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Identifying and rationally modulating cellular drivers of enhanced and diminished immunity

Abstract: Immune homeostasis requires constant collaboration between a diverse and dynamic set of cell types. Within our immune tissues, distinct cellular subsets must work together to defend against pathogenic threats, maintain tolerance, and establish memory. While surveying multiple healthy individuals enables exploration of potential ensemble immune solutions, contrasts against outliers of health and disease can reveal deviations that underscore diagnostic, therapeutic, and prophylactic features of enhanced function or dysfunction. Here, I will discuss how we can leverage single-cell genomic approaches – and, in particular, single-cell RNA-Seq – to explore the extensive functional diversity among immune cells within and across individuals, and uncover, from the bottom-up, distinct cell types and states associated with improved or impaired immunity. Moreover, I will discuss emerging experimental and computational strategies for altering ensemble cellular responses through targeted intra- or extracellular induction or suppression of these preferred or unwanted types and states, respectively.