

Modulation of Adaptive Immune Responses

- Studies in infectious diseases and immune disorders Thesis summary:

One cornerstone of good health is a well-functioning immune system. Immune cells interact via direct contact between cells as well as by secretion of signaling molecules which reach distant cells throughout the body. This complex system needs to be flexible and well controlled at the same time. If parts of the immune system are missing or defective, immunodeficiency disorders might develop. In order to elucidate regulatory mechanisms of the immune system, we investigated the interaction between regulatory T cells (Tregs) and effector T cells on a functional level. We identified specific activation kinetics which determine the suppressive potential of Tregs and we observed distinct changes in intracellular signaling events in immune effector cells in presence of suppressive Tregs. In addition we found out that the susceptibility of effector T cells to suppression depends on earlier contact between these two cell types and the ability of effector cells to have escaped suppression earlier. We also investigated the possibility to use existing drugs as treatment adjuvants for patients with different types of immune defects to improve immune responses or boost current therapies. In this context we treated blood samples from patients that suffer from infectious diseases such as tuberculosis or HIV with MEK pathway inhibitors prior to cell activation. While we were able to reduce Treg numbers and block the upregulation of the FoxP3 transcription factor which determines Treg suppression, disease-specific effector T cell function did not improve as hypothesized. In samples from patients with common variable immunodeficiency we could show a positive effect on T and B cell immune responses when antagonizing the cAMP/PKA signaling pathway prior to cell activation. In order to treat patients with immune disorders in the best possible way in the future, it is important to establish an understanding of immune responses and investigate the use of immune modulating agents.