An overarching theme of our research is the cellular, molecular and signalling processes underpinning immune homeostasis.

Central and peripheral tolerance. To eliminate self-reactive T-cells, transcription regulator Aire promotes expression of tissue-restricted antigens in the medullary thymic epithelial cells (mTECs). In this context, we have shown that if not removed in the thymus, self-reactive enteric α-defensin-recognizing T cells in the periphery can destroy Paneth cells, leading to intestinal microbiome dysregulation and enhanced inflammatory Th17 responses. Using single-cell RNA-sequencing, we have also studied the process of cooperative antigen transfer and its importance for the generation of T-regulatory cells (Voboril et al, Nature Communications, in revision).

Interestingly, AIRE is not exclusively expressed in mTECs, but also in extrathymic cells present in the lymph nodes, spleen and testes. To enable cell type-specific ablation of the Aire gene, we generated transgenic mice with a LoxP-flanked Aire locus. We have also identified Aire-expressing cells in lymph nodes with typical group 3 innate lymphoid cell (ILC3) characteristics. They express MHCII, costimulatory molecules, and present antigens to CD4⁺ T cells. These findings define a novel type of ILC3-like cells with potent APC features.

Toll-like receptors and embryonic haematopoiesis. We have shown that TLRs are expressed during early embryogenesis (Fig. 1). The expression of TLR2 on E7.5 c-kit⁺ cells mark the emergence of precursors of erythroid-myeloid progenitors (EMPs). Using in vivo fate mapping, we demonstrated that at E8.5, the Tlr2 locus is already active in emerging EMPs and in progenitors of adult haematopoietic stem cells (HSC). Together, we showed that the activation of the Tlr2 locus tracks the earliest events in the process of EMP and HSC specification.

TCR proximal signalling. We continue in our effort to understand the earliest events leading to the activation of T cells (Fig. 2). Toward this end, we have contributed to studies on membrane heterogeneities in T cells.

Selected publications: