Notch2 controls developmental fate choices between germinal center and marginal zone B cells upon immunization

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Follicular (FO), marginal zone (MZ), and germinal center (GC) B cells play a central role in humoral immunity, but their developmental dynamics and the mechanisms of their maintenance are not clearly defined. We developed and continue to develop integrative approaches combining mathematical modeling with long-term, dedicated experiments to understand the rules governing B cell homeostasis. Our work has revealed how the host environment drives cell-extrinsic, age-related changes in the generation and maintenance of B cells and provides crucial insights into how our immunoglobulin repertoires evolve as we age.

Relevance: These findings bring us closer to developing a comprehensive understanding of the processes that shape and maintain our protective antibody-mediated immunity.

Towards a unified model of naive T cell dynamics across the lifespan

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The size and clonal diversity of T lymphocyte subsets are determined by the interplay of production, proliferative renewal, death, and differentiation. By combining mathematical modeling with a wide range of datasets derived from diverse experimental systems, we demonstrate that the time since T cells' ancestors developed in the thymus—post thymic cell age—has a profound effect on their life expectancy. This finding challenges the widely held view of feedback regulation of T cell homeostasis and reveals a remarkably simple picture of their maintenance, in which they adapt to increase their survival capacity.

Relevance: In combination with results from my previous publications, which show a progressive decline in T cell responsiveness with age, our results here provide a potential explanation for the age-associated decline in T cell-mediated immunity, in which functionally impaired old naive T cells accumulate preferentially as we age.

Spatiotemporal modeling of the key migratory events during the initiation of adaptive immunity.

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In another cross-disciplinary project, we tackled the challenge of modeling the trafficking of dendritic cells between skin and lymphatic tissues during an active immune response. This work provides a detailed quantitative assessment of the residence and transit times of dendritic cells in skin tissue surrounding the point of infection and the lymph nodes draining the immune cells back and forth to the infection site.

Relevance: Our results have strong relevance for developing strategies to modulate antigen accessibility during vaccinations and in treating infections and auto-immune pathologies.