**Project Narrative**

Marginal zone B cells are key players in defending against bacteria and viruses that enter the circulation; generating a reservoir of antibodies against common pathogens, and regulating tolerance to our own proteins and lipids. A quantitative understanding of their homeostasis will provide unparalleled insights into determinants that shape their pool size and clonal repertoire, across our lifespan and during immune responses. Leveraging or manipulating these determinants to modulate antibody-mediated protection – for example, to boost the efficacy of vaccines or potency of immune-regulative treatments – will have direct *relevance to human health*, guiding the development of therapeutics against systemic infections, immunodeficiencies, and autoimmunity.