

## Ancestral function of the imprinted Grb10 gene

**Lead Supervisor:** Prof Andrew Ward, Department of Biology & Biochemistry

### Project description:

Around 100 mammalian genes are subject to genomic imprinting, a form of epigenetic regulation that restricts expression to only one of the two parental alleles. Major goals are to understand: how and why imprinting has evolved; how imprinted genes influence health and disease, including cancer and obesity.

Dlk1 is expressed from the paternally inherited allele, promotes growth and inhibits adipose deposition. Conversely, maternally expressed Grb10 inhibits growth and promotes adipose deposition. We have shown using mouse genetics that Dlk1 and Grb10 act antagonistically in a common pathway. Importantly, their actions are independent of the insulin like growth factor (IGF) pathway, which includes another pair of imprinted genes with antagonistic growth functions. Whereas growth regulation through IGF signalling is likely conserved in all animal species the functions of Dlk1 and Grb10 are unknown in non-mammalian species. Thus, this project aims to determine gene function in zebrafish, a model species without imprinting, to establish whether growth regulation is an ancestral function of Dlk1 and Grb10 or has been acquired along with imprinting during mammalian evolution. Former students have discovered multiple functions of Dlk1 and Grb10 in mouse (see references, below).

The project will involve zebrafish genetics and phenotypic characterisation, with techniques from embryology, physiology, molecular biology and bioinformatics.

### Candidate:

Applicants should hold, or expect to receive, a First Class or high Upper Second Class UK Honours degree (or the equivalent qualification gained outside the UK) in a relevant subject. A master's level qualification would also be advantageous.

### Applications:

Informal enquiries should be directed to Prof Andrew Ward, [bssaw@bath.ac.uk](mailto:bssaw@bath.ac.uk).

Formal applications should be made via the University of Bath's [online application form](#).

On the application form, please ensure that you quote 'Evolution Education Trust' in the Finance section and the supervisor's name and project title in the 'Your research interests' section. Should you wish to be considered for more than project, quote the projects in order of preference and upload a separate personal statement relevant to each one.

Please see our Doctoral College website for [more information on how to apply](#) for a PhD at Bath.

**Application deadline: 30 April 2019.**

**Interviews will take place in Bath on 14 June 2019.**

**Anticipated start date: 30 September 2019.**

### References:

Madon-Simon et al. 2014, BMC Biology, BMC Biology 12, 771 (22p).  
Cowley et al. 2014, PLoS Biology, 12, e1001799 (13p).  
Garfield et al. 2011, Nature, 469, 534-538.  
Smith et al. 2007, Mol. Cell. Biol., 27, 5871-5886.  
Charalambous et al. 2003, Proc. Natl. Acad. Sci. U.S.A., 100, 8292-8297