

Intracellular delivery of peptides using lipid-based nanoparticles

Newcastle University, Chemistry/School of Natural & Environmental Sciences

Supervisory Team

- **Prof. Akane Kawamura, Chemistry, Newcastle University (Lead)**
- **Prof. Moein Moghimi, School of Pharmacy, Newcastle University**
- **Prof. Steven Cobbs, Durham University**

Project overview/context

Peptides are gaining attention as attractive class of molecules in biomedical research and drug discovery. Peptides offer complex 3D scaffolds covering immense chemical diversity, and can bind to protein targets with high potency and selectivity, including for challenging protein targets such as protein-protein interactions. Recent advances in peptide chemistry and display technologies means that it is now possible to rapidly develop high affinity peptide ligands against target proteins of interest. However, one of the important challenges facing peptide therapeutics discovery is establishing rules for reliable cell-penetration. In this project, we will explore the use of lipid-based nanoparticles to develop generic strategies for the delivery and functional assessment of peptides in cells.

Research Project

For drugs and molecules that act on intracellular targets, they first need to cross the cell membrane. While there are several examples of natural product peptides that can act on intracellular targets (e.g. romidepsin, cyclosporin), peptides often display poor cell permeability. In contrast to small molecules, there are currently no established rules for cell penetration for peptides, and engineering cell-permeability can be time-consuming and challenging. Thus, there is an urgent need to develop robust strategies to deliver peptides into cells in order to realise their enormous potential in drug discovery.

The overall aim of this project is to develop lipid-based nanoparticle cellular delivery systems for peptides for hit and target validation in cells. We will explore the use liposome and lipid nanoparticles as generic delivery strategies for different types of peptide cargoes. Once the delivery strategies and cytosolic release steps of peptides are optimised, we will validate the approach by applying to peptide hits and therapeutic protein targets of interest at Newcastle. We will confirm cellular target engagement and evaluate their cellular response.

This project will suit someone with a strong chemical background who is interested in working at the interface of chemistry and biology.

Training & Skills

The student will receive extensive training in cutting-edge methods and chemical biology techniques, including encoded peptide library technologies, peptide chemistry, biophysical and biochemical and cellular assays, and will be supported by academic supervisors. The student will be mainly based in the recently refurbished state-of-the-art chemical biology laboratories in the Bedson building at Newcastle University, and will work alongside a interdisciplinary team of experienced chemists, chemical biologists and molecular/cell biologists. The project will involve working closely with nanoparticle drug delivery experts in the King George VI building in the School of Pharmacy, and peptide chemists at Durham University.

The student will benefit from bespoke research and life skills training programme provided by the Centre for Doctoral Training.

Further Information

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How to Apply

You must apply through the University's [online application system](#).

When applying to Newcastle University please select the Course Code **8207F (PhD in Molecular Sciences)**

You will need to:

- Insert the **programme code 8207F** in the programme of study section
- Select '**PhD in Molecular Sciences**' as the programme of study
- Input (only) the **studentship reference code (e.g. 22_05)** that you are applying for in the studentship/partnership reference field when prompted (all codes are outlined in the individual project adverts

and can be found on the MoSMed website: <https://research.ncl.ac.uk/mosmed/phdstudentships/>)

- Attach all documents that are requested including a CV and cover letter. The cover letter must **clearly** state the project reference code, the full title of the studentship and state how your interests and experience relate to the project
- Attach degree transcripts and certificates and, if English is not your first language, a copy of your English language qualifications

Should you have any queries regarding the application process to Newcastle University please contact Selina McCarthy, MoSMed CDT Manager: Selina.McCarthy@newcastle.ac.uk or email mosmed.cdt@newcastle.ac.uk

Within the MoSMedCDT we are committed to building a diverse community based on excellence and commitment. To that end in our recruitment of Doctoral Researchers we welcome applications from outstanding candidates of all backgrounds regardless of ethnicity, disability, gender identity, sexual orientation and will consider all applications equally based on merit.



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