Visualizing the dynamics of T cell receptor signaling throughout thymocyte development

Positive selection of thymocytes is essential for the generation of a functional population of mature T cells capable of recognizing foreign antigen in the context of MHC. Although it is known that weak T cell receptor (TCR) recognition of self-peptides presented by MHC molecules on cortical thymic epithelial cells is necessary for positive selection, the quality and quantity of TCR signaling that governs this process in situ remains largely unknown. I will describe the use of a thymic slice system in combination with two-photon microscopy and chemical-genetic systems to characterize the dynamic behavior of thymocytes undergoing positive selection within the true spatial and temporal context of the three-dimensional thymus. This work also highlights the differences between in vitro and in situ systems for understanding immune cell function and behavior.