Investigating conserved long noncoding RNA functions during melanocyte development in zebrafish and human melanoma

This project is one of a number that are in competition for funding from the South West Biosciences Doctoral Training Partnership (SWBio DTP) which is a BBSRC-funded PhD training programme in the biosciences, delivered by a consortium comprising the Universities of Bath, Bristol, Cardiff and Exeter, along with the Rothamsted Research Institute. The partnership has a strong track record in advancing knowledge through high quality research and teaching, in collaboration with industry and government.

Studentships are available for entry in September/October 2019.

All SWBio DTP projects will be supervised by an interdisciplinary team of academic staff and follow a structured 4-year PhD model, combining traditional project-focussed studies with a taught first year which includes directed rotation projects.

Lead supervisor: Dr Keith Vance, Department of Biology & Biochemistry
University of Bath, email k.w.vance@bath.ac.uk

Co-supervisors: Prof Robert Kelsh (University of Bath), Prof Mark Lindsay (University of Bath)

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

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 cancer. 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.

Funding

Studentships provide funding for a stipend at the standard UKRI rate (currently £14,777 per annum, 2018/19 rate), research and training costs and UK/EU tuition fees for 4 years.

UK and EU applicants who have been residing in the UK since September 2016 will be eligible for a full award; a limited number of studentships may be available to EU applicants who do not meet the residency requirement. Applicants who are classed as Overseas for tuition fee purposes are not eligible for funding.

Applications

Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or the equivalent qualifications gained outside the UK, in an appropriate area of science or technology.

Applications should be submitted on the University of Bath's online application form for a PhD in Biosciences. Please ensure that you quote the supervisor's name and project title in the 'Your research interests' section. You may apply for more than one project if you wish but you should submit a separate personal statement relevant to each one.

The deadline for the receipt of applications is Monday 3 December 2018.