

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 - Immune regulation by DNA damage-response Pathways in Dendritic Cells**

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**Key words:** Dendritic cell, immunity, DNA-repair, ATM, IL-23, Th17, regulatory T-cell, transcription factor

T-helper 17 (Th17) cells play central roles in autoimmunity and cancer and are regulated by polarizing cytokines secreted by dendritic cells (DC). This project addresses the novel role played by DNA damage-response (DDR) proteins in regulating Th17 polarizing cytokines in DC. We identified a novel pathway where the DDR proteins including ATM (Ataxia Telangiectasia Mutated) kinase control secretion by DC of the cytokines IL-1, -6 and -23 (J. Immunol. 2013 190: 3246-55). More recently we have now discovered that other DNA-repair systems also immuno-regulatory roles (Wang et al, submitted). Our work shows that these DDR proteins act as rheostats and can be inhibited with small molecules or activated by stress to amplify or attenuate Th17 responses. We have already identified some potential molecular targets in this pathway and will further characterise these before testing these in pre-clinical models. A comprehensive understanding of these pathways will identify further molecular targets to switch on or off Th17 responses. We therefore have a potential therapeutic strategy for cancer immunotherapy and autoimmunity.

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)**