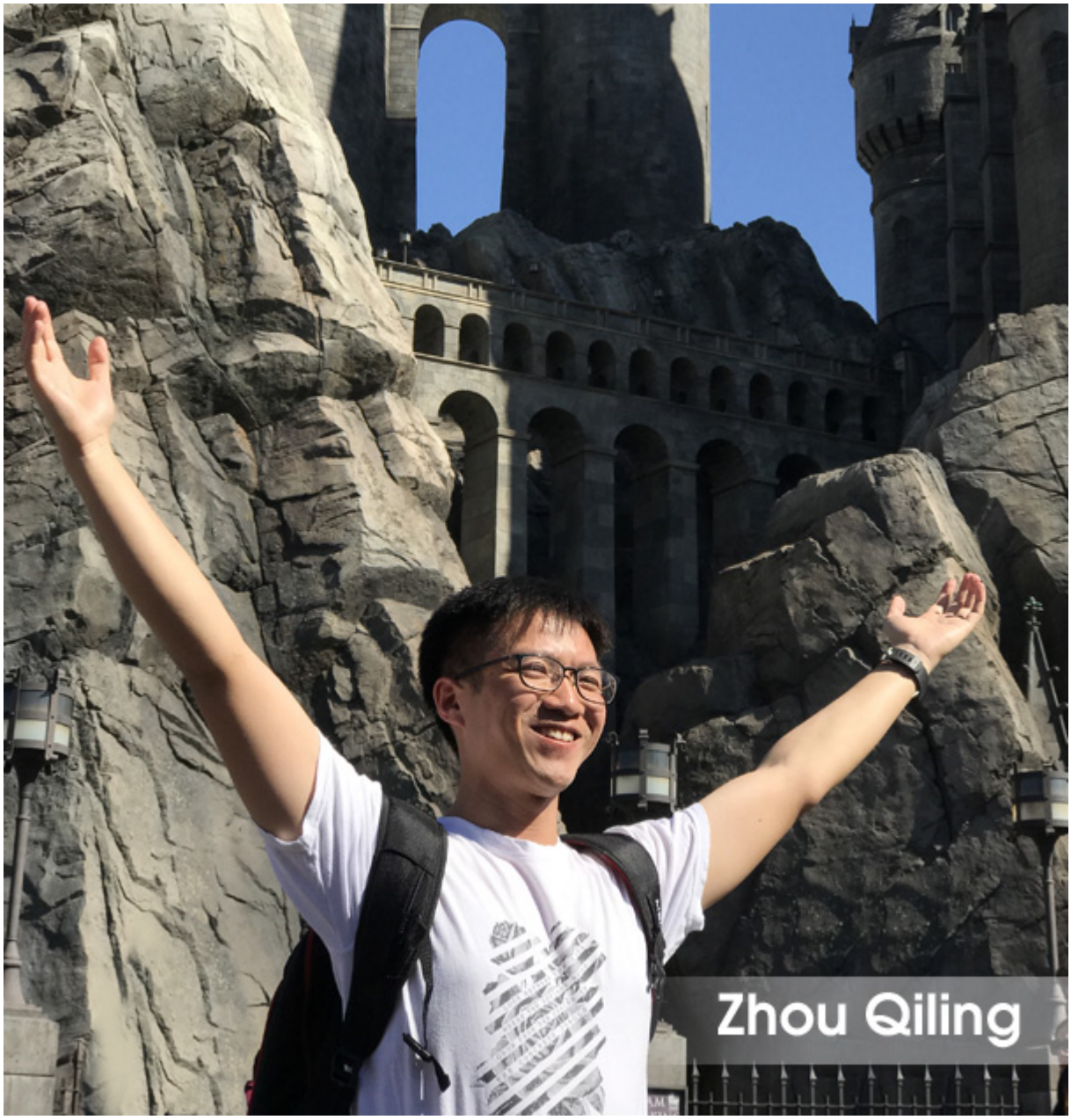
Congratulations to IMCB's latest PhD graduate - Zhou Qiling

Thursday, 02 May 2019



Thesis Title: Hematopoietic stem cell integrity is dependent on chromosome structure maintained by ZNF143

Motile cilia are localised to tissues and cells where fluid movement and cellular locomotion is required. Mutations in genes associated with ciliogenesis and cilia motility give rise to diseases called ciliopathies. Primary Ciliary Dyskinesia (PCD), a heterogeneous genetic disorder, is the most common form of ciliopathy that arises from defects in motile cilia. Several systematic approaches have led to the identification of numerous genes with putative function in ciliogenesis and ciliary motility. We interrogated existing data and identified several novel candidate genes temporally associated with ciliogenesis. Expression of these genes were analysed in mouse airway epithelial cells during mucociliary differentiation at the air liquid interface (ALI) and different mouse tissues. This thesis focuses on a poorly characterized gene encoding the protein 'PIERCE1'.

Transcriptional analysis of *Pierce1* revealed an expression pattern temporally associated with ciliogenesis during differentiation of ALI mouse airway epithelial cells. *Pierce1* also shows enriched expression in motile ciliated mouse tissues. Transient morpholino knock down of *pierce1* in zebrafish showed phenotypes consistent with abnormalities in motile cilia and live imaging showed severe cilia motility defects in Kupffer's vesicle. Finally, we generated maternal zygotic loss-of-function alleles at the zebrafish *pierce1* locus using the CRISPR/Cas9. These mutants showed mild laterality defects. A custom-made antibody against mouse full length PIERCE1 protein, was used to carry out immunofluorescence microscopy on ALI cultured mouse airway epithelial cells. It revealed that PIERCE1 is a cytoplasmic protein specifically expressed in motile ciliated cells. A yeast 2-hybrid assay carried out on human lung and testis libraries identified PIAS2, as a possible interacting partner of PIERCE1. With these findings, we propose that PIERCE1 may be involved in the assembly and transport of components required for cilia motility.

Supervisor

Prof. Vinay TERGAONKAR

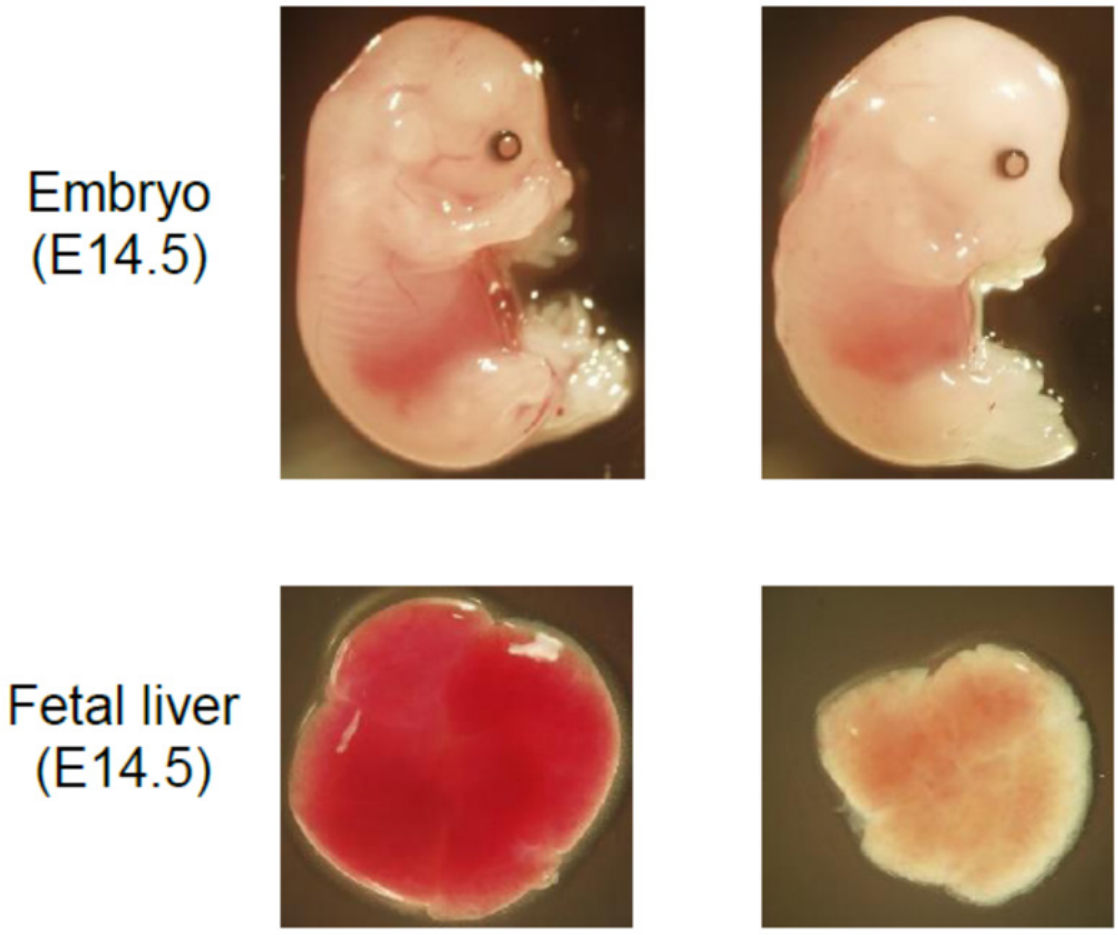


Figure Legend: Genetic depletion of Znf143 leads to fatal hematopoietic failure at embryonic stage. Intact embryo (upper panel) and fetal liver from wild type (Znf143 f/f) and Znf143 excised (Znf143 -/-) embryos were isolated at E14.5 day