UNNC – SIMM, CAS Doctoral Training Partnership

Available PhD topics

PhD topic 1	**AI Enabled Drug Discovery of Anti-cancer Drugs**
SIMM Supervisor(s)	Prof Xiaojie Lu
UNNC Supervisor(s)	Dr Bencan Tang
Short introduction & description of PhD	Machine learning is an interdisciplinary study of statistical model that solves problems by making data-based predictions and deductions. The significance of machine learning and artificial intelligence used in drug discovery has been emphasized by recent papers published in high ranking journals. This research aims to develop advanced machine learning algorithms for the screening of anti-cancer agents. It involves bench chemistry as well as artificial intelligence. A candidate with chemistry or medical chemistry background with strong interest in machine learning would be ideal.
Contact points	Please contact Dr Bencan Tang (Bencan.Tang@nottingham.edu.cn) and Prof Xiaojie Lu (xjlu@simm.ac.cn) before sending the application via 'How to apply' section.
PhD topic 2	**Application of Graphene in quality control and production of Liver Organoids**
SIMM Supervisor	Prof Guoyu PAN
UNNC Supervisor(s)	Prof Cheng Heng PANG
Short introduction & description of PhD	**Background:** The in vitro model of hepatocytes is an essential tool for the evaluation of drug metabolism and drug toxicity. Hepatocytes are easy to lose their original traits, morphology, structure and function due to the limited conditions of in vitro hepatocyte culture. As a result, it cannot reflect the efficacy and toxicity of in vivo drugs, and does not fulfil the needs of clinical and scientific research. 3D culture can better reflect the interaction between cells and matrix, especially the recent rise of organoid technology, which may mimic the in vivo environment and reflect physiological changes when a diverse population of cells is present. With the help of novel organoid technology, 3D culture can better reflect the interaction between cells and substrates, simulate the in vivo environment, and reflect physiological changes. However, how to maintain the integrity and physiological function of organoids in vitro has always been the focus of translational medicine and materials science. From the perspective of new drug development, the best choice for hepatotoxicity and liver drug screening is hepatic-like cell organoids, which is capable of long-term preservation of liver function. However, this in vitro model is far from mature to be employed by pharmaceutical industry.

	To solve this problem, a 3D culture material matrix with better biocompatibility is required; on the other hand, a rapid, comprehensive, and non-invasive quality control method is a prerequisite for industrialization of liver organoid culture. **Possibilities analysis of Graphene application in liver organoid culture and quality control:** Graphene is a honeycomb carbon structural material formed by carbon atoms connected by Sp2 hybridization, and has a hexagonal honeycomb layered structure. The surface properties, low toxicity to cells, and good biocompatibility of Graphene make it useful as a platform for cell adhesion and even inducing cell proliferation. As a scaffold, Graphene can increase the quantity of adhesion points and cell proliferation while increasing intracellular tension. Compared to 2D Graphene film, the 3D Graphene scaffold not only provides a porous structure, but also possesses microscale topographic features and electrical conductivity. Graphene can be used as an excellent carrier material for co-culture of various cells. It has a unique function for the morphological retention of organoids. However, the relationship between liver organoids and Graphene has not been systematically studied. Non-invasive continuous quality control of organoids is a prerequisite for large-scale production of organoids which cannot be achieved by current quality control methods. Due to the unique biochemical components of cells, tissues and organs, Raman spectroscopy is expected to be a powerful tool for organoid culture quality control. Raman spectroscopy is restricted in its application to larger organoids because of its sensitivity. Surface-enhanced Raman spectroscopy can be more effective and more sensitive than conventional Raman spectroscopy to help us distinguish between normal and diseased cells or tissues. Due to the two-dimensional ultrathin structure and high specific surface area of Graphene, Graphene has strong adsorption to molecules. These excellent properties make it possible to chemically enhance the response signal of Raman spectroscopy. It was found that the surface plasmon properties of silver nanoparticles (AgNPs) can also enhance the absorption range of Raman light. It was reported that the combination of silver nanoparticles with Graphene can simultaneously exert the electromagnetic enhancement of AgNPs and the chemical enhancement of Graphene, the Raman signal of the detected molecule can be enhanced by several orders of magnitude. This provides a unique possibility for Raman spectroscopy application in quality control of liver organoid cultures. **Brief Research Proposal:** This project aims to establish a novel liver organoid culture method with novel materials in scaffolds. With the help of 3D Graphene or related materials, it may improve the metabolic enzyme activities and transport protein abilities in hepatic-like cell organoids, which can meet the needs of clinical and scientific research purposes. Silver Nanoparticles (AgNPs) composited with Graphene and alternative compositions may generate a novel surface-enhanced Raman spectroscopy material with high sensitivity and good stability for quality control in the production of organoid chip. It can realize the detection of physiological and pathological states of liver organoids under different culture conditions. The work may accelerate the pharmaceutical research and environmental toxicological investigation.
Contact points	Informal inquiries may be addressed to Prof Guoyu Pan (gypan@simm.ac.cn) and Prof Cheng Heng Pang (ChengHeng.Pang@nottingham.edu.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 3	**Design and application of graphene coupled antibody detection kit**

SIMM Supervisor	Prof Chunhe Wang
UNNC Supervisor(s)	Prof Cheng Heng PANG
Short introduction & description of PhD	Graphene has very bright prospects in biomedicine and drug delivery. Graphene's unique two-dimensional structure makes it have bright application prospects in the field of sensing and detection. Its large surface area makes it very sensitive to the surrounding environment, which shows that graphene has high detection sensitivity. Antibody, also known as immunoglobulin, is a large Y-shaped protein mainly secreted by plasma cells and used by the immune system to identify and neutralize foreign substances such as bacteria, viruses and other pathogens. An antibody can uniquely recognize a specific foreign object through its variable region, which is called an antigen. When the antibody is coupled with graphene, the detection kit can be made according to the targeting of antibody and the ultra-high sensitivity of graphene, which has great prospect and research value.
Contact points	Informal inquiries may be addressed to Prof Cheng Heng PANG (ChengHeng.Pang@nottingham.edu.cn) and Prof Chunhe Wang (wangc@simm.ac.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 4	**DNA Encoded Library(DEL) Enabled Drug Discovery of Anti-cancer Drugs**
SIMM Supervisor(s)	Prof Xiaojie Lu
UNNC Supervisor(s)	Dr Bencan Tang
Short introduction & description of PhD	DNA encoded library (DEL) technology has become a useful tool for the hit identification for many biologically interesting targets for the drug discovery. Several hit compounds discovery by the DEL has been further optimized and move forward to the phase1-2 clinical stage. The success of the DEL was heavily relied on the chemical diversity of libraries, more DNA compatible reactions and biologically interested scaffolds are urgently needed to expand the DEL chemical space. This research aims to develop more DNA encoded libraries for the screening of anti-cancer agents. It involves bench synthetic chemistry as well as computational chemistry. A candidate with chemistry or medical chemistry background with strong interest in computational chemistry would be ideal.
Contact points	Please contact Dr Bencan Tang (Bencan.Tang@nottingham.edu.cn) and Prof Xiaojie Lu (xjlu@simm.ac.cn) before sending the application *via* 'How to apply' section.
PhD topic 5	**Drug Discovery of Anti-cancer Drugs**
SIMM Supervisor(s)	PI in drug discovery in SIMM - TBC
UNNC Supervisor(s)	Dr Bencan Tang
Short introduction & description of PhD	This project will use medicinal chemistry to guide the synthesis of new molecules with potential to be developed into anti-cancer drugs. The project will focus on the discovery of anti-cancer candidates. The project may involve the application of machine learning, computational chemistry or PROTAC. It will also involve synthesis of predicted molecules for testing by collaborators in biology. A good medicinal chemist or a synthetic chemist would be an ideal candidate for this project.
Contact points	Please contact Dr Bencan Tang (Bencan.Tang@nottingham.edu.cn) before sending the application via 'How to apply' section.
PhD topic 6	**Intelligent drug delivery system and cancer immunotherapy**

