CEITEC MU – overview of the topics

1	CEIPEX RESEARCH TOPIC LEVEL2
2	NAME OF THE RESEARCH GROUP
3	TOPIC/TOPICS
4	SHORT SUMMARY
5	WEBPAGE OF THE GROUP/CONTACT

	GL leader	**Assoc. Prof. Pavel Plevka, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Structural Biology: structural virology**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	Structural Virology
3	**TÉMA/TÉMATA**	Postdoctoral Researcher in Structural Virology
4	**ANOTACE K TÉMATU/TÉMATŮM**	The post-doc will participate in a research project focused on characterizing the processes of cell entry and genome delivery of non-enveloped viruses from families Picornaviridae, Polyomaviridae, Papillomaviridae, Adenoviridae, and Parvoviridae, using cryo-electron microscopy and tomography. The project will also include structural studies of endocytosis of well-characterized markers of various types of endocytosis, such as transferrin (clathrin-mediated endocytosis), anti-b1-adrenergic receptor (fast endophilin-mediated endocytosis), anti-CD44 antibody (clathrin-independent endocytosis). We aim to determine the mechanisms of virus cell entry and genome delivery, and possible means of preventing it.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://plevkalab.ceitec.cz/

	GL leader	**Petr Těšina, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Structural Biology: coupled transcription & translation, translational control**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Translation Control**
3	**TÉMA/TÉMATA**	**Translation Control**
4	**ANOTACE K TÉMATU/TÉMATŮM**	Problems in translation due to faulty mRNA or other modes of cellular stress lead to ribosomal collisions which are sensed by specific cellular factors for stress signaling and for clearance of problematic mRNAs and incomplete nascent polypeptides. Our research utilizes cryogenic electron microscopy together with cellular and biochemical methods and aims at providing mechanistic understanding of these translation control processes,

		defining working principles of their components and their disease-causing mutations. We also study the molecular mechanisms by which viruses affect host translation control.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://www.ceitec.eu/translation-control/rg396

	GL leader	**Prof. Marek Mráz, MD, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Téma č. 1: Molecular Medicine: microenvironment of immune cells** **Téma č. 2: Molecular Medicine: cancers of the blood**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Microenvironment of Immune Cells**
3	**TÉMA č. 1**	**LONG NON-CODING RNAs (lncRNAs) IN MICROENVIRONMENTAL INTERACTIONS OF B CELL CHRONIC LYMPHOCYTIC LEUKEMIA**
	TÉMA č. 2	**ROLE OF TRANSCRIPTION FACTORS IN ONSET AND PROGRESSION OF B-CELL MALIGNANCIES**
4	**ANOTACE k tématu č. 1**	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.
	ANOTACE k tématu č. 2	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	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://mrazlab.ceitec.cz/

	GL leader	**Prof. Jiří Fajkus, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Genomics & Proteomics of Plant Systems: stress in plant system**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	Chromatin Molecular Complexes
3	**TÉMA/TÉMATA**	**Environmental “double trouble”: Elucidating plant molecular responses to heavy metal and PFAS co-contamination**
4	**ANOTACE K TÉMATU/TÉMATŮM**	As sessile organisms, plants face continuous exposure to environmental pollutants that are readily absorbed from soil and water, harming plant health and posing health risks to livestock and humans through bioaccumulation in edible plant parts. It is estimated that approximately 14 to 17% of farmland globally exceeds safe agricultural thresholds for at least one heavy metal (HM), exposing over a billion people living in those regions to the consequences of HM pollution (*1*). However, heavy metal pollution is not the only concern for farmland. Per- and polyfluoroalkyl substances (PFAS)—man-made organic compounds with broad industrial

		applications—are persistent pollutants with long half-lifes, strong bioaccumulative properties, long-range transport potential, and known adverse effects on biota (*2–4*). Although some PFAS, such as perfluorooctanoic acid (PFOA), are being phased out, replacement PFAS compounds, like GenX, exhibit similarly concerning adverse effects (*5*, *6*). These two types of contaminants likely co-occur, especially in industrialized areas. Therefore, understanding their combined effects is essential for crop improvement to reduce PFAS uptake and its transport to edible parts in co-contaminated environments with HMs. The project will investigate molecular responses of plants to co-contamination with cadmium (Cd) and selected PFAS compounds. Using *Arabidopsis thaliana* and *Oryza sativa*, plants will be grown under environmentally relevant concentrations of these contaminants on agar plates and in hydroponic systems. A wide range of methods will be employed: transcriptome profiling, biochemical assays, photosynthetic performance metrics, phenotypic analysis, ionomics, as well as spatially resolved spectroscopy techniques such as laser ablation-inductively coupled plasma-mass spectrometry (LA-ICP-MS) and laser-induced breakdown spectroscopy (LIBS). These approaches will enable investigation of PFAS and Cd uptake, translocation under co-contamination, and their effects on nutrient composition. Integrating transcriptomic and ionomic data through systems biology approaches will allow identification of candidate genes involved in pollutant transport and stress response for downstream functional validation. Analysing phylogenetically distant species is expected to reveal conserved mechanisms, potentially transferable to other plants, while species-specific effects may apply to closely related crops. This study is expected to provide novel insights into the mechanisms of PFAS translocation in plants and their interactions with heavy metals, offering targets for crop improvement in contaminated environments.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://www.ceitec.eu/chromatin-molecular-complexes/rg51

