Developing a multimodal analysis pipeline for the assessment of cardiac dysfunction in aged and diseased adult zebrafish

Supervisory team:
Main supervisor: Dr Beck Richardson (University of Bristol)
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Host institution: University of Bristol

Project description:
Zebrafish are recognised as an excellent model in which to study development, gene function and tissue regeneration. They have a remarkable ability to naturally regenerate damaged tissues such as the heart and, due to other advantages such as fecundity and ease of genome manipulation (e.g. via CRISPR/Cas technology), they have also become a valued model for studying gene function and for drug screening and discovery (1,2). The vertebrate cardiovascular system is a complex network of blood, interconnected vessels and the heart and zebrafish have contributed much to our understanding of the development, patterning and maturation of this system (3). Cardiovascular disease in humans remains the leading cause of death worldwide and study of the zebrafish model could provide crucial new understanding of changes to cardiac function in pathological states. However, despite the advantages of this model system, very few studies have investigated the function of the cardiovascular system in adult zebrafish and during natural ageing. It is, therefore, vital that we have robust techniques to assess the function of the zebrafish heart, as the major organ of the cardiovascular system, during old age and pathological states.

This project aims to develop new approaches to assess functional cardiac parameters in adult zebrafish. The student will develop protocols to use echocardiogram, live imaging (lightsheet) (4), electrocardiogram (ECG), and swim testing/behavioural equipment already available in the supervisors labs to assess cardiac function in different adult zebrafish cardiac pathology models including aged fish (<2.5 yrs – already available in the main supervisors lab), fish recovering from cardiac injury (5) and new fish models carrying mutations linked to valve disease, heart failure and cardiac arrhythmias. The student will gain excellent training in working with this advantageous in vivo model, multiple functional analysis techniques, which can be applied to other model systems, and will have the chance to develop new computational analysis software via collaboration with data analysis specialist Dr Stephen Cross. This student will join two dynamic teams with complementary expertise in tissue regeneration, cardiovascular biology, translational pharmacology, genetic engineering and regenerative medicine and will gain expertise that would allow a future career in any of these fields.

References:
1 – Dooley & Zon, 2000. Curr Opin Genet Dev. 10(3):252-6
2 – Patton et al., 2021. Nat Rev Drug Discov. 20(8):611-628.
3 – Bakkers, 2011. Cardiovasc Res. 91(2):279-88
4 – Winter et al., 2021. Br J Pharmacol. 178(13):2671-2689
5 – Bevan et al., 2020. Cardio Res. 116(7): 1357-1371

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.