

Topic Proposal

Doctoral study program: Molecular Medicine

Research area: Cancer biology

Supervisor: Assoc. Prof. Marek Mraz, MSc., M.D., Ph.D.

Topic title: Role of FoxO1 transcription factor in B-cell malignancies

Annotation:

The project is focused on FoxO1 transcription factor and its role in the pathophysiology of chronic lymphocytic leukemia (CLL). Although the therapy of CLL has made several remarkable improvements, the disease still remains incurable. Current therapeutic approaches mainly include the use of so-called B-cell receptor signaling inhibitors (ibrutinib, idelalisib) leading to disruption of pro-survival and pro-proliferative interactions in immune niches, and the use of venetoclax, which "inhibits" BCL2 anti-apoptotic protein. We have previously described that FoxO1 protein is crucial for homing capacity of CLL cell to immune niches and tonic Akt activity supporting the survival of malignant B cells (Seda et al...Mraz, Blood, 2021). Results from the FoxO1 knockout CLL cell line suggest that FoxO1 is involved in adaptation to targeted therapy (our unpublished data). The project aims to investigate further the role of FoxO1 in microenvironmental interactions, regulation of apoptosis, and adaptation to targeted therapy. The student will use techniques such as genome editing (CRISPR), CHIP seq, RNA sequencing, drug testing in vitro, primary CLL samples obtained on therapy, and functional studies with various in vitro and in vivo models. The research is also relevant for the pre-clinical development of novel drugs and their combinations (several patents submitted by the lab).

Recommended literature:

Seda V. et al...**Mraz**. FoxO1-GAB1 Axis Regulates Homing Capacity and Tonic AKT Activity in Chronic Lymphocytic Leukemia. Blood, 2021, <https://doi.org/10.1182/blood.2020008101>.

Ondrisova L, **Mraz M**. Genetic and Non-Genetic Mechanisms of Resistance to BCR Signaling Inhibitors in B Cell Malignancies. Front Oncol. 2020 Oct 26;10:591577.

Kipps et al. Chronic lymphocytic leukaemia. Nat Rev 2017 <https://pubmed.ncbi.nlm.nih.gov/28102226/>

Seda V, **Mraz M**. B-cell receptor signalling and its crosstalk with other pathways in normal and malignant cells. Eur J Haematol. 2015 Mar;94(3):193-205. doi: 10.1111/ejh.12427. Epub 2014 Sep 13. PMID: 25080849 Review.

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Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary)

Requirements on candidates:

- 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.

Keywords: CLL, FoxO1, targeted therapy, microenvironment, apoptosis

Information on the supervisor:

H-index 27 (citations > 3500, 46 publications with IF), currently principal investigator of 5 grants (AZV 2x, **ERC**, GACR, NPO). Dr. Mraz has currently 7 PhD students, with 2-3 finishing soon). international collaborations: University of Southampton, Univ. California-San Diego, Mayo Clinic, Dana-Farber Cancer Institute, EMBL, University of Turin (student internship available), member of EHA Comitte, reviewer in scientific journals: Blood, Leukemia, Leukemia Research; <https://is.muni.cz/auth/osoba/101627>;

More information on the laboratory ceitec.cz/mrazlab

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Topic Proposal

Doctoral study program: Life Sciences

Research area: Cancer biology

Supervisor: Assoc. Prof. Marek Mraz, MSc., M.D., Ph.D.

Topic title: MICROENVIRONMENT MODELS AND THEIR USE TO STUDY AGGRESSIVENESS AND TARGETED THERAPY IN B CELL MALIGNANCIES

Annotation:

Chronic lymphocytic leukemia (CLL) cells and indolent lymphomas are known to be dependent on diverse microenvironmental stimuli providing them signals for survival, development, proliferation, and therapy resistance. It is known that CLL cells undergo apoptosis after cultivation *in vitro*, and therefore it is necessary to use models of CLL microenvironment to culture CLL cells long-term and/or to study their proliferation. Several *in vitro* and *in vivo* models meet some of the characteristics of the natural microenvironment based on the coculture of malignant cells with T-lymphocytes or stromal cell lines as supportive cell, but they also have specific limitations.

