

Stemness and maintenance of CD4+ regulatory T cell (Treg) responses in homeostasis, inflammation and ageing

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Department/Institute: Pathology

Industrial Partner: AstraZeneca

Research area: Immunology, inflammation, ageing, T cell biology, regulatory T cells

Project outline:

CD4+ Regulatory T (Treg) cells are rare immune cells with powerful immunoregulatory functions. Treg cells are required throughout the lifespan prevent lethal inflammation. Defects in their function are associated with autoimmunity and allergy. There is intense scientific and translational interest in exploiting the powerful functions of Treg cells but efforts to do so have thus far been disappointing – indicating the need to develop a better understanding of their underlying biology.

While much is now known about how Treg cells develop, we lack understanding of how Treg responses are maintained. A majority of Treg cells develop in early life, but maintenance of Treg responses is required throughout life and into age to promote immune homeostasis. Maintenance of Treg responses is also critical to efficacy of Treg-targeted therapies, including Treg cell therapy and tolerogenic vaccines. In many tissues, cellular populations are maintained by quiescent stem cells which self-renew while giving rise to shorter-lived progeny. Our recent published work (Grant et al., J Exp Med 2020) shows that a critical characteristic of stem cells – quiescence – is required for Treg cells to be maintained over long periods of time.

Using cutting-edge new mouse genetic models which enable Treg cell subpopulations to be precisely fate-tracked and depleted, this studentship will test the hypothesis that long-lived Treg responses are hierarchically organised, with quiescent self-renewing progenitor cells giving rise to shorter-lived functionally active progeny. It will define molecular mechanisms by which quiescent Treg cells are maintained into age to promote lifelong immune and tissue homeostasis.

BBSRC DTP main strategic theme: Bioscience for an integrated understanding of health

BBSRC DTP secondary strategic theme: Understanding the rules of life