	GL leader	**Prof. Marek Mráz, MD, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Molecular Medicine: cancers of the blood**
2	**RESEARCH GROUP**	**Microenvironment of Immune Cells**
3	**TOPICS/FOCUS**	**ROLE OF TRANSCRIPTION FACTORS IN ONSET AND PROGRESSION OF B-CELL MALIGNANCIES**
4	**SUMMARY**	Transcription factors (TFs) are important regulators of cell growth, development, and hematopoietic cell differentiation. Disrupting the mechanisms that are responsible for the proper function of the transcription apparatus can lead to the onset of blood cell malignancies. The abnormal function of TFs due to dysregulation or genomic aberrations are often associated with the development of leukemias, including chronic lymphocytic leukemia (CLL) and other B-cell malignancies. Much evidence from the latest research shows that CLL cells have an extra deregulated chromatin structure and show an increased incidence of activated enhancer and promoter areas, allowing TFs to bind and subsequently aberrantly activate potential oncogenes. Moreover, specific post-translational modification of some TFs have been noted as a result of dysregulated signaling in the leukemia microenvironment and this also contributes to disease progression. However, it remains largely unknown which TFs and how they contribute to the development and aggressiveness of CLL and other B malignancies. This project aims to describe the role of candidate TFs in the development and progression of B-cell malignancies with emphasis on CLL while also testing targeted therapy options, e.g. using specific inhibitors of TFs or chromatin modification regulators that are currently available or in development. We have identified several TFs that might act as novel regulators of the B cell survival, proliferation and crosstalk with other immune cells. The PhD student will further investigate this using techniques such as genome editing (CRISPR), RNA sequencing, use of primary samples, and functional studies with various in vitro and in vivo mouse models. The research is also relevant for understanding resistance mechanisms to targeted therapy.
5	**RG WEBPAGE/CONTACT**	https://mrazlab.ceitec.cz/