Téma DSP – akademický rok 2019/2020, zahájení studia jaro 2020

Program: Biomedicínské vědy / Biomedical Sciences

Specializace: Molekulární medicína / Molecular Medicine

Forma studia: prezenční

Pracoviště: Středoevropský technologický institut, Centrum molekulární medicíny, Výzkumná skupina Mikroprostředí imunitních buněk

Školitel: doc. Marek Mráz

Téma: **REGULATION OF BCR SIGNALLING BY DNA DAMAGE RESPONSE AND P53 PROTEIN**

Počet stipendijních míst: 1

Annotation:
PROJECT: We are looking for a motivated PhD student that would like to work on the following project funded by the ERC (European Research Council) Starting grant. The variable clinical course of several B cell malignancies largely depends on p53 functionality and B-cell receptor (BCR) signalling propensity; however, it is unclear if there is any crosstalk between these pathways. We showed for the first time that there is a connection between p53 pathway and regulation of BCR signalling (Cerna et al…Mraz, Leukemia, 2018). We described that DNA damage response (DDR) activation leads to down-modulating the transcriptional factor FOXP1, which functions as a positive BCR signalling. It seems that the low FOXP1 levels limit BCR signalling partially via allowing for upregulation of a CD22 cell-surface, whose intracellular part serves as a docking site for phosphatases that limit BCR activation on the cell membrane. The student will further explore the connection between DNA damage response and the BCR signalling regulation. Additionally, the p53 aberration could also affect the basal levels of CD22/phosphatases, and thus contribute to the "tonic" BCR signalling, and general aggressiveness of the B cells. In vitro studies using Crispr technology and inducible shRNAs for p53 will be conducted. Additionally, we have collected over 100 samples obtained during the administration of chemo-immuno therapy in B-cell chronic lymphocytic leukaemia (CLL) patients, and these can be used to validate the in vitro observations.
Key words: DNA damage, p53, BCR signalling, leukemia, chronic lymphocytic leukemia, B cells
Literature: Cerna et al…Mraz, Leukemia, 2018, Mraz et al., Blood, 2014; Musilova et al…Mraz, Blood, 2018; Mraz and Kipps, 2013, Musilova and Mraz, Leukemia, 2015
WHAT DO WE OFFER:

- modern laboratories, project funded by the prestigious ERC grant = high risk and high gain, state-of-the-art instrument, stable funding, competitive scholarship
- You will work in a team of young investigators that challenge some long standing problems in the field of hematology. We do basic science, but with the objective to help patients in the future (we have access to primary samples with hem. malignancies, and we suggest novel clinical trials).

WHAT WILL YOU LEARN/DO:

- How to think and work independently as a scientist
- Writing of abstracts and papers (and course in grant writing and presentation of data)

- How to present data and will attend conferences to present your research
- You will spend 1-2 months visit(s) in collaborating labs in Europe or US
- Collaboration with experts in wet lab research and bioinformatics
- Novel methods such as Next Generation Sequencing (Illumina) and genome editing (Crispr).
- How to critically analyze scientific data (regular journal clubs)
- Classical methods of molecular biology (e.g. immunoblotting, flow cytometry, qRT-PCR, cell cultures, cloning), and you will use our in vitro models for microenvironmental interactions, and artificial activation/inhibition signalling pathways to decipher the gene regulatory loops.
- You can supervise bachelor and diploma students if interested

HOW TO APPLY:

- To apply please contact the supervisor and submit a CV by email to: marek.mraz@email.cz (Subject: PhD School).

OTHER INFO: The research is funded by ERC grant, and will be conducted at CEITEC MASARYK UNIVERSITY (campus Bohunice). Our laboratory extensively collaborates with the University Hospital Brno in the same campus to obtain primary samples from patients. The campus provides a vibrant, multidisciplinary and highly collaborative scientific environment. The lab is located in Brno, the second-largest city in Czech Republic that has the biggest concentration of biomedical research in the region. Brno is one of the major cultural hubs, with a vibrant and lively atmosphere housing ~60.000 students. The city has a very good public transport and plenty of interesting places to visit within the reach of trains (within small distance of several major cities such as Prague, Vienna, Bratislava, Budapest) and close to international airports.

Požadavky na uchazeče:

- Motivated smart people that have the “drive” to work independently, but also willing to learn from other people in the lab and collaborate.
- Candidates should have a master’s degree in Molecular biology, Biochemistry, or similar field and have deep interest in molecular biology and cancer cell biology.

Informace o školiteli: aktuální informace o školiteli jsou zveřejněny na https://www.ceitec.cz/doc-mudr-mgr-marek-mraz-ph-d/u26692

ceitec.cz/mrazlab