### Division
Cellular and Molecular Pathology

### Supervisor
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### Project title
Characterization of clonal evolution of T-cell lymphoma

### Project abstract for advert
(Max 100 words)
It has long been assumed that malignant T-cell lymphoma is a monoclonal disease. i.e. the tumour grows and expands from a single cell. In contrast to this traditional view, our ongoing investigations show for the first time evidence of bi- or oligo-clonal T-cell populations in angioimmunoblastic T-cell lymphoma and its related entities. It is imperative to investigate whether each of these different clonal T-cell populations in a T-cell lymphoma is neoplastic, derived from a common progenitor cell population, and how they impact on disease presentation and treatment responses.

### Full details
(Max 250 words. Will be published on Departmental website; do not include confidential information)
Angioimmunoblastic T-cell lymphoma (AITL) is a neoplastic proliferation of mature T follicular helper cells with clinical and histological presentations strongly suggesting a role of antigenic drive in its development. Genetically, the lymphoma development is characterized by a step-wise acquisition of somatic mutations. Early mutations involve epigenetic regulators (*TET2*, *DNMT3A*) and occur in haematopoietic stem cells, most likely causing “clonal haematopoiesis” and increasing risk of lymphomagenesis. Subsequent genetic changes involve cellular signaling molecules (*RHOA*, *VAV1*, *PLCG1*, and *CD28*, and the *CTLA4-CD28*, *ITK-SYK* and *VAV1-STAP2* fusion), and occur probably in committed T-cells, thus important for malignant transformation and clonal expansion. By investigating both somatic mutation and TCR gene rearrangement, we found bi- or oligo-clonal T-cell populations in AITL, particularly in cases with multiple *TET2* mutations. This raises the possibility of independent malignant transformation from the haematopoietic stem cells carrying *TET2* mutation. We propose to characterize further the clonal composition, their temporal and spatial evolution during AITL development, and examine the impact of bi- or oligo-clonality on disease presentation and progression.

### Image(s) related to project
(For use in adverts and on Departmental website)