The aim of this research is to develop and use models mimicking lymphoid microenvironment to study mechanisms leading to aggressiveness in B cell malignancies and/or novel therapeutic options, e.g. drugs targeting CLL proliferation, development of resistance in long-term culture or combinatory approaches, which cannot be analyzed in experiments based on the conventional culture of CLL/lymphoma primary cells. This project will utilize models developed in the laboratory and will further optimize and modify them. The biology of CLL and responses to targeted treatment will be interrogated using the developed models. The student will utilize various functional assays, Crispr editing, RNA sequencing, genome editing, drug screening etc., with the use of primary patient's samples and cell lines. The research might bring new insights into the microenvironmental dependencies and development of resistance to targeted therapy.

Recommended literature:

Hoferkova E, Kadakova S, Mraz M. In Vitro and In Vivo Models of CLL-T Cell Interactions: Implications for Drug Testing. *Cancers* (Basel). 2022 Jun 23;14(13):3087.

Sharma et al. ...**Mraz**. miR-29 Modulates CD40 Signaling in Chronic Lymphocytic Leukemia by Targeting TRAF4: an Axis Affected by BCR inhibitors. *Blood* 2021. <https://pubmed.ncbi.nlm.nih.gov/33171493/>

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Seda V. et al...**Mraz**. FoxO1-GAB1 Axis Regulates Homing Capacity and Tonic AKT Activity in Chronic Lymphocytic Leukemia. *Blood*, 2021, <https://doi.org/10.1182/blood.2020008101>.

Kipps et al. Chronic lymphocytic leukaemia. *Nat Rev* 2017 <https://pubmed.ncbi.nlm.nih.gov/28102226/>

Seda V, **Mraz M**. B-cell receptor signalling and its crosstalk with other pathways in normal and malignant cells. *Eur J Haematol*. 2015 Mar;94(3):193-205. doi: 10.1111/ejh.12427. Epub 2014 Sep 13. PMID: 25080849 Review.

Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary)

Requirements on candidates:

- 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.

Keywords: lymphoma, microenvironment, models

Information on the supervisor:

H-index 27 (citations > 3500, 46 publications with IF), currently principal investigator of 5 grants (AZV 2x, **ERC**, GACR, NPO). Dr. Mraz has currently 7 PhD students, with 2-3 finishing soon). international collaborations: University of Southampton, Univ.California-San Diego, Mayo Clinic, Dana-Farber Cancer Institute, EMBL, University of Turin (student internship available), member of EHA Comitte, reviewer in scientific journals: *Blood*, *Leukemia*, *Leukemia Research*; <https://is.muni.cz/auth/osoba/101627>; More information on the laboratory ceitec.cz/mrazlab

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Topic Proposal

Doctoral study program: Life Sciences

Research area: Cancer Biology

Supervisor: Assoc. Prof. Marek Mraz, MSc., M.D., Ph.D.

Topic title: LONG NON-CODING RNAs (lncRNAs) IN THE PATHOGENESIS OF MATURE B CELL MALIGNANCIES

Annotation:

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. It has been shown that short non-coding RNAs significantly contribute the onset, progression, and therapy resistance in multiple B cell leukemias and lymphomas. We have recently described the role of miRNAs in microenvironmental interactions and aggressiveness of chronic lymphocytic leukemia and follicular lymphoma (Sharma et al...Mraz, Blood, 2021; Musilova et al...Mraz, Blood, 2018; Cerna et al...Mraz, Leukemia, 2019). However, the role of long non-coding RNAs in the pathogenesis of these diseases remains completely unknown.

In this project, the student will decipher how lncRNAs regulated BCR signaling and microenvironmental interactions in B cell malignancies. We are mainly interested in chronic lymphocytic leukaemia (CLL) and follicular lymphoma (FL). CLL is the most common leukemia in adults and FL is the most common indolent non-Hodgkin lymphoma. The clinical course of CLL/FL patients can be surprisingly variable (survival from months to decades), and both diseases still remain incurable. The course of the diseases is characterized by repeated relapses leading to the evolution of resistant disease or to the high-grade transformation to a more aggressive diffuse large B-cell lymphoma/Richter. This is associated with a poor prognosis and a high risk of early death. Number of studies showed that multiple genetic lesions are associated with CLL/FL aggressiveness or transformation; however, precise molecular mechanisms underlying these processes are largely unclear. The project aims to reveal the molecular mechanisms involving lncRNAs and/or miRNAs responsible for CLL/FL aggressiveness, especially activation of BCR signaling and B-T cell interactions. The primary samples will be analyzed on the level of protein-coding as well as non-coding genes (NGS with Illumina, preliminary data available). This will be followed by searching for the function of lncRNAs using CRISPR interference, mouse models, and molecular biology technics. This will help to better understand the disease biology and possibly to identify novel molecular targets that could be used therapeutically.

