastic candidate with deep interest in science. Prior laboratory experience is advantageous.

Laboratory of Germ Cell Development

http://www.img.cas.cz/research/zdenek-trachtulec/

Project title:

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

PhD project: Investigation of the relationship between the alleles of some genes and low copy number repeat variation in various mouse and rat models of reduced fertility. The applied methods will include: fertility phenotyping (dissections, sperm count and malformation assays), fluorescent and light microscopy (cytology and histology of testes and ovaries)), genotyping, gene expression analyses.

Research Topic: The PRDM9 (PR-domain 9) 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 rodent models of complete sterility, time-dependent (semi)sterility reduced sperm count, and mild meiotic arrest.

Candidate profile: M.Sc. or equivalent in molecular genetics and/or reproductive biology, experience in work with rodents, basic bioinformatics, active English

Guest group of Genome Dynamics and Neurodegeneration

Project title:

The mechanistic interplay between DNA strand break repair, RNA processing, and human neurological disease

Supervisor: Hana Hanzlikova (h.hanzlikova@sussex.ac.uk)
Co-supervisor: Keith Caldecott (k.w.caldecott@sussex.ac.uk)

Project description:

DNA single-strand breaks (SSBs) are the most frequent DNA lesions arising in cells and are a major threat to cell survival and genetic integrity, as indicated by the elevated genetic deletion, embryonic lethality, and neurological disease observed if single-strand break repair (SSBR) is attenuated[1]. Based on our recent exciting data[2] we will address the extent to which the impact of SSBs extends to other neurodegenerative diseases and to normal human ageing. In addition, the project will address the mechanisms by which SSBs trigger neurodegeneration, and will employ cutting edge techniques in molecular and cellular biology, including genome editing by CRISPR-Cas9 technology. The successful applicant will join a dynamic and well-funded laboratory with training opportunities in laboratories in both Prague and the UK.

An overview of research in the Caldecott lab can be found at www.sussex.ac.uk/lifesci/caldecottlab.

1. Caldecott, K.W. Single-strand break repair and genetic disease. ***Nat. Rev. Genet***. 9, 619–631 (2008).
2. Hoch, N.C., Hanzlikova, H. *et al*. XRCC1 mutation is associated with PARP1 hyperactivation and cerebellar ataxia. ***Nature***. 541(7635), 87-91 (2017)

Candidate's profile (requirements):
The successful applicant will be highly motivated, enthusiastic and willing of working within a multidisciplinary team. Previous experience with methods in molecular and cell biology and biochemistry, eukaryotic cell cultures and fluorescence microscopy will be an advantage.