

Cell- and Tissue-targeted cyclic peptide discovery platform

Newcastle University (Chemistry), Durham University, Novo Nordisk

Supervisory Team

- **Prof Akane Kawamura, Newcastle University (Lead)**
- **Dr Martin Münzel, Novo Nordisk A/S**
- **Dr James Knight, Newcastle University**
- **Prof Steven Cobb, Durham University**

Project overview/context

Targeted drug delivery is a strategy where medicines (drugs) are specifically delivered to the site of disease in the body. The strategy allows the drug to maintain a local therapeutic concentration at the disease site to act on the target, and avoids any interaction with the healthy tissues – which can otherwise lead to off-target side effects. In this project, we will establish novel strategies to develop bespoke cyclic peptides that bind specific cells / tissues over others with high affinity and selectivity (e.g. cancer vs healthy cells), in order to use them as delivery vehicles for drugs or for bioimaging.

Research Project

Antibodies are powerful reagents that are widely used in biomedical research and in drug discovery. In particular, cell-targeted antibodies have gained significant attention as delivery reagents for targeted therapeutics (e.g. antibody-drug conjugates) and for imaging (e.g. PET-imaging) / diagnostic applications. However, antibodies can be limiting due to their size (150kDa) and restricted chemical diversifications (e.g. modifications, conjugations). Cyclic peptides (CPs), on the other hand, are smaller (2-3kDa), have better tissue/cellular penetration, and are synthetically tractable whilst achieving potency and selectivity that can match antibodies. Thus CPs represent an attractive alternative modality for cell- and tissue-specific drug delivery.

The overall aim of this project is to develop an innovative screening platform to identify precision CPs for specific cell and tissue-targeting applications, using

mRNA-display technology¹. We will establish methodologies for mRNA-display screening in cellular context, building on our expertise in *in vitro* selection, then to optimise for more complex, lysate-, cell- and tissue- specific applications. Initial focus will be on developing CPs targeting cancer cells / tissues. The targeted CPs will further be explored for clinical imaging/ diagnostic applications and CP-drug/label conjugation in vivo disease models. This project provides an exciting opportunity to develop new peptide-based targeting approaches for chemical biology and drug discovery.

We are looking for a highly motivated, creative and enthusiastic candidate, with a strong background in chemistry/biochemistry or closely related subjects, who is passionate about working at the interface of chemistry, biology and medicine, and have interest in therapeutics discovery.

Reference: ¹ Chem. Rev. 2019 119 17 10360-10391

Training & Skills

The student will be based in the recently refurbished state-of-the-art chemical biology laboratories in the Bedson building at Newcastle University, and will work alongside a team of experienced chemists, chemical biologists and molecular/cell biologists. The student will receive extensive training in cutting-edge methods in chemical biology, including encoded library technologies, peptide chemistry / synthetic chemistry, bioinformatics, biophysical/biochemical and cellular assays, and will be supported by academic and industrial supervisors. The student will work closely with Novo Nordisk, a global pharmaceutical company specialising in diabetes care and peptide therapeutics discovery, and will have the opportunity to visit Novo

Nordisk in Copenhagen, Denmark, for industrial placements during the course of their PhD.

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

Further Information

For further information, please contact the lead supervisor, Professor Akane Kawamura: akane.kawamura@ncl.ac.uk

How to Apply

If applying to a **Newcastle project**, you must apply through the University's [Apply to Newcastle Portal](#). Once registered select '**Create a Postgraduate Application**'.

Use '**Course Search**' to identify your programme of study:

- search for the 'Course Title' using the programme code: **8207F**
- select '**PhD Molecular Sciences for Medicine (SNES)**' as the programme of study

You will then need to provide the following information in the '**Further Questions**' section:

- a 'Personal Statement' (this is a mandatory field) - upload a document or write a statement directly into the application form. Please include the full title of the studentship, the studentship code, and how your interests and experience relate to the project.
- the relevant studentship code (**mos23_07**) in the 'Studentship/Partnership Reference' field.

If you wish to apply for additional studentships, please make sure to add the relevant studentship reference each time, before submitting each separate application. For example, you may wish to apply for mos23_07 AND mos23_08. **You must include the relevant code for your application to be considered.**

- when prompted for how you are providing your research proposal - select 'Write Proposal'. You should then type in the title of the [relevant research project](#). You do not need to upload a research proposal.
- An up to date CV.
- Please upload all documents in PDF format.

Equality, Diversity and Inclusion (EDI)

Within the MoSMed CDT 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.

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



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