SIMM Supervisor	Prof Haijun Yu
UNNC Supervisor(s)	Dr Binjie HU
Short introduction & description of PhD	Immunotherapy has emerged as a promising clinical modality for cancer therapy due to its ability to initiate an antitumor immune response. However, current immunotherapy is severely impaired by immunosuppression of host T-cell antitumor activity through the programmed cell death 1 ligand (PD-L1) and programmed cell death receptor 1 (PD-1) (PD-L1/PD-1) immune checkpoint. In this project, we will dedicate to developing novel drug delivery system for tumor-specific delivery of various immune modulators. The drug delivery systems will be designed for on-demand drug release or activation at the tumor site, thus achieve precise immunotherapy. For example, Boolean logic nanoparticles will be developed for tumor-targeted co-delivery of immune modulators (e.g., immune activator and immune inhibitor) and combination immunotherapy. A library of stimuli-activatable units will be fabricated yielding YES/AND logic outputs by adjusting the input combinations, including extracellular matrix metalloproteins 2/9, intracellular acidity, and reduction in the tumor microenvironment. The drug delivery systems will be administrated through systemic injection, oral This Ph.D. program is a multi-disciplinary, which covers broad fields of materials sciences, nanomedicine, pharmaceutics and oncology. The potential candidate should be self-motivated and have strong background in material sciences, pharmacological sciences or onco-immunology.
Contact points	Informal inquiries may be addressed to Dr Binjie HU (Binjie.HU@nottingham.edu.cn) and Prof Haijun Yu (hjyu@simm.ac.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 7	**New drug development targeting brain tissue against stroke**
SIMM Supervisor	Prof Baohong Jiang
UNNC Supervisor(s)	Dr Binjie Hu
Short introduction & description of PhD	Stroke continues to be the major global health problem associated with considerable mortality and morbidity. Developing new strategies to alleviate the lesion of stroke is urgent need. Our research will concentrate on new drug development against stroke. This research involves set up of animal model, efficiency evaluation based on infarct volume, neurobehavioral scores and histopathological examination. The new administration methods and drug delivery systems will be explored to penetrate blood brain barrier in order to target brain tissue for therapy of stroke. This Ph.D. program is a multi-disciplinary, which covers broad fields of materials sciences, nanomedicine, pharmaceutics, pharmacodynamics and histopathology. The potential candidate should be self-motivated and have strong background in material sciences, pharmacological sciences or pathological sciences.
Contact points	Informal inquiries may be addressed to Prof Baohong Jiang (jiangbh@simm.ac.cn) and Dr Binjie Hu (Binjie.HU@nottingham.edu.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 8	**Structure of nano-particles and space distribution in cells and tissues of inflammatory bowel disease visualized by synchrotron radiation micro-computed tomography and fluorescence micro-optical sectioning tomography**
SIMM Supervisor	Prof Jiwen Zhang

