

The $\gamma\delta$ T cells are a minor subset of T cells, they comprise usually around 5% of total T cells in human peripheral blood. Due to their ability to rapidly respond to stimuli, they comprise one of the most important parts of anti-viral and anti-cancer surveillance. Up to date, there have been several clinical trials using $\gamma\delta$ T cells with promising results in some studies e.g. in non-small cell lung cancer, renal cell carcinoma or prostate cancer. Nevertheless, a better understanding of $\gamma\delta$ T cells is necessary to make full use of their immunotherapeutic potential in various human diseases.

Myeloid-derived suppressor cells (MDSC) are a heterogenous group of immature myeloid cells that are especially frequent in cancer patients and have high suppressive potential. Monocytic MDSC population is especially expanded in a number of haematological malignancies, including chronic lymphocytic leukemia (CLL). They suppress the T cell response to the cancerous cells thus promoting cancer progression. Elevated percentage of MDSC cells is linked to the worse prognosis.

Vitamin C was noted to significantly enhance cytokine production by $\gamma\delta$ T cells, promote the proliferation of purified $\gamma\delta$ T cells in response to phosphoantigen stimulation and regulate cell-cycle. Vitamin D is known to enhance the maturation of myeloid cells, increasing expression of HLA-DR, thus probably decreasing the suppressive potential of monocytic MDSC.

Cancer is a serious problem of the modern world, according to recent estimates, there is approximately 40% chance that an individual will develop some kind of malignancy during their life. Chronic lymphocytic leukemia (CLL) and non-Hodgkin small lymphocyte lymphoma are considered to be one single entity with different clinical manifestation – in the former cancer cells can be found mainly in blood and bone marrow, while in the former in lymph nodes. Together CLL/SLL is the most common haematological malignancy among adults. Globally, approximately 200,000 new cases are diagnosed each year as well as approximately 60,000 CLL/SLL-related deaths are recorded.

Current project aims to describe the functional relations between monocytic MDSC and $\gamma\delta$ T cells as well as the impact of vitamin C and vitamin D supplementation thereon. As the current knowledge about the interactions between monocytic MDSC and $\gamma\delta$ T cells is almost non-existent, this project may significantly broaden our knowledge and is of relatively high novelty. Better understanding of monocytic MDSC- $\gamma\delta$ T cell interactions in malignancy is of high importance for the success of immunotherapy with *in-vitro* expanded $\gamma\delta$ T cells.

This project comprises a wide range of different cell cultures, including both monocytic MDSC and $\gamma\delta$ T cells. To some cultures vitamins C and D will be added to evaluate their effect. Material will be evaluated or treated using a wide range of state-of-the-art methods, including multicolour flow cytometry, flow cytometry cell sorting, magnetic activated cell sorting, beads arrays to measure levels of cytokines, RT-qPCR for the quantitative evaluation of gene expression and microRNA expression and finally also Next-Generation-Sequencing with the smallest available sequencer – Oxford Nanopore MinION.