Human T cell regulation – from the mechanistic basis to translational applications

The Zielinski lab is interested in the fundamental basis of how protective and pathogenic T cell memory responses are shaped in human health and disease. Our long-term goal is to develop novel therapeutic strategies in settings of chronic infections, autoimmunity and cancer. Our research has unraveled novel T cell subsets with major implications for human health and disease and proposed novel molecular checkpoints, which determine their regulation and which might serve as therapeutic candidate targets.

- How do T cells adapt to the challenges of pathogen encounter?
- How can we exploit their regulatory checkpoints for therapeutic interventions?
- How do T cells crosstalk with the local tissue microenvironment?
- How do T cells communicate with other immune compartments system-wide over a lifetime?

We are in particular interested in the mechanisms by which a tissue resident immunological memory is generated and maintained in the human tissue. The reciprocal interactions of T cells with the tissue microenvironment including fungi, microbiota, metabolites and even ions are of particular interest. They shape the functionality of the tissue resident memory T cell compartment, “imprint” tissue-tropic migration and residence and represent interesting targets for novel immunomodulatory therapies.

To address our goals, we use a translational and interdisciplinary approach, combining the analysis of healthy and pathological tissue samples with novel cutting-edge technologies, gene editing and high-dimensional data analysis. We are studying patients undergoing extensive *in vivo* perturbation of their immune system, i.e. by systemic therapies with immunomodulatory drugs or by stem cell transplantation. We also take advantage of studying patients with genetic immunodeficiency syndromes.

Together, our research aims to provide a fundamental basis of human T cell regulation and translational applications for the design of pharmaceutical targets and adoptive T cell therapies in settings of infections, autoimmunity and cancer.