The role of polyamines for immunosenescence in Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is the most common inflammatory joint disease affecting up to 1% of the western population. A pivotal role in the disease pathogenesis is assigned to premature immunosenescence of T-cells including inadequate accumulation of terminally differentiated effector-memory $CD28^-$ T-cells in peripheral blood as well as at sites of inflammation. Recent findings suggest that premature immunosenescence goes hand in hand with T-cell DNA hypomethylation as observed in RA T-cells. Excessive consumption of S-adenosylmethionine (SAM) – the major methyl donor - by polyamine pathway is thought to contribute to global DNA hypomethylation

In this project we aim to investigate the role of polyamine metabolism on T-cell immunosenescence in RA. Therefore, we attempt to show that RA T-cells exhibit reduced levels of SAM, show a reduction in DNMT1 mRNA as well as higher levels of AMD1 mRNA, have reduced DNA methylation and inhibition of Dnmt1-activity by 5-Azacytidine *in vitro* leads to a more senescence-like phenotype and function of healthy T-cells.

We anticipate that the conclusions drawn from this study will link immunosenescence, DNA methylation and T-cell metabolism and improve current understanding in the pathogenesis of RA.