Project title: Investigating the immunomodulatory effect of intervention therapy for T-cell leukaemia in the premalignant stage

Project Summary:

Cancer prevention is the optimal strategy to minimise the vast and growing burden of cancer and is a focus of the government's 10 Year Health Plan. **To achieve this, we urgently need effective, well-tolerated treatments for premalignancy.** Infection with Human T-cell Leukaemia Virus type-1 (HTLV-1) causes Adult T-cell Leukaemia/Lymphoma (ATL) in 5-10% of carriers. Our previous research has shown that premalignant cells appear in the blood up to 10 years before ATL. We translated this observation from bench to bedside to develop a prognostic test which identifies 'high-risk' HTLV-carriers who have >30% transformation risk within 5 years, and have launched an academic Phase 2 multi-centre trial to treat high-risk carriers with the anti-CCR4 antibody mogamulizumab, to eradicate premalignant T-cells.

We are searching for a candidate to join our interdisciplinary team to investigate whether the antiviral immune response, or the lack thereof, contributes to the emergence or control of ATL. Immunocompromise is a hallmark of ATL, and malignant T cells have a regulatory T cell phenotype, thus malignant T-cells may directly suppress immune responses. Mogamulizumab depletes both CCR4-expressing premalignant T-cells and conventional regulatory T-cells. **We hypothesise that mogamulizumab treatment restores dysfunctional anti-HTLV- immune responses, resulting in durable suppression of premalignant cells after the drug is cleared.**

This project will assess the depth and duration of response to treatment by quantifying premalignant T cells in blood samples before, during, and after treatment. Quantification of key immune cell subsets and antiviral immune responses at the same time points will be carried out to test for an association between the restoration of antiviral immune responses and durable control of premalignant disease. The results of this study will provide critical evidence to guide future strategies for cancer prevention, improve risk stratification for HTLV-1 carriers by identifying novel immune biomarkers, and inform clinical management of premalignancy.

Supervisory Team:

Dr Aileen Rowan (ICL)
Dr Lucy Cook (ICNHT/ICL)
Dr Maggie Cheang (ICR)

Clinical Specialities:

Haematology/Oncology