UNNC Supervisor(s)	Prof Cheng Heng PANG
Short introduction & description of PhD	Inflammatory bowel disease (IBD) is a chronic and recurring long-term gastrointestinal tract disorders, which causes severe destruction of the intestinal epithelial barrier. IBD has been recognized as a global disease, accompanied by rising high incidence. Ulcerative colitis (UC) is one of the most common clinical forms of IBD which involves involuntary diarrhea, hematochezia and weight loss affecting life quality of patients seriously. The conventional treatment of IBD relies on large doses of immunosuppressive and anti-inflammatory drugs, which cause serious adverse effects due to poor specificity. To overcome these glitches, many researchers have designed various types of colon-targeted preparations to improve drug accumulation at the target site. Furthermore, there is a growing demand on understanding the thorough colon architectures, as well as, the accurate distribution patterns in vivo and retention mechanisms of the colon-targeted materials at three-dimensional (3D), in situ, and single-particle level. Thus, a novel strategy that reveals the spatial distribution of colon-targeted particles precisely at multi-scale ranging from sub-micron to the whole colon scale needs to be established. However, to date, the cross-scale study of precise colon structure and its inner inhaled particles distribution still faces considerable obstacles. Although the in vivo imaging system (IVIS) has been utilized as a routine method to provide the distributing situation of colon-targeted particles at organ-scale, it only can ascertain the particles distribution at 2D level. Therefore, there still remains a lack of detection on the accurate spatial distribution of colon-targeted particles at the whole-colon scale with subcellular resolution. In the study of PhD, high-precision cross-scale visualization of entire colon anatomy was acquired by the advanced Micro-Optical Sectioning Tomography (MOST) system coupled with whole colon nissl-staining. In addition, suitable fluorescent dye labelled colon-targeted material were synthesized and characterized as model particles, and dual-color and colon-wide datasets were acquired by fluorescence-micro-optical sectioning tomography (f-MOST) system. More importantly, the sophisticated architectures of the mouse colon and the region-specific distribution patterns and structure associated deposition of the colon-targeted particles in colon were revealed simultaneously for the first time, providing new approaches for understanding the retention behavior and distribution of colon-targeted materials in vivo. This research will provide precise anatomical data for in vitro simulations and contribute to fill the gap between in vitro and in vivo analyzing results, which will facilitate the clinical translations of novel colon-targeted vehicles.
Contact points	Informal inquiries may be addressed to Prof Jiwen ZHANG (jwzhang@simm.ac.cn) and Prof Cheng Heng PANG (chengheng.pang@nottingham.edu.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 9	**The morphology effect of Nano- and microspheres encapsulations on inhaled drug delivery and the application for lung disease therapy**
SIMM Supervisor	Prof Yongzhuo Huang
UNNC Supervisor(s)	Dr Binjie Hu
Short introduction & description of PhD	Inhaled formulations provide a self-administered and safe method for lung disease therapy, with an advantage of local drug delivery that can directly target the organ and thus reduce the unwanted drug exposure to healthy tissues. Nano- or microspheres encapsulations can be used as inhaled delivery carriers for achieving drug extended release and protection for degradation. Their morphology plays an important role in

	determining the in vivo fate of the drugs. For example, the different size and shape could result in various biodistribution in the target organ. Furthermore, Surface modification of the carriers can render the functional alteration. In this project, the morphology effect of nano- and microspheres on the biodistribution and therapeutic efficacy will be explored, and subsequently, the morphology will be modified by a physical or chemical method to achieve an optimal treatment efficacy in various diseases (e.g., acute respiratory distress syndrome, pulmonary fibrosis, and chronic obstructive pulmonary disease). And inhaled vaccine delivery using of nano- and microspheres encapsulations will also be explored.
Contact points	Informal inquiries may be addressed to Dr Binjie Hu (binjie.hu@nottingham.edu.cn) and Prof Yongzhuo Huang (yzhuang@simm.ac.cn), but formal applications should follow the instructions in 'How to apply' section.
PhD topic 10	**Single cell glycan analysis combined with droplet microfluidics**
SIMM Supervisor	Prof Wei Huang
UNNC Supervisor(s)	Dr Weihua Meng Dr Mainul Haque
Short introduction & description of PhD	Glycosylation is a carbohydrate-based post-translational modification associated with the regulation of multiple cellular processes in different cell types and species, such as cell proliferation, differentiation, migration, signal transduction, and immune homeostasis. It makes great sense to develop and establish a method to analyze cell surface glycans directly on a single cell. Different methods have been utilized to analyze glycans, such as MS, HPLC, NMR, and CE. However, these methods still remain great challenges at a single-cell level. The droplet microfluidic system is a good strategy for single-cell analysis. Monodisperse aqueous droplets flow in an inert carrier oil in microfluidic channels on a chip and each droplet functions as an independent microreactor. Two groups of barcodes are designed, one for carbohydrate-binding lectins, and another for beads. One droplet contains a single cell, conjugated with a glycan-lectin-barcode complex, and a bead linked with another unique barcode. An oligonucleotide chain is generated with two barcodes from lectin and bead respectively. Computational and bioinformatic tools will be employed for data process. The major goal of this project is to profile the distinct glycans at single-cell level and to elucidate the role of glycan in stem cell differentiation.
Contact points	Informal inquiries may be addressed to Dr Weihua Meng (Weihua.Meng@nottingham.edu.cn) and Prof Wei Huang (huangwei@simm.ac.cn), but formal applications should follow the instructions in 'How to apply' section.