	GL leader	**Prof. Šárka Pospíšilová, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Molecular Medicine: medical genomics**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Medical Genomics**
3	**TÉMA/TÉMATA**	**Genetic predispositions to development of hematological malignancies**
4	**ANOTACE K TÉMATU/TÉMATŮM**	Hematological malignancies are closely related to various types of somatic mutations in blood cells, which often accumulate during the course of the disease. Recent findings point to the increasing importance of inherited genetic predispositions that influence the development of lymphoid and myeloid leukemias and other neoplasms. They could play a causal role in the development of the disease and be related to its early onset, patient prognosis and the effect of therapy. The description of novel germline mutations as risk factors for disease progression therefore has clear clinical implications and benefits for patients and their families. The underlying biological mechanisms leading to leukemic transformation are specific for each genetic variant and should be further investigated. The most frequent and severe genetic variants predisposing to hematological

		malignancies will be selected from a novel genome-wide analysis of the Czech/European population analyzed within the Genome of Europe project, which is currently underway in our laboratory.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://www.ceitec.eu/medical-genomics/rg34

	GL leader	**Mgr. Michal Šmída, Dr. rer. nat.**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Molecular Medicine: cancers of the blood**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Functional Genomics**
3	**TÉMA/TÉMATA**	Investigation of novel possibilities for targeted therapy in acute myeloid leukemia
4	**ANOTACE K TÉMATU/TÉMATŮM**	Acute myeloid leukemia (AML) is a hard-to-treat malignancy of myeloid blood cell lineage, whose therapy was for decades relying primarily on intensive chemotherapy. Only recently, the first targeted agent venetoclax (an inhibitor of BCL2 antiapoptotic protein) has been approved. Nevertheless, majority of patients does not benefit from venetoclax therapy in long-term, leaving them no other therapeutic options. Our research aims to reveal the molecular mechanisms underlying venetoclax resistance, identify novel targets of therapy and propose new means of targeted treatments with higher success rate, tailored for individual groups of patients. State-of-the-art technologies are applied in our research such as CRISPR/Cas9 gene editing, genome-wide CRISPR/Cas9 knockout screening, large-scale drug screening, CAR-T cell engineering technology, RNA sequencing, single-cell RNAseq and many other cell biology and molecular biology techniques.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://www.ceitec.eu/functional-genomics/rg214

	GL leader	**Karel Říha, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Genomics & Proteomics of Plant Systems: stress in plant system**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	Plant Molecular Biology
3	**TÉMA/TÉMATA**	Molecular mechanisms of heat stress adaptation: The function of ribonucleoprotein condensates in plant reproduction
4	**ANOTACE K TÉMATU/TÉMATŮM**	Elevated temperatures pose a major challenge to plant reproduction, threatening crop fertility and yield. Meiosis is particularly vulnerable to heat stress, which can disrupt homologous recombination and chromosome segregation, leading to pollen abortion and infertility. To cope with these conditions, plants employ intricate

		molecular mechanisms that safeguard gene expression and protein function. Among these, ribonucleoprotein (RNP) condensates have emerged as dynamic regulatory hubs that respond to diverse stress conditions by sequestering and protecting RNAs and proteins, thereby fine-tuning gene expression for adaptation. We have recently identified an RNA-binding protein that forms RNP condensates, which act as key regulators of meiotic protein expression, influencing processes such as chromosome pairing, cytokinesis, and callose metabolism. Importantly, these condensates are responsive to temperature, suggesting a critical role in plant adaptation to heat stress. The main goal of this project is to elucidate how these RNP condensates coordinate stress responses and contribute to heat stress adaptation. Ultimately, this knowledge will be leveraged to manipulate these mechanisms to enhance plant reproductive resilience and seed yield under elevated temperatures.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://riha.ceitec.cz/

