

## Differentiated normal cell identity and epigenetic barriers to trans-differentiation and reprogramming

### Supervisory team:

**Main supervisor:** Prof Adele Murrell (University of Bath)

**Second supervisor:** Dr Karim Malik (University of Bristol)

**Non-academic (CASE) supervisor:** Dr Mark Kotter and Dr Tuzer Kalkan (Bit.Bio)

**Host institution:** University of Bath

**CASE partner:** Bit.Bio

### Project description:

How does a cell maintain its differentiated identity and carry out its specific functions? What prevents a normal cell from losing its identity and transforming into a less differentiated cell or even another cell type? Understanding these fundamental questions about cell identity will advance the diverse applications of stem cell research, and the utility of stem cells in improving health across the life-course.

In this PhD project we will investigate how two epigenetic mechanisms come together to constitute cell identity and provide the cell with a memory of its developmental origins. The two mechanisms that will be studied are: (i) Demethylation of DNA through the conversion of 5-methylcytosine to 5-hydroxymethylcytosine (5-hmC) and (ii) The methylation of arginine residues on histones. We will use induced pluripotent stem cell and hepatocyte differentiation models to investigate how these epigenetic marks are established and maintained during differentiation and reprogramming.

During this PhD you will gain the following skills and experience: 1) Cell biology skills using high content quantitative microscopy, iPSC culture and in vitro differentiation. 2) Epigenetic biochemistry, detection of DNA methylation, 5hmC, histone modifications, making sequencing libraries, bioinformatics and computational analysis of data 3) Mathematical probabilistic modelling to describe the interplay between gene expression, chromatin modifications and DNA methylation and derive gene regulatory networks 4) Industrial collaboration to apply epigenetic profiling to in-vitro differentiation.

This cross disciplinary project will co-supervised at Universities of Bath and Bristol and includes an industrial placement in a Cambridge-based Biotech company. Informal enquiries can be made to [amm95@bath.ac.uk](mailto:amm95@bath.ac.uk).