The University of Nottingham School of Medicine
Division of Cancer & Stem Cells
(http://www.nottingham.ac.uk/medicine/about/cancerandstemcells/index.aspx)
Host-Tumour Interactions Group
(http://www.nottingham.ac.uk/research/groups/hosttumourinteractions/index.aspx)

PhD Project - The Impact of Tumour Microenvironment on crosstalk between Antigen Presenting Cells and Stromal Fibroblasts

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Cross talk between antigen presenting cells (APC) and stromal cells has a marked impact on their function resulting if the differential induction of immune responses. This extra dimensionality of immune regulation provides a means to communicate micro-environmental signals to the immune system and therefore is of interest in organ-specific pathology and diseases such as cancer. We recently described a role for stromal fibroblasts (FB) in controlling key aspects of the function of the principal APC, namely dendritic cells (DC) (J. Leukocyte. Biol. 2016 100: 381-9). In this system, the expression of key signal 3 cytokines by activated DC was inhibited by ionising radiation. However, signals derived from co-cultured FB were able to restore the function of DC and their production of IL-23, a major Th17 supporting cytokine. This has potential ramifications for understanding the immune response to local radiotherapy. These findings underscore the need to account for the impact of micro-environmental factors, including stromal cells, in understanding the control of immunity.

This PhD will investigate intercellular communication between APC (namely DC and macrophage) and stromal fibroblasts. Tissue culture models will be established to replicate the tumour microenvironment by using primary FB from normal and malignant areas and their impact on the immune function of DC and M1 and M2 macrophages will be determined. A range of assays will be employed to investigate the regulation of signals governing the polarisation of CD4+ T-cells to Th1, Th17, Tr1 etc.

The successful student would join the Host-Tumour Interactions Group co-directed by Dr Andrew Jackson and Professor Poulam Patel. The group currently comprises PhD students, clinical research fellows and technicians, and has an international standing in the field. The group is based on the City Hospital Campus in laboratories shared with other immunology and cancer biology research groups.

(Added: November 2016)