Recommended literature:

Sharma et al. ...**Mraz**. miR-29 Modulates CD40 Signaling in Chronic Lymphocytic Leukemia by Targeting TRAF4: an Axis Affected by BCR inhibitors. Blood 2021.
<https://pubmed.ncbi.nlm.nih.gov/33171493/>

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Musilova et al. ...**Mraz**. miR-150 downregulation contributes to the high-grade transformation of follicular lymphoma by upregulating FOXP1 levels . **BLOOD**. 2018 **NOV 29**;132(22):2389-2400. <https://pubmed.ncbi.nlm.nih.gov/33786575/>

Musilova K, **Mraz M**. MicroRNAs in B-cell lymphomas: how a complex biology gets more complex. *Leukemia*. 2015 May;29(5):1004-17

Zeni and **Mraz** LncRNAs in adaptive immunity: role in physiological and pathological conditions. *RNA Biol*. 2021 May;18(5):619-632. <https://pubmed.ncbi.nlm.nih.gov/33094664/>

Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary)

Requirements on candidates:

- 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.

Keywords: Long non-coding RNA, lymphomas, DLBCL, miRNA

Information on the supervisor:

H-index 27 (citations > 3500, 46 publications with IF), currently principal investigator of 5 grants (AZV 2x, **ERC**, GACR, NPO). Dr. Mraz has currently 7 PhD students, with 2-3 finishing soon). international collaborations: University of Southampton, Univ.California-San Diego, Mayo Clinic, Dana-Farber Cancer Institute, EMBL, University of Turin (student internship available), member of EHA Comitte, reviewer in scientific journals: *Blood*, *Leukemia*, *Leukemia Research*; <https://is.muni.cz/auth/osoba/101627>; More information on the laboratory ceitec.cz/mrazlab

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Topic Proposal

Doctoral study program: Life Sciences

Research area: Cancer biology

Supervisor: Mgr. Miroslav Boudny, Ph.D.

Consultant: Marek Mraz, MD, Ph.D.

Topic title¹: Regulation of microenvironmental interactions in chronic lymphocytic leukemia by microRNAs

Annotation:

Aberrant expression of miRNAs has been observed in almost every type of cancer. The first link between miRNA dysfunction and cancer development was discovered in chronic lymphocytic leukemia (CLL) where miR-15/16 are deleted in most CLL cases, and this contributes to aberrant expression of the anti-apoptotic BCL2 molecule.

Recently, it has been recognized that a characteristic feature of CLL is that cell survival and proliferation fully depend on signals from the microenvironment, especially T-cell interactions and B-cell receptor signaling (summarized in Hoferkova et al., *Cancers* 2022). It was shown that the proliferation of CLL cells in the microenvironment is a key determinant of the disease aggressiveness. To study miRNAs involved in microenvironmental interactions, we performed a global miRNA profiling of “resting” vs “activated” CLL cells (NGS with Illumina, preliminary data available). We hypothesize that differently expressed miRNAs are directly or indirectly involved in cell signaling induced by contact with the microenvironment and thus contribute to the regulation of CLL cell survival and proliferation. We have described for the first time that miRNAs are involved in the regulation of CLL interactions with T cells (Sharma et al., *Blood* 2021).

The project's goal will be to study regulation through miRNAs and the function of selected miRNAs in the context of the CLL microenvironment. Experimentally, the project will include techniques such as immunoblotting, qPCR, transfections, cloning, viral transductions, genome editing (RNA interference or CRISPR), luciferase assay or RNA sequencing. Work with both cell lines and primary cells from patients will be included.

Recommended literature:

Kipps et al. Chronic Lymphocytic Leukaemia. *Nature Reviews Disease Primers*, 2017, <https://doi.org/10.1038/nrdp.2016.96>.

Sharma et al. Mir-29 Modulates CD40 Signaling in Chronic Lymphocytic Leukemia by Targeting TRAF4: An Axis Affected by BCR Inhibitors. *Blood*, 2021, <https://doi.org/10.1182/blood.2020005627>.

Hoferkova et al. In Vitro and in Vivo Models of CLL–T Cell Interactions: Implications for Drug Testing. *Cancers*, 2022. <https://doi.org/10.3390/cancers14133087>.

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Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary).

