CRUK Cambridge Centre MRes rotation project

Rotation Project Title	Role of GNA13 in lymphoid malignancies
Head of Laboratory (PI) Name	Daniel Hodson
Second supervisor if applicable	
Programme	Haematology
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Laboratory Location	CSCI

Project Outline	Positive selection CRISPR screens in our lab have identified a potent tumour suppressor function for the G protein alpha subunit GNA13 in lymphoid malignancies. GNA13 is commonly inactivated by mutation in Diffuse lymphoma and Burkitt lymphoma. A previous study has proposed a mechanism based on lymphocyte homing and regulation of PI3K activity. Our data suggests that other mechanisms account for the function of GNA13 mutations in lymphomas. This has implications for the molecular classification and potential therapy of these malignancies. This project will investigate the downstream pathways regulated by GNA13 in human lymphocytes. The MRES project will construct and validate the molecular tools required for these experiments.
Experimental plan	During the three-month MRES rotation the student will generate molecular biology tools to manipulate GNA13 activity. This will include cloning individual lentivirial sgRNA constructs and retroviral expression constructs for WT GNA13, dominant negative GNA13 and the antagonistic molecule GNAI2. These will be transduced into cell lines and primary cells and their function tested by Western blotting and flow cytometry. Future work (PhD project) will employ these tools for RNA-Seq and intracellular signalling experiments.
Main Techniques	Molecular Biology Tissue Culture Flow Cytometry CRISPR/Cas9
Key References	Muppidi JR et al. Loss of signalling via Gα13 in germinal centre B-cell-derived lymphoma. Nature 2014 516(7530)254-8