Imaging analysis of muscle progenitor and stem cell activation in differentiation and repair

Supervisory team:
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Project description:
How progenitor cells and resident stem cells enter a differentiation pathway is a key question for stem cell biology and tissue repair. This project asks this question for muscle, both during normal development and during repair after injury. It uses the classic model organism Drosophila melanogaster alongside cultured cell lines. Drosophila is the system of choice for this project: in addition to the speed and power of genetic techniques, it is highly suited to imaging of both its accessible muscle progenitor cells and repairing muscle fibres. You will analyse flight muscles, formed from a discrete population of Adult Muscle Progenitors (AMPs) in the Drosophila larva. Recent data has unexpectedly revealed that this AMP population is taking the very earliest steps into the differentiation pathway and so has become an excellent system for examining muscle progenitor cell activation during development. You will also analyse satellite cells, the resident stem cells of adult muscle activated from quiescence in response to injury to repair damaged muscle. Satellite cells were only recently discovered in Drosophila and the potential of developing the Drosophila experimental system for new discoveries is high.

The conserved transcription factor Mef2 plays a major role in orchestrating muscle differentiation and is central to the work. We have used CRISPR/Cas9 to tag the endogenous Mef2 with GFP and have already visualised it in AMPs and satellite cells. The project will build on this foundation to analyse the dynamics of protein and cell behaviour on activation into the muscle differentiation pathway. Using the same CRISPR technology, we have already tagged two Mef2 regulator proteins, and you will also use other regulators and other emerging Fluorescent Protein (FP) tags coupled with live markers of cell features to track cell behaviour. Cell-by-cell analysis, including live imaging, will then evaluate levels of expression, subcellular localisation, and protein interactions through the application of confocal and light sheet microscopy available in our Departmental Bioimaging Hub. A crucial aspect will be analysis in space and time, e.g. with respect to entry into the differentiation pathway.

A critical feature of the project will be to use cell lines as a test-bed to develop image analysis skills and to explore different FPs-fusions and methodologies before taking them into the in vivo Drosophila system. This first live imaging of these progenitor/stem cells will reveal new cell and protein behaviours as these cells enter the differentiation pathway.

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.