Requirements on candidates:

- Master's degree in Molecular biology, Biochemistry, or similar field of study
- Experience of working in a laboratory
- The ability of collective work as well as independent project planning
- Desire to learn new things

Keywords: miRNA, CLL, T cell, microenvironment

Information on the supervisor:

Nine years of experience in chronic lymphocytic leukemia research, first-author publications in Q1 journals (Boudny, Haematologica 2019; Boudny, Cancer Treatment Reviews 2020; total 29 citations), internship at the University of Birmingham in research group of Tatjana Stankovic, supervision of students (supervisor of 1 diploma and 2 bachelor students, co-supervisor of 1 diploma student). Extensive experience in the fields of cancer biology, hematology, immunology.

More at: <https://is.muni.cz/auth/person/393305>.

More information about the research group: <http://mrazlab.ceitec.cz/>

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Topic Proposal

Doctoral study program: Molecular Medicine

Research area: Cancer biology

Supervisor: RNDr. Josef Vecera, Ph.D.

Topic title¹: ROLE OF TRANSCRIPTION FACTORS IN ONSET AND PROGRESSION OF B-CELL MALIGNANCIES

Annotation:

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 leukaemias, including chronic lymphocytic leukaemia (CLL) and other B-cell lymphomas. 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 signalling in the leukaemia microenvironment and this also contributes to disease progression. This project should 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 candidate TFs that might act as novel regulators of the B cell survival, proliferation, and crosstalk with other immune cells. This will be further investigated by the Ph.D. student using technics such as genome editing (CRISPR), RNA sequencing, CHIPseq (cut-and-run), the use of primary CLL samples, and functional studies with various *in vitro* and *in vivo* models. The research is also relevant for understanding resistance mechanisms to targeted therapy.

Recommended literature:

Beekman et al. The reference epigenome and regulatory landscape of chronic lymphocytic leukemia. Nature Medicine 2018
<https://pubmed.ncbi.nlm.nih.gov/29785028/>

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Kipps et al. Chronic lymphocytic leukaemia. Nat Rev 2017
<https://pubmed.ncbi.nlm.nih.gov/28102226/>

Seda et al. FoxO1-GAB1 Axis Regulates Homing Capacity and Tonic AKT Activity in Chronic Lymphocytic Leukemia. Blood 2021 March (epub).
<https://pubmed.ncbi.nlm.nih.gov/33786575/>

Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary)

Requirements on candidates:

- 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.

Keywords:

CLL, transcription factor, epigenetics, microenvironment

Information on the supervisor:

H-index 11, citations at WOS: 287, 16 publications in impacted journals. Former principal investigator of GACR funding. Fellowship at Karolinska Institutet (Stockholm) in research group of Dr. Emma Andersson and prof. Urban Lendahl. Supervision of diploma (4) and bachelor (11) students. 3 years of experience in the CLL and hematological malignancies field. 10 years of expertise in immunology, molecular physiology, stem cell research and mouse model developmental studies.

More information on the Marek Mráz Research Group (mrazlab.ceitec.cz).

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Topic Proposal

Doctoral study program: Molecular Medicine

Research area: Cancer biology

Supervisor: Mgr. Miroslav Boudny, Ph.D.

Consultant: Marek Mraz, MD, Ph.D.

Topic title¹: REGULATION OF BCR SIGNALLING BY DNA DAMAGE RESPONSE AND P53 PROTEIN

Annotation:

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., 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.

Recommended literature:

Cerna et al. MicroRNA miR-34a Downregulates FOXP1 During DNA Damage Response to Limit BCR Signalling in Chronic Lymphocytic Leukaemia B Cells. Leukemia, 2019, <https://doi.org/10.1038/s41375-018-0230-x>.

Cerna and Mraz P53 Limits B Cell Receptor (BCR) Signalling: A New Role for miR-34a and FOXP1. Oncotarget, 2018, <https://doi.org/10.18632/oncotarget.26376>.

Kipps et al. Chronic Lymphocytic Leukaemia. Nature Reviews Disease Primers, 2017, <https://doi.org/10.1038/nrdp.2016.96>.

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Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary).

Requirements on candidates:

- Master's degree in Molecular biology, Biochemistry, or similar field of study
- Experience of working in a laboratory
- The ability of collective work as well as independent project planning
- Desire to learn new things

Keywords: BCR signalling, DNA damage response, p53

Information on the supervisor:

Nine years of experience in chronic lymphocytic leukemia research, first-author publications in Q1 journals (Boudny, Haematologica 2019; Boudny, Cancer Treatment Reviews 2020; total 29 citations), internship at the University of Birmingham in research group of Tatjana Stankovic, supervision of students (supervisor of 1 diploma and 2 bachelor students, co-supervisor of 1 diploma student). Extensive experience in the fields of cancer biology, hematology, immunology.

