Lineage Tracing to Model B Cell Response Dynamics Using Paired Single-Cell Transcriptomics and BCR Sequencing

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B lymphocytes produce highly specific antibodies that resolve infections and underpin effective vaccines. They do this through affinity maturation: tightly regulated cycles of somatic hypermutation (SHM) and selection within the splenic germinal centers that refine the B cell receptor (BCR). At the same time, B cells differentiate into different functional phenotypes, such as antibody-secreting plasma cells or long-lived memory cells. However, how B cell clones transition, persist, and evolve across these states remains poorly understood. By analyzing data derived from single-cell gene expression and V(D)J sequencing post-immunization, we construct clonal trajectories of responding B cells and analyze their differentiation patterns across time. Effectively, we will use this analysis to pinpoint mutation patterns that define key developmental branch points and characterize molecular players governing clonal expansion and diversification. This comprehensive informatics framework dissects the molecular and evolutionary logic of the B-cell immune response, with implications for vaccine design, autoimmunity, and B-cell malignancy.