UNNC – SIMM, CAS Doctoral Training Partnership

It's essential that you have contacted the UNNC and/or SIMM supervisors before applying.

Formal applications should follow the instructions in 'How to apply' section.

Research areas

- Pharmaceutical science and related fields

Available PhD topics

PhD topic	**Biomimetic nanoparticles targeting immune cells to improve MHC-I-deficiency tumor tolerance**
SIMM Supervisor	Prof. Yaping Li
UNNC Supervisor(s)	Prof. Yong Ren
Short introduction & description of PhD project	Immunotherapy resistance is the main reason for the poor clinical efficacy of anti-tumor immunotherapy. The downregulation of MHC-I expression leads to the inability of $CD8^+$ T cells to be fully activated. Therefore, choosing a treatment that does not rely on $CD8^+$ T cells may improve the immunotherapy resistance of tumors and help to enhance the therapeutic effect of anti-tumor immunity. As an antagonist of apoptotic protein inhibitor, LCL161 can effectively promote the activation of natural killer cells and kill tumor cells. However, LCL161 is poorly soluble in water and can cause cytokine storm. There is an urgent need to design a carrier to increase its bioavailability and deliver it to the tumor site to exert anti-tumor effects. Based on the above, we consider to deliver LCL161 by using cyclodextrin as a carrier, encapsulated with tumor cell membrane modifying PH-M70. When entering the blood circulation, the nanoparticles are targeted to tumor tissue. In the acidic microenvironment of tumor tissue, M70 breaks the membrane and releases the core cyclodextrin carrier. Cyclodextrin delivers LCL161 to dendritic cells, promoting the increased release of IL12, which then activates natural killer cells to promote their direct killing of tumors. At the same time, the interaction of CD47 on the membrane surface with SIRPα of tumor-associated macrophages blocked phagocytosis checkpoint and promoted phagocytosis and killing of tumor cells by macrophages.
Contact points	Informal inquiries may be addressed to Prof. Yaping Li (ypli@simm.ac.cn) and Prof. Yong Ren (Yong.Ren@nottingham.edu.cn).
PhD topic	**Discovery and biosynthesis of antibiofilm peptides**

SIMM Supervisor	Baofu Xu
UNNC Supervisor(s)	Enrico Marsili
Short introduction & description of PhD project	Antimicrobial resistance has been causing tremendous concern in public healthcare. In addition to the overuse of antibiotics, biofilm also enhances the resistance of pathogens to commonly used antibacterial agents. Biofilm-based infections are associated with 80% of microbial infections. However, no commercial antimicrobial drugs targeting biofilm have been developed, probably due to the lack of high efficient biofilm testing platform. At University of Nottingham Ningbo China (UNNC), assoc. Prof. Enrico Marsili has pioneered the bioelectrochemical characterization of biofilms and testing of antimicrobial and antibiofilm agents. These methods allow cost-effective and real-time testing under realistic conditions, both on the standard surface and biomedical devices by developing techniques for biofilm analysis with bioelectrochemical instruments. With the well-developed and easy-to-use biofilm testing platform in hand