Project: Initial Training Network for Neurological Disorders orchestrated by cytokines (NeuroKine)

Research Topic: Antigen-specific immunotherapy

One of the major features of the autoimmune disease Multiple Sclerosis (MS) is that T cells mistakenly recognize and attack self-peptides of the myelin sheath. Antigen-specific immunotherapy of MS aims to restore immune tolerance while avoiding the use of non-specific and potentially toxic immunosuppressive drugs. Effective tolerance induction in the Tg4 TCR-transgenic murine model for MS, experimental autoimmune encephalitis (EAE), involves repeated administration of a self-peptide in a dose escalating manner to re-educate pathogenic T cells to become protective interleukin-10 (IL-10)-secreting regulatory T cells. By breeding the Tg4 T cell receptor onto an IL-10-GFP reporter mouse, it is possible to further investigate the spatiotemporal distribution of IL-10 secreting cells in lymphoid and non-lymphoid tissue during the course of tolerisation and during the progression of EAE. A further aim is to boost the IL-10 secretion by making use of tolerance enhancers like glycogen synthase kinase-3 inhibitors. Moreover, the project investigates the role of the spleen in peripheral tolerance induction because peptide administration targets CD11c dendritic cells in the spleen. Finally, the ability of the IL-10 secreting cells to exhibit bystander suppression, in which responses of autoreactive lymphocytes are inhibited although the specificity of both cell types differ, is investigated.

Principal Investigator: Prof. David C. Wraith

Research Fellow: Anja Wegner

Apitope Technology (Bristol) Ltd
Innovations Centre, Bristol & Bath Science Park
Dirac Crescent, Emersons Green
Bristol BS16 7FR, United Kingdom