Shaping bioscience research training in the East of Scotland

Delivery of Raman active nanoparticles to dopaminergic neurons to investigate age-related protein aggregation

4-year (48 months) Studentship to start in October 2018.
Supervisors: Alison Hulme, Tilo Kunath

The studentship will cover fees, stipend, research training support costs of £5,000 per year (reduced to £2,000 in the final year) and a small travel and conference allowance. Students are a part of the EASTBIO training programme and are required to undertake enhanced subject-specific, core bioscience and generic skills training and 3-month professional internship (PIPS) outwith academia or a placement with their CASE partner. They are required to submit their thesis within 4 years.

Project description:

This project will investigate age-associated protein aggregation within neurons using Raman active 'loaded' nanoparticles delivered both to human dopaminergic neurons in culture, and into the brain of a genetic rat model that has α-synuclein aggregation.

The first aim of the project will be to produce and test Raman active polymer analogues of poly(lactic-co-glycolic acid) to manufacture the nanoparticles. These particles will be functionalised with surface proteins, such as lactoferrin, to specifically target them to dopaminergic neurons. The Raman active and standard nanoparticles loaded with fluorescent dyes will be used to treat a mixture of human stem cell-derived cortical and dopaminergic neurons to investigate neuronal specificity, and to determine the optimum imaging modality. The nanoparticles will further be used for intranasal delivery in rats to investigate regional brain uptake.

The second aim of the project is to investigate the delivery of cargo with diagnostic potential. In collaboration with Mathew Horrocks (Cambridge University), the PhD student will load the nanoparticles with validated DNA aptamers that specifically bind to α-synuclein oligomers. The DNA aptamers will be covalently linked to fluorescent dyes or to small active Raman tags with a different vibrational frequency to the nanoparticle polymer. The latter will be used for 'dual colour' imaging with Stimulated Raman Scattering microscopy [1]. This diagnostic α-synuclein tool will be used to detect α-synuclein aggregates in stem cell-derived dopaminergic neurons with familial PD mutations [2], and delivered intranasally to ageing rats with an α-synuclein mutation that causes protein aggregation. Finally, the functionalized nanoparticles will be loaded with small molecule modulators of α-synuclein aggregation to investigate their ability to alter the state of the protein in human neurons and in the rat α-synuclein model.

Working in world-leading laboratories at Edinburgh, the student will receive training across the fields of chemistry, cell biology and imaging. The ideal applicant will have a strong academic record, and a BSc or MChem/MSc degree in Chemistry, Biochemistry or related fields, with experience of working in an interdisciplinary environment.

Our application guidance is here: http://www.eastscotbiodtp.ac.uk/how-apply-0
Paperwork needed for each student is EASTBIO application form; undergraduate transcript and MSc transcript if available, in English; CV if available; EASTBIO Supervisor Support Statement.
Formal applications are made through the University's EUCLID system.
http://www.chem.ed.ac.uk/studying/postgraduate-research/applications-and-entry-requirements

The School of Chemistry holds a Silver Athena SWAN award in recognition of our commitment to advance gender equality in higher education. The University is a member of the Race Equality Charter and is a Stonewall Scotland Diversity Champion, actively promoting LGBT equality. The University has a range of initiatives to support a family friendly working environment. See our University Initiatives website for further information. University Initiatives website:
https://www.ed.ac.uk/equality-diversity/help-advice/family-friendly

The deadline for applications is 5.00 pm 4th December 2017