

## **Biomolecular sciences**

Our focus is on multi-disciplinary approaches to complex health and wellbeing research using a wide range of methodological approaches.

### **Faculty of Health and Wellbeing**

Research is co-ordinated through the Health and Wellbeing Research Institute and delivered through five research centres:

- [Centre for Health and Social Care \(CHSCR\)](#)
- [Centre for Sport and Exercise Science \(CSES\)](#)
- [Centre for Sport Engineering Research \(CSER\)](#)
- [Sport Industry Research Centre \(SIRC\)](#)
- [Biomolecular Sciences Research Centre \(BMRC\)](#)

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### **How to apply**

Applicants are requested to email a [postgraduate application form](#) to [m.n.lyons@shu.ac.uk](mailto:m.n.lyons@shu.ac.uk) by 12 noon on Friday 29 January 2016.

Where English is not your first language, you must show evidence of English language ability to the following minimum level of proficiency: an overall IELTS score of 6.5 or above, with at least 6.0 in each component or an [accepted equivalent](#). Please note that your test score must be current, i.e. within the last two years.

For full details on the eligibility criteria, see: [www.shu.ac.uk/studentships/eligibility](http://www.shu.ac.uk/studentships/eligibility)

### **Selection process**

Interviews will take place in the week commencing 22 February 2016.

Applicants are required to give a short 10–15 minute presentation followed by an interview. Interview panel members will include the postgraduate research tutor and a prospective director of studies. Where travel to Sheffield is not possible, interviews may be conducted by Skype or conference call.

### **Research topics**

Each project is loosely connected to a particular research centre. However the majority are supervised by staff drawn from research teams across the faculty, and in some cases, the University.

### **Project B1: A study of small molecule probes for the lysine specific demethylase 1 (LSD1) enzyme**

The importance of LSD1 has been highlighted in the growth of tumours and cancerous tissues, as well as gene regulation in pluripotent stem cells. This makes LSD1 a target for inhibitor synthesis and biochemical pathway investigation. The MOA-inhibitor drug, tranylcypromine, can be modified with the addition of an alkyne tag which allows it to be visualised using "click chemistry" to attach a fluorescent azide dye. This probe has been observed in adherent cells, localising in the cell nucleolus where it reacts with the LSD1 enzymes in chromatin modifying complexes. This probe molecule can be used as a visualisation probe for the LSD1 enzyme. Optimization of the fluorescent probe and elucidation of the covalent mechanism of MAO inhibition will be investigated by a combination of synthetic techniques and quantum chemical (DFT) calculations. The function and synthetic origins of these molecular probes makes them ideal for studying the distribution and function of LSD1 in selected biochemical problems.

For enquires contact: [s.turega@shu.ac.uk](mailto:s.turega@shu.ac.uk)

### **Project B2: Functionalised metal nanoparticles for mitochondria targeted radiotherapeutics**

Chemotherapy and radiotherapy are the principal treatments for most cancers. Both treatment regimens have a number of drawbacks, mainly acute side effects, damage to peripheral tissues, and tumour resistance. Nanotechnology has the potential to make a significant impact on cancer by enabling therapies to be targeted to cancer cells and subcellular organelles, such as mitochondria, in a controlled manner thus reducing the side-effects of the treatment. The aim of the project is to produce metal nanoparticles functionalised with organophosphorus ligands that can be targeted to the mitochondria of cancer cells and which are able to act as radiosensitisers - stimulation of the particles by X-rays excites the particles producing free radicals and heat leading to cell death. The project will integrate aspect of chemical synthesis, cell biology and analytical techniques. Radiotherapy studies will be carried out in conjunction with the Open University in Milton Keynes.

For enquires contact: [n.bricklebank@shu.ac.uk](mailto:n.bricklebank@shu.ac.uk)

### **Project B3: Investigation of plant products for the development of new antimicrobial drugs**

The increasing incidence of antibiotic-resistant pathogens and the likelihood that existing antibiotics will become progressively less effective has created an exigent need for new antimicrobial drugs. One massive potential source of novel antimicrobials is the plant kingdom where secondary metabolites represent an untapped reservoir of new compounds. Our team comprises microbiologists and chemists across two universities, in collaboration with Blueberry Therapeutics Ltd., a company developing new medicines to treat a range of infections. We have previously isolated and characterised three molecules from seeds of an edible salad vegetable with promising antifungal and antibacterial activities. This PhD project will determine the mechanism of action of these compounds to assess their potential for future development as pharmaceuticals, as well as studying derivatives to establish structure-activity relationships. Additional antimicrobial molecules will also be isolated and characterised. The student will work in a lively research collaboration and gain experience of cutting-edge techniques of molecular microbiology and separation technology.

For enquires contact: [t.j.smith@shu.ac.uk](mailto:t.j.smith@shu.ac.uk)

### **Project B4: Pharmacological mechanisms underlying the effects of lurasidone on body weight regulation**

Lurasidone is a new antipsychotic drug that has some valuable clinical properties including a favourable metabolic profile; it shows a relative lack of the weight gain that is common to many antipsychotic drugs, the consequences of which include increased risk of diabetes and cardiovascular disease. This project aims to investigate the pharmacological mechanisms underlying this protective metabolic effect, using ex vivo and in vitro techniques. The hypothesis is that lurasidone has its protective effects via its partial agonist actions at 5-HT<sub>1A</sub>, and perhaps other 5-HT receptors, which stabilise neuronal function in the hypothalamic regions controlling body weight and food intake. Initial studies will use ex vivo brain tissue to investigate the effect of lurasidone on hypothalamic markers of neurons involved in control of body weight. Molecular biology techniques (qPCR, pyrosequencing) and immunohistochemical and western blotting techniques will be used. The subsequent focus will be to undertake in vitro experiments to determine directly the pharmacological basis of lurasidone's relative freedom from weight gain using neuronal cells in culture; further complementary work will include investigation of adipose cells in culture.

Candidates for this project should have experience of relevant molecular biology and cell biology techniques. A background in neuroscience and/or neuropharmacology would be an advantage.

For enquires contact: [c.f.dalton@shu.ac.uk](mailto:c.f.dalton@shu.ac.uk)

**Project B5: Natriuretic peptide signalling in intervertebral disc degeneration.**

Natriuretic peptides have beneficial effects on the health musculoskeletal tissues. This project will investigate natriuretic peptide signalling as a potential therapeutic avenue to dampen inflammation and promote tissue repair in IDD.

For enquires contact: [n.peake@shu.ac.uk](mailto:n.peake@shu.ac.uk)