Understanding the Role of Extracellular Vesicle/Exosome Transport in the Visual System

Supervisory team:

Main supervisor: Dr Ben Mead (Cardiff University)
Second supervisor: Prof Aled Clayton (Cardiff University)
Prof James Uney (University of Bristol)

Host institution: Cardiff University

Project description:

Cellular communication has typically been understood as cells secreting messenger proteins, known as cytokines and growth factors, which bind to receptors on recipient cells and elicit their desired effect. A great deal of research over the last 50 years into treatments for disease has also been trying to modulate these signals, inhibiting, altering, or increasing them. A new signalling mechanism has recently been discovered, and due to its novelty, is still poorly understood. Along with cytokines/growth factors, cells also secrete extracellular vesicles (EVs), which include exosomes and microvesicles. These membrane-bound particles contain huge numbers of proteins as well as genetic material in the form of RNA (mRNA and miRNA). While their existence has been known for many years, only recently have EVs been effectively shown to be able to deliver their cargo into other cells, with those recipient cells able to utilize said cargo. Importantly, this mRNA forms the blueprint for new protein synthesis whereas the miRNA acts in opposition, inhibiting protein synthesis. Cells can therefore regulate the gene expression and ultimately, the protein make-up of recipient cells via the secretion of EVs. Due to our poor understanding of this process, this project seeks to better understand the role this signalling mechanism plays within the normal physiology of the eye. The eye is an easily accessible tissue, making it a highly amenable model to study EV communication. EVs have been implicated in disease and this includes detrimental factors that further the pathogenesis as well as potential therapies. Not enough data exists on their normal function within the healthy body and eye, making these implications difficult to study.

This project begins by isolating/analyzing EVs including their size, numbers and cargo. This cargo includes their mRNA, miRNA, and proteins. Since every cell releases different types of EVs, it will be important to identify which retinal cells are releasing which EVs and track where they are going in the eye including their ultimate destination. Human retina will be generated from embryonic stem cell lines and will serve as a useful comparison to ensure results are applicable to human physiology. We will also determine what happens in the eye as we begin inhibiting the release of EVs or the packaging of specific cargo, allowing us to ascribe specific functions to EVs. It is also necessary to analyse the target retinal cells and better understand what changes occur when an EV delivers its cargo.

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.