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More information about the research group: <http://mrazlab.ceitec.cz/>

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Topic Proposal

Doctoral study program: Life Sciences

Research area: Cancer biology

Supervisor: Mgr. Václav Šeda, Ph.D.

Co-Supervisor: doc. MUDr. Mgr. Marek Mráz, Ph.D.

Topic title¹: REGULATION OF CELL MIGRATION AND ITS THERAPEUTIC TARGETING IN B CELL LEUKEMIAS

Annotation:

The project goal is to understand the molecular machinery that regulates the migration of malignant B cells between different niches such as lymphoid and bone marrow niche and peripheral blood. Deciphering general mechanisms of cancer cell migration is of great interest, especially in chronic lymphocytic leukemia (CLL), which is a disease dependent on the recirculation between peripheral blood and supportive microenvironment in lymphoid compartments (reviewed in Seda and Mraz, 2015; Seda et al, 2021). Migration is a complex process guided by chemokine receptors, integrins, and various intracellular proteins. However, it remains largely unknown how CLL cells integrate multiple migratory signals and how they “decide” to return to supportive immune niches. This is of note since inhibiting this process is one of the major mechanisms of action for B-cell receptor (BCR) inhibitors such as ibrutinib and idelalisib. We and others have currently described that CLL cells in peripheral blood may activate the non-genetic mechanisms of CLL cells' adaptation to BCR inhibitors shortly after treatment initiation. This provides supportive signaling improving CLL cell survival. Our lab established several models for in vitro and in vivo studies of microenvironmental interactions and their interplay (unpublished in vivo model; Pavlasova et al. Blood, 2016; Pavlasova et al. Leukemia, 2018; Musilova et al. Blood, 2018; Mraz et al. Blood, 2014; Cerna et al. Leukemia, 2019).

We have identified candidate molecules that might act as novel regulators of the B cell migration or the balance between homing and survival in peripheral blood. This will be further investigated by the PhD student using technics such as genome editing (CRISPR), RNA sequencing, use of primary samples, functional studies with various in vitro and in vivo models, and transplantation of genetically edited cells to mice. The research is also relevant for understanding resistance mechanisms to BCR inhibitors, pre-clinical development of novel drugs and their combinations (several patents submitted by the lab).

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Recommended literature:

- 1) Seda et al.: FoxO1-GAB1 Axis Regulates Homing Capacity and Tonic AKT Activity in Chronic Lymphocytic Leukemia. *Blood* 2021 March. <https://pubmed.ncbi.nlm.nih.gov/33786575/>
- 2) Ondrisova et al.: Genetic and Non-Genetic Mechanisms of Resistance to BCR Signaling Inhibitors in B Cell Malignancies. *Front Oncol* 2020 Oct. <https://pubmed.ncbi.nlm.nih.gov/33154951/>
- 3) Seda and Mraz.: B-cell receptor signalling and its crosstalk with other pathways in normal and malignant cells. *Eur J Haematol* 2015 Mar. <https://pubmed.ncbi.nlm.nih.gov/25080849/>

Funding:

Part-time salary (min. 0,5 FTE) on AZV/ERC/GACR grants + national scholarship (equals approx. half-time salary).

Requirements on candidates:

- 1) Smart and motivated people that work independently, but also willing to learn from other people in the lab and collaborate.
- 2) Candidates should have a master's degree in Immunology, Molecular biology, Biochemistry, or similar field and have deep interest in molecular biology and cancer cell biology.
- 3) Candidates should have good wet-lab skills related to molecular biology.

Keywords: CLL, BCR signaling, Therapy, adaptation, resistance

Information on the supervisor:

Nine years of experience in chronic lymphocytic leukemia research; H-index 7 (citations at WOS 284; publications with IF: 9); patent application: 1; Supervisor of 1 diploma thesis; Co-supervisor of 3 diploma thesis; Co-supervisor of 1 bachelor thesis. Internship at Centre Esther Koplowitz in Subero lab, Spain. Genome Engineering: CRISPR/ Cas course at European Molecular Biology Laboratory (EMBL), Germany. Holder of Certificate of professional competence to design experiments and experimental projects for work with animals. Reviewer in scientific journals: *Blood Cancer Journal*, *Frontiers in Oncology*. Award for the best presentation Young Investigator meeting, International workshop on CLL (iwCLL), Poland. Award for the best publication published in impacted journal, Purkyně foundation.

More information about the research group: <http://mrazlab.ceitec.cz/>

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