Investigating novel interactions of the Merlin gene in cell behaviour.

Supervisory team:
Lead supervisors: Prof Benjamin Housden (University of Exeter) and Prof David Parkinson (University of Plymouth)
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Collaborators: Prof Oliver Hanemann (University of Plymouth)

Host institution: University of Exeter (Streatham) / University of Plymouth
Submit applications for this project to University of Exeter

Project description:
The aim of this project is to investigate the functions of the Merlin/NF2 protein using a combination of Drosophila, mouse and human resources and approaches, giving the student on this project a huge range of expertise with many different techniques and model organisms. This project is important because the Merlin protein is a key scaffolding protein, which controls many aspects of cell growth, adhesion, proliferation, differentiation and migration as well as being dysregulated in many tumour types and tumour syndromes.

While the function of NF2/Merlin in regulating Hippo signalling is relatively well characterised, there is evidence that the protein has multiple other functions that have not been fully explored. Understanding these alternate roles of the protein as well as completely unknown functions will lead to a better understanding of how basic cell behaviour is controlled during tissue development and disease. The wide range of mutations within the NF2/Merlin gene in disease also gives us ideal models to track such new interactions.

In this project, the student will use a combination of Drosophila, mouse and human model systems to investigate novel functions of the NF2/Merlin protein. We will start by investigating the genetic interactions of the NF2/Merlin gene in Drosophila cells, which will provide insight into gene function. This will identify genes that depend on NF2/Merlin to fulfil their own functions and, combined with statistical enrichment analysis of the genetic interactions, will provide new knowledge into the various biological pathways that are dysregulated by NF2/Merlin loss.

Next, the identified pathways will be investigated in human cell lines and primary cells to assess the conservation of the newly identified functions of NF2/Merlin. Finally, mouse models will be used to test the new functions of NF2/Merlin using an in vivo system.

By the end of the project, we expect to have uncovered new functions of the NF2/Merlin gene that will improve our understanding of how cells control their growth, proliferation and behaviour. Given the important role of this gene in disease, we expect that this new knowledge will lead to the discovery of new therapies for NF2/Merlin related tumours in the future.

This project will combine cell culture, molecular biology, biochemistry, statistical analysis and in vivo experiments. This broad range of experience and skills will provide a strong basis for the successful candidate's future career development.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.