Investigating conserved long non-coding RNA functions during melanocyte development in zebrafish and human melanoma

Supervisory team:
Main supervisor: Dr Keith Vance (University of Bath)
Second supervisor: Prof Robert Kelsh (University of Bath)

Collaborators: Prof Mark Lindsay (University of Bath), Prof Colin Goding (University of Oxford), Dr Karim Malik (University of Bristol)

Host institution: University of Bath

Project description:
The vertebrate genome expresses many thousands of long non-coding RNAs (lncRNAs). LncRNAs can act as gene expression regulators of important biological processes and have been implicated in different diseases. However, very few lncRNAs have so far been shown to be critical for vertebrate development in vivo.

During development, neural crest cells give rise to a number of different cell types including pigment producing melanocytes. Mutations within these cells can give rise to melanoma, a highly aggressive form of skin cancer. In this project, we will use zebrafish as a model to investigate cell type specific functions of conserved human-zebrafish lncRNAs in melanocyte development in vivo. We will perform RNA-sequencing to identify lncRNAs that are expressed in zebrafish neural crest cells and compare these with human melanoma associated lncRNAs to map orthologous transcripts. CRISPR interference (CRISPRi) will then be performed to deplete the expression of selected conserved lncRNAs in zebrafish and determine their function during neural crest cell differentiation and melanocyte development in vivo. A number of genes important for melanocyte development are also dysregulated in melanoma. We will therefore use CRISPRi to deplete orthologous lncRNA expression in human melanoma cells and investigate their role in controlling the metastatic potential of melanoma cells in culture. Rescue experiments will then identify conserved lncRNA functions. This work will generate important insights into lncRNA mediated mechanisms of cellular growth and differentiation control during melanocyte development and will have implications for understanding the role of lncRNAs in melanoma.