POSTDOC

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. We seek new colleagues who will join our young team and share with us enthusiasm for basic science. The ideal candidate will have a PhD degree in biology or biochemistry, will be able to communicate in English and think independently. We offer an interesting work in an international team, salary scale based on performance, access to modern equipment in core facilities and benefits for IMG employees. Positions are available for 2 years with possible extension. See below for specification of available projects and do not hesitate to contact Dr. Libor Macurek for further details at macurek@img.cas.cz or Tel: +420 241063210.

Topic I: Defects in DNA damage response as predisposing factors for cancer development

Mutations in genes involved in DNA repair commonly predispose to breast, ovary and other solid tumors. In the same time these mutations influence sensitivity of the tumor to therapy. Besides well-known genes BRCA1/2, PALB2 and CHK2, new variants are now being identified in cancer patients by next generation sequencing approaches. In this project we will study new variants of uncertain significance in genes involved in homologous recombination and other DNA repair pathways and we will evaluate their impact on genome integrity. We will develop reliable cellular models using CRISPR/Cas9 mediated gene editing in human nontransformed cell lines. This project will be performed in collaboration with a clinical department providing unique data from cancer patients. Professional experience with DNA damage response and repair pathways is great advantage.

Topic II: Role of PPM1D/WIP1 phosphatase in oncogenesis using a mouse model

Protein phosphatase PPM1D/WIP1 is a negative regulator of the tumour-suppressor p53 and contributes to termination of the DNA damage response pathway. Truncated form of PPM1D/WIP1 is present in a fraction of patients with breast and colon carcinoma. We observe increased formation of tumours also in a newly established mouse model carrying truncated PPM1D/WIP1. We will use this mouse model to study the role of oncogene-induced senescence in prevention of cancer development. We will also evaluate the impact of truncated PPM1D/WIP1 on behaviour of stem cells and organoids. This project is suitable for a postdoctoral fellow with previous experience with mouse models and cancer biology.

Topic III: Role of PLK3 kinase in cell response to DNA damage and in cell cycle

Protein kinases of the Polo-like family are involved in many events of nuclear and cell division. Project will focus on the least explored member of this kinase family PLK3 that is likely involved in other cellular functions including DNA repair. Role of PLK3 will be studied in nontransformed cells using CRISPR/Cas9 mediated gene editing and using ATP analogue sensitive mutants allowing selective inhibition of PLK3. New substrates will be identified using mass spectrometry using SILAC labeling. We expect that these new approaches of cell/molecular biology will allow discovery of so far unknown functions of PLK3 in human cells. Previous experience with protein kinases, interest in protein-protein interactions and mass spectrometry will be considered as advantage but project is suitable also for fresh graduates.