	GL leader	**Martin Lamoš, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Brain & Mind Research: deep brain stimulation**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	Multi-modal and Functional Neuroimaging
3	**TÉMA/TÉMATA**	Next-generation noninvasive neurostimulation technologies for treatment of neurodegenerative disorders
4	**ANOTACE K TÉMATU/TÉMATŮM**	This fellowship is based at the Multimodal and Functional Neuroimaging at Masaryk University (Martin Lamoš, Ivan Rektor) Our research focuses on developing novel noninvasive electrical stimulation methods for the central nervous systems, using advanced high-frequency (kHz) supraphysiological waveforms aimed at improving treatments for Parkinson's disease and related movement disorders. We combine clinical studies in patients and healthy volunteers with theory and computational modelling. Our teams have access to advanced electrophysiology, medical imaging, and unique opportunities to work with patients carrying deep brain stimulation (DBS) implants, enabling both acute and chronic recordings from implanted electrodes. Collaboration with the Bioelectronics Materials and Devices group (Prof. E. Glowacki) at the Brno University of Technology CEITEC campus is also envisioned as a part of this project. A successful fellowship can be tailored to individual expertise, ranging from theoretical and computational modelling, through fundamental biophysics of kHz stimulation, to preclinical electrophysiology and clinical studies with human participants
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://mafil.ceitec.cz/en/

	GL leader	**Jiří Nováček, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Structural Biology: protein structure and dynamics; protein-DNA interactions**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Cryo-Electron Microscopy and Tomography Core Facility**
3	**TÉMA/TÉMATA**	Advancing Time-Resolved Cryo-EM to Elucidate Insulin Receptor Inhibition Mechanisms
4	**ANOTACE K TÉMATU/TÉMATŮM**	The proposed project will aim to provide insight into the activation mechanism of the insulin receptor (IR), a key regulator of glucose homeostasis and a prototypical receptor tyrosine kinase. Despite the availability of high-resolution structures of apo and fully bound IR, the sequence and timing of intermediate conformational states remain poorly understood. We will implement a comprehensive time-resolved cryo-electron microscopy (trEM) workflow to capture structural snapshots from receptor activation on both microsecond and millisecond timescale. For that, we will first adapt an integrated cryo-fluorescence microscope, developed in the CEITEC cryo-EM core facility (CEMCOF), into a microsecond-resolved cryo-sample preparation platform. This will enable precise triggering (e.g., pH or photochemical stimulus), localized laser melting, and revitrification of the sample. The system will be calibrated using a pH-dependent conformational transition of a virus from the Picornaviridae family, a process with well-characterized microsecond-scale dynamics. Concurrently, we will benchmark a time-resolved cryo-EM plunger, currently under development at CEMCOF, which will utilize mix–spray–plunge vitrification >100ms time scale and calibrate its performance using a well-studied case of bacterial ribosomal subunits association. These two complementary approaches will then be applied to study the insulin receptor activation process at multiple temporal resolutions. By capturing intermediate states during insulin binding and receptor conformational changes, we aim to reconstruct the sequence of structural events that underlie IR activation. The project will not only advance mechanistic understanding of insulin signaling but will also establish a validated infrastructure for time-resolved cryo-EM as a service to the broader research community.
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://cryo.ceitec.cz/

	GL leader	**Assoc. Prof. Jozef Hritz, PhD**
1	**CEIPEX RESEARCH TOPIC LEVEL2**	**Structural Biology: protein structure and dynamics; protein-DNA interactions**
2	**NÁZEV VÝZKUMNÉ SKUPINY**	**Protein Structure and Dynamics**
3	**TÉMA/TÉMATA**	Structural Changes in Intrinsically Disordered Proteins Relevant to Neurodegenerative Diseases
4	**ANOTACE K TÉMATU/TÉMATŮM**	Our research is centered on intrinsically disordered proteins (IDPs) such as Tau and α-Synuclein, which are known to undergo conformational changes that result in the formation of pathological fibrils. These fibrillar aggregates are hallmark components of neurofibrillary tangles in Alzheimer's disease and Lewy bodies in Parkinson's disease. We investigate, in detail, how post-translational modifications, buffer conditions, and interactions with binding partners—particularly 14-3-3 proteins—influence these structural transitions. For the characterization of soluble protein states, we employ biomolecular NMR spectroscopy (CF NMR CEITEC - Ceitec.cz). Structural studies of fibrillar forms are conducted using atomic force microscopy (AFM) and cryo-electron microscopy (cryo-EM). Importantly, beyond in vitro models, we analyze patient-derived pathological fibrils directly within tissue samples from Alzheimer's and Parkinson's disease patients using cryo-EM tomography (CF Cryo-Electron Microscopy and Tomography - Ceitec.cz). To gain deeper mechanistic insights, we integrate experimental data with computational simulations. Our work is supported by multiple international research grants, most notably the *Excellence Hubs* project ADDIT-CE, coordinated by Jozef Hritz (ADDIT-CE - Ceitec.cz).
5	**WEBPAGE VÝZKUMNÉ SKUPINY/KONTAKT**	https://www.ceitec.eu/protein-structure-and-dynamics/rg110