

**Chronic Myeloid Leukemia (CML)** is a blood cancer with constitutes 20% of all leukemias. The onset is asymptomatic, caused by chromosomal mutation leading to creation of mutated protein – BCR-ABL and cancer development. The average lifespan of untreated patient is 4-5 years. In 2001 a breakthrough in the treatment has been made, new drug – Imatinib has been introduced into clinics. Imatinib specifically inhibits the survival and proliferation of cancer cells, extending the average lifespan of about 20 years. Unfortunately, some patients who do not respond to treatment from the beginning, and others (sooner or later) acquire resistance during the treatment. Therefore it is extremely important to search for new ways to improve the treatment. This resistance to treatment is frequently a result of activation of prosurvival pathways in cancer cells. JAK/STAT signalling pathway is known to be one **of such mechanism related with disease progression and resistance to treatment** leading to cancer cell survival.

**Our previous research has led to the identification of new prosurvival pathway in CML cells, activated as a response to stress stimuli coming from cancer microenvironment. Our preliminary results suggest that in CML cells this stress-driven prosurvival mechanism stimulates cytokine release.** In healthy cells cytokines are highly important for proper functioning. However, when released in an uncontrolled manner by cancer cells, they stimulate its growth and proliferation.

Our preliminary results suggests that the inhibition of stress response “middleman” decreases cytokines release, slows down the progression of disease and sensitizes cancer cells to therapy, what makes these signaling pathways a potential therapeutic target. **That is why the goal of our project is to check the hypothesis, whether stress response secreted cytokines activate prosurvival JAK/STAT signaling promoting CML cells survival and resistance to treatment. We plan to use cell lines as well as laboratory mice in order to examine the role of cytokines released by CML cells in leukemia development. Additionally we plan to test new potential treatment which seems to have the potential to inhibit this prosurvival signaling and serve as a new weapon in eradication of the disease.**