THE UNIVERSITY of EDINBURGH
School of Chemistry

EastBio DTP – New methods for metalloenzyme modelling to combat antimicrobial resistance

Antimicrobial resistance (AMR) is a silent pandemic endangering the efficacy of antimicrobial agents such as antibiotics against infectious diseases. Understanding how resistance mechanisms occur and how to intervene in them without the need to develop new antibiotics is an appealing strategy in this antimicrobial resistance crisis.

Computational methods such as molecular simulations can give insights into atomistic resistance mechanisms and help design new inhibitors against antimicrobial targets. Both machine learning methods [1] and simulation-based alchemical free energy methods [2] are used for the identification of potential inhibitors for antimicrobial resistance targets. Often these methods do not perform well for proteins involving metal ions in their active site. Metallo-beta-lactamases (MBLs) are Zinc proteins that give rise to resistance by breaking down antibiotics. Understanding how MBLs function and how to inhibit this function will help combat AMR.

The project starting point will be based on preliminary work on alchemical free energy methods [3] for metalloproteins. The goal is to develop new methods combining quantum machine learning potentials [4] with alchemical free energy methods to improve how we can model not only MBLs implicated in AMR.

The Mey Group is recruiting an enthusiastic candidate to work on the interface of biomolecular modelling and machine learning; applied to challenges in antimicrobial resistance for a 4-year fully funded PhD studentship.

References

[1] Gorantla et al. J. Chem. Inf. Model. 64 (6), 1955-1965 (2023)

[2] Mey et al. Living J. Comp. Mol. Sci. 2 (1), 18378 DOI (2020)

[3] Güven et al. chemRxiv-204-9ksxr (2024)

[4] Rufa et al. bioRxiv (2020)

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