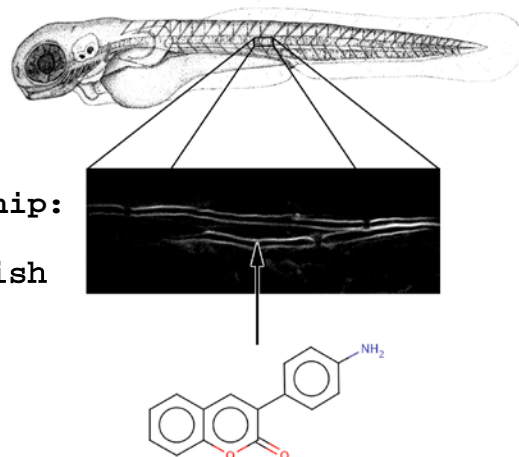


University of Edinburgh PhD studentship:
Chemical systems biology in zebrafish

Supervisors: Dr. David Lyons and Prof. Manfred Auer.



We are seeking applications from highly motivated candidates, with a physical sciences background, and an interest in biology, to establish zebrafish as a model organism for chemical systems biology with which to carry out high-throughput chemical biology screens.

The zebrafish is a well-established vertebrate model organism due to its amenability for genetic screens, and its fantastic qualities for live imaging. Embryonic zebrafish also represent an almost ideal system for the study of small molecule function *in vivo*, due to their small size, aquatic existence, availability in large numbers, and molecular, cellular and system level similarities to higher vertebrates including humans. As with genetic screens, it is possible to employ different small molecule screening strategies using zebrafish. One can perform phenotypic screens, whereby one first identifies an interesting phenotype caused by a small molecule, and subsequently identifies the biological target(s) of effective compounds. In so doing one can discover new mechanisms of small molecule function, and, importantly, also identify new roles for known and novel proteins during biological processes. One can also carry out reverse pathway engineering whereby one selects a known target protein (possibly a drugable target), rationally designs a chemical library likely to affect this target, finds high affinity binders or inhibitors *in-vitro* and then tests the ability of candidate chemicals to affect the target *in vivo*, after which its biological effects can be studied.

This PhD project will be part of an ongoing collaboration between Dr. David Lyons (CNR) and Prof. Manfred Auer (CMVM, DPM, CIR), and will benefit from a unique combination of expertise in model organism biology, screening methodologies, chemistry and biophysics. Dr. Lyons's lab focuses on the genetic and cellular basis of nervous system formation in zebrafish, with extensive experience in zebrafish biology and screening regimes. Prof. Auer is a biophysical chemist, who has 20 years of experience in the development of drug discovery technologies. Prof. Auer's lab designed, established and runs a unique chemical biophysics platform for lead compound discovery and chemical target validation. They can produce large scale tagged or untagged one-bead one-compound libraries, which they test against drug targets in bead based, chip based, cellular and now model organism assays. Small molecule compound function will be investigated in the PhD project in zebrafish using a systems approach. The molecular basis of biological systems will be studied using optical and phenotypic zebrafish models screened against fluorescently labelled small molecule and peptidomimetic libraries. Combined with top of the line mass spectrometry and single molecule microspectroscopy we hope to identify and validate new target compound pairs in a systematic approach. The successful applicant will therefore join a unique interdisciplinary environment, with ambitious long-term goals to carry out rapid cost effective high throughput screening of small molecule function at a whole organism systems level.

The ideal candidate will have a first class honours undergraduate degree, or an MSc with distinction in a relevant subject. Due to the ambitious and broad ranging challenges of this project significant laboratory expertise (> 1year) in a relevant area such as chemistry, biochemistry, or biophysics is required.

Interested candidates should first send a Curriculum Vitae and statement of specific interest to Dr. Lyons (david.lyons@ed.ac.uk) and Prof. Auer (manfred.auer@ed.ac.uk), to discuss their potential suitability for the position. Short listed candidates will then be invited to apply formally through the Centre for Neuroregeneration website before panel interview.