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| | **GL leader** | **Prof. Marek Mráz, MD, PhD** |
| **1** | **CEIPEX RESEARCH TOPIC LEVEL2** | **Molecular Medicine: microenvironment of immune cells** |
| **2** | **RESEARCH GROUP** | **Microenvironment of Immune Cells** |
| **3** | **TOPICS/FOCUS** | **LONG NON-CODING RNAs (lncRNAs) IN MICROENVIRONMENTAL INTERACTIONS OF B CELL CHRONIC LYMPHOCYTIC LEUKEMIA** |
| **4** | **SUMMARY** | Marek Mraz research group has a long-term interest in non-coding RNAs and microenvironmental interactions of malignant B cells, and this research has been supported by an ERC Starting grant (2019-2024). We have previously described novel regulators of microenvironmental interactions including short non-coding RNAs, microRNAs (Sharma et al…Mraz, Blood, 2021; Musilova et al…Mraz, Blood, 2018; Cerna et al…Mraz, Leukemia, 2019). MicroRNAs were shown to play a pivotal role in B cell functions; however, the functions of long non-coding RNAs (lncRNAs) remain unclear. We aim to decipher for the first time the role of lncRNAs in B cell receptor (BCR) signaling and B-T cell interactions. Human genome contains large numbers of lncRNAs that can regulate various physiological cellular processes or contribute to the onset or aggressiveness of cancer. We will study lncRNAs in the context of chronic lymphocytic leukemia (CLL), which is driven by aberrations in the BCR pathway and B-T interactions. Regulation of BCR pathway and B-T cell interactions by lncRNAs is likely of relevance for CLL, but is also transferable to the biology of other B cell malignancies, autoimmune diseases and normal B cells. We identified 3 candidate lncRNAs involved in microenvironmental interactions of CLL. We will decipher the molecular functions of these lncRNAs using biochemical and cellular approaches and via a novel lncRNA knock-out mouse model. We have engineered mice for genetic loss of one of these lncRNAs, and the student will analyse the phenotype of these mice and breed them with known CLL mouse models (Eu-TCL1). Detailed biochemical/molecular studies will complement these data and we will also analyze primary samples from patients with B cell malignancies. We will identify functions of lncRNAs using CRISPR interference, RNA pulldown experiments, mouse models, and molecular biology technics. Furthermore, we developed a novel co-culture model inducing robust primary CLL cell proliferation (~50%) in vitro (Hoferkova et al, Leukemia, 2024). We aim to utilize this game-changing tool to perform the first-ever CRISPR screening of lncRNAs/genes regulating primary CLL cell proliferation. This will help better understand the disease biology and possibly identify novel molecular targets for therapy. |
| **5** | **RG WEBPAGE/CONTACT** | https://mrazlab.ceitec.cz/ |