

## **Study of the Graft versus Lymphoma Effect in Mycosis Fungoides**

Mycosis fungoides (MF) is a CD4+T-cell lymphoma of the skin that is incurable in its advanced stages. Preliminary data from our ongoing programme of reduced intensity conditioning allogeneic haemopoietic stem cell transplantation (RIC-HSCT) for advanced stage MF suggest a significant graft-versus-lymphoma (GVL) effect associated with long term remission but often accompanied by graft-versus-host disease (GVHD).

The aims of this application are: First, to gain additional experience in the management of patients with RIC-HSCT. Second, to develop specific and transferable expertise in the management of patients with advanced stage cutaneous T-cell lymphomas and third, to commence a laboratory project with the ultimate goal of identifying the tumour or minor histocompatibility antigens (mHA) capable of inducing a GVL but only a mild/moderate graft versus host effect. By employing TCRBV chain spectratyping of tumour bed non-malignant and blood T cells selected for their skin homing potential, we will identify clonal expansions with anti-tumour potential. Using mAb specific for these clonal expansions, T cell clones will be generated; their specificity for mHA and their GVL and GVH potential will be determined by their relative reactivity against tumour, recipient and donor haemopoietic cells and recipient keratinocytes. This approach will allow the characterisation of mHA-specific T cell responses without a requirement for prior knowledge of the identity of the mHA themselves.

The well described approach of expression cloning using cDNA libraries generated from patient B-cell lines and primary tumour cells and transfected into COS-1 cells will be used to identify mHA presented by HLA class I to tumour-reactive CD8+ T cells. It is expected that the work proposed here will form the basis for a better understanding of the GVL effect in MF and will allow the development of refined immunotherapeutic approaches that retain powerful GVL potential but are associated with clinically manageable GVHD.