



EastBio DTP – The development of coherent vibrational microscopy methods for the study of youthful and aged dopaminergic neurons

In the last decade, coherent vibrational microscopy techniques, such as stimulated Raman scattering (SRS) microscopy, have emerged as exciting experimental technologies that provide label-free imaging of cells and tissues [1]. The data acquired complements that derived from other emerging label-free imaging technologies such as holotomography and Quantitative Phase Imaging (QPI). In contrast to conventional Raman microscopy, SRS can be performed on a timescale that is compatible with live-cell imaging, and in hyperspectral mode (hSRS) it can give quantitative information about the chemical composition of cells and tissues. In this project, we will determine the phenotypic vibrational characteristics of youthful and aged human dopaminergic neurons using label-free hSRS imaging. Small molecule cocktails that are known to enhance neuronal senescence will be screened for their effects [2], and AI used to determine hallmarks of neuronal cellular age.

During this project the EastBio DTP student will gain experience from world leaders in neuronal cell culture and differentiation [3], label-free small molecule and cellular imaging by SRS [4], and AI bioanalysis [5]. The student will be embedded within research groups in the School of Chemistry and the Institute for Regeneration and Repair at the University of Edinburgh, giving a truly multidisciplinary experience and placing the student at the forefront of understanding the chemical signatures of cells through bioimage analysis.

References

- [1] 'Recent advances in the use of stimulated Raman scattering in histopathology': M. Lee, C. S. Herrington, M. Ravindra, K. Sepp, A. Davies, A. N. Hulme, V. G. Brunton, *Analyst*, 2021, 146, 789.
- [2] 'Identifying novel age-modulating compounds and quantifying cellular aging using novel computational framework for evaluating transcriptional age': C. Zhang, et al., *BioRxiv*, 2023, doi:10.1101/2023.07.03.547539.
- [3] 'An Isogenic Collection of Pluripotent Stem Cell Lines with Elevated α -Synuclein Expression Validated for Neural Induction and Cortical Neuron Differentiation': A. Natalwala, R. Behbehani, R. Yapom, T. Kunath, *Front. Cell Dev. Biol.*, 2022, 10, 898560.
- [4] 'Utilizing stimulated Raman scattering microscopy to study intracellular distribution of label-free ponatinib in live cells': K. Sepp, M. Lee, M. T. J. Bluntzer, G. V. Helgason, A. N. Hulme, V. G. Brunton, *J. Med. Chem.*, 2020, 63, 2028.
- [5] 'Complementing machine learning-based structure predictions with native mass spectrometry': T. M. Allison, M. T. Degiacomi, E. G. Marklund, L. Jovine, A. Elofsson, J. L. P. Benesch, M. Landreh, *Protein Science*, 2022, 31, e4333.

Funding Notes

This opportunity is open to UK and international students and provides funding covering stipend and UK level tuition fees. The University of Edinburgh covers the difference between home and international fees meaning that the EastBio DTP offers fully-funded studentships to all appointees. There is a cap on the number of international students the DTP recruits. It is therefore important for us to know from the outset which fees status category applicants will fall under when applying to the University.

Please refer to UKRI website for full eligibility criteria: 'Get a studentship to fund your doctorate – UKRI'
<https://www.ukri.org/apply-for-funding/studentships-and-doctoral-training/get-a-studentship-to-fund-your-doctorate/>



How to Apply

Closing date is Friday 17 January 2025, 11.59 pm GMT.

This 4-year PhD project is part of a competition funded by EastBio BBSRC Doctoral Training Partnership (DTP). For detailed guidance on the application process and the EastBio Application and Reference Forms, please see:

<https://biology.ed.ac.uk/eastbio/how-to-apply>

Please send your completed EastBio Application Form and a copy of your academic transcripts in pdf format to the Chemistry Graduate School, email: chemistry.gradschool@ed.ac.uk

Please also contact your referees and ask them to submit their references on the EastBio reference form template to Chemistry Graduate School, email: chemistry.gradschool@ed.ac.uk by the application deadline of 17 January 2025.

Equality and Diversity

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.

For further information, please see our University Initiatives website:

<https://equality-diversity.ed.ac.uk/inclusion/family-and-carer>