# Role of cholesterol and cholesterol metabolites in brain development

**Supervisory team:**
**Main supervisor:** Dr Helen Waller-Evans (Cardiff University)
**Second supervisor:** Dr Yasir Syed (Cardiff University)
Prof Emyr Lloyd-Evans (Cardiff University)

**Host institution:** Cardiff University

**Project description:**
Cholesterol is known to be vital in the developing brain, both as a membrane component and signalling molecule. It is a major constituent of myelin, is needed to form synapses, and is critical for signalling via Sonic Hedgehog, which controls how, where and when different parts of the brain are formed. Genetic disruption of the genes involved in cholesterol biosynthesis cause defects in brain development and neurodevelopmental disorders such as autism, further underscoring its importance. Despite this obviously vital role, very little is known about when and where cholesterol is needed during brain development – it is not known which cells and regions of the brain are most dependent on cholesterol or whether there are critical timepoints at which cholesterol is needed. This PhD will use genetic techniques and drug treatments to investigate and better understand the role of cholesterol and cholesterol metabolites in brain development. This project will characterise the expression of genes and proteins involved in cholesterol biosynthesis and regulation in different cells and regions of the developing zebrafish brain and in cerebellar organoids. We will then investigate the effects of modulating these genes and proteins on brain development, including regional patterning and cell migration, and on cell function, including effects on cholesterol homeostasis and synapse formation. The student will gain experience in developmental biology, cell biology, and lipidology. The student will learn a wide range of techniques, including cutting edge super-resolution confocal and lightsheet microscopy, intracellular signalling, protein and lipid biochemistry, molecular biology, and organoid culture. The project will utilise state-of-the art facilities at the Medicines Discovery Institute and Neuroscience and Mental Health Innovation Institute at Cardiff University, where the student will be embedded in a multidisciplinary research environment encompassing cell biology, chemistry, structural biology and genetics. Understanding the role of cholesterol and cholesterol metabolites in brain development will not only improve our knowledge of this fundamental process, but also help us understand how disruptions to cholesterol homeostasis contribute to neurodevelopmental disorders and whether any treatments developed for these disorders are likely to be effective if given after diagnosis. This project would be suitable for applicants with a degree in a biological subject.

**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.**