Investigating the impact of neuroactive drug exposure on the developmental and functional neurobiology of the vertebrate brain

Supervisory team:
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Host institution: University of Exeter (Streatham)

Project description:
Many chemicals, including pharmaceuticals, heavy metals, and some pesticides are found in environment and are known to have an effect on the development and function of the brain. Some of these 'neuroactive' or 'neurotoxic' chemicals have been linked to the incidence of neurodevelopmental disorders in humans, such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Despite these links, relatively little is known about how these chemicals act on the brain, and what aspects of brain function they affect. This is where the use of a small tropical fish, the zebrafish, may prove invaluable. The zebrafish brain is relatively simple compared with the human brain but contains many of the same components. Importantly, in younger animals the skull is see-through and, therefore, using advanced microscopy and molecular markers of different cell types, we can visualise how the brain and its interconnectivity develop, and also how this changes when exposed to chemicals which may be harmful. We can also measure specific behaviours in zebrafish such fear, aggression and learning, which as the ultimate expression of brain function, may also change after exposure to such chemicals.

In this exciting PhD project, a very wide range of cutting-edge techniques will be used, including transgenic animal use, functional brain imaging using light sheet and confocal fluorescence microscopy, advanced image analysis, behavioural assessment and histopathology. The student will be trained in these techniques and will then characterise how early life exposure to neuroactive/ neurotoxic chemicals affects brain development, activity within and between certain regions of the brain, and how this affects resultant behaviours compared with 'normal' unexposed animals. Similar approaches will also be applied in older zebrafish to assess the later-life consequences of chemical exposure on more complex behaviours. For example, how zebrafish behave within a shoal, whether their learning is impaired, or whether they behave appropriately during courtship and mating.

Due to the wide range of techniques being used, this will provide an exceptional training opportunity for the successful student who will become part of large and vibrant postgraduate student population at Exeter. The skills and training obtained will also provide the student with expertise in understanding the biological consequences of exposure to chemicals that act on the brain, which is applicable to both human health and environmental protection sectors. This diversity in techniques and topics will hugely enhance the student's future employment prospects across multiple biosciences research themes.

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.