Elucidating the role of mechano-sensitive miRNAs in cartilage homeostasis: a multi-organism study

Supervisory team:
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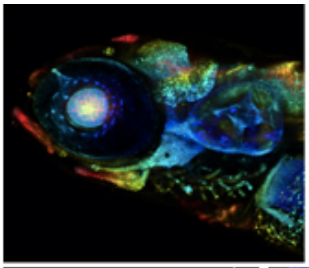
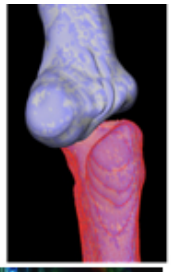
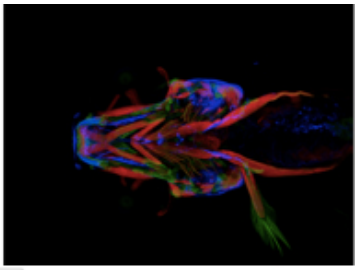
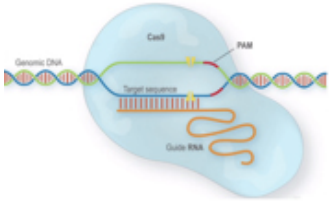
Host institution: Cardiff University

Project description:
This studentship will investigate the role of microRNAs (miRNAs) in regulating cell and tissue-dependent responses in synovial joints subjected to mechanical load. Using a range of state-of-the-art techniques and two model organisms (mouse and zebrafish), this proposal will apply a novel approach to mechanistically investigate the role of these mechanically-regulated miRNAs in cartilage chondrocyte homeostasis. A pivotal factor in maintenance of cartilage tissue homeostasis is mechanical load, effected by chondrocytes. Moderate 'physiological' loads, are essential to maintain cartilage homeostasis by promoting anabolic activities e.g. increased production of ECM molecules, whereas abnormal 'non-physiological' joint loading, characterised by either over-load or insufficient load, disrupts the homeostatic balance favouring catabolism and cartilage degeneration. Recent evidence demonstrates that mechanical forces can impact cellular responses, with a primary contributor being the miRNAs which control the post-transcriptional regulation of one third of all genes. Using in vitro and in vivo models of mechanical loading, we have previously identified a subset of miRNAs which are either (i) sensitive to mechanical forces or (ii) are regulated by abnormal loading only. Using this dataset, the project will validate these findings in the mouse loading model, prior to investigating their relevance in cartilage homeostasis using the zebrafish model; miRNA expression will be manipulated using mimics (over-expression) and inhibitors (knock down) and effects characterised in the presence or absence of mechanical load. This project will provide the student with an excellent cross-disciplinary skill set utilising techniques such as in vivo models, RNAseq, live cell imaging and finite element modelling, and will interface between Cardiff University and the University of Bristol providing a stimulating research environment for the studentship.

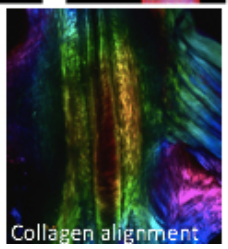




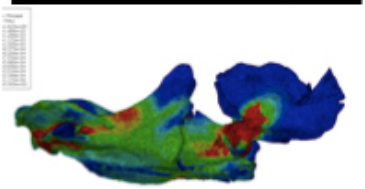




Hard tissue uCT



Collagen alignment



Finite element modelling