Yap-Wnt in gastrulation

Project ID: 3505

Supervisory team

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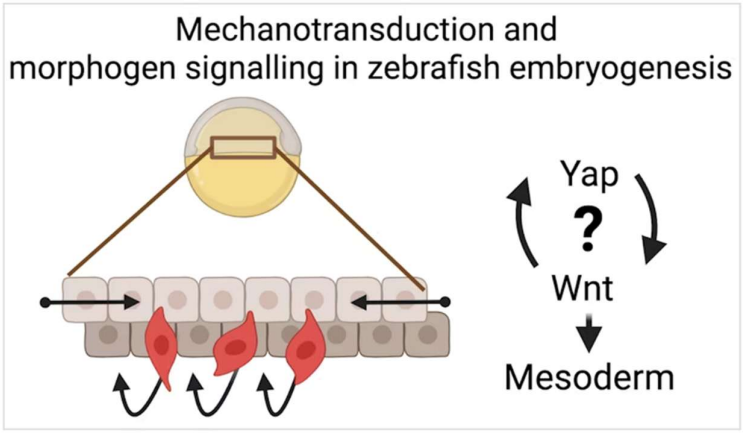

Project description: Dissecting the Yap–Wnt mechanoregulatory program during zebrafish gastrulation - How do cells sense physical forces and translate them into the molecular signals that shape an embryo?Gastrulation is a fundamental stage of vertebrate development during which cells move and rearrange to establish the body axis and form the germ layers that will generate future tissues and organs. In zebrafish, prospective mesoderm and endoderm cells roll over the germ ring in a process called involution. These cells loosen connections with their neighbours, change shape and direction, and migrate towards the animal pole. Although these movements are well described, we do not understand how cells interpret changes in their mechanical environment or how mechanical cues influence cell fate. This PhD project will investigate whether Yap, a key sensor of cell shape and mechanical tension, connects the physical forces generated during gastrulation with Wnt signalling, a major regulator of mesoderm formation. We hypothesise that changes in cell shape, adhesion and tension alter Yap activity, which in turn regulates Wnt8a expression as cells enter and integrate into the developing mesoderm.The student will combine advanced imaging, developmental biology and computational modelling. Light-sheet and confocal microscopy will be used to visualise cell shape, movement and Yap/Wnt signalling in living zebrafish embryos. Brillouin microscopy will enable non-invasive measurements of tissue mechanics and allow these properties to be correlated with signalling dynamics in vivo. Cell-grafting and genetic perturbation experiments will test how cells respond to different mechanical environments and whether Yap–Wnt regulation is required for normal embryo patterning.Experimental data will be integrated with computational vertex models to predict how changes in cell shape, adhesion and mechanical stress influence tissue behaviour, providing a quantitative understanding of how mechanics and signalling interact during development.The student will receive supportive, structured training in zebrafish embryology, light-sheet and confocal microscopy, quantitative image analysis, molecular and genetic methods, cell grafting, and mathematical modelling. They will join an interdisciplinary community spanning developmental biology, mechanobiology, biophysics and computational science, with opportunities to work across Exeter and Bristol, attend research meetings and develop communication and career skills. Applicants are not expected to have experience in every technique. We welcome applicants from biological, physical, mathematical, engineering or computational backgrounds who are curious about development and keen to learn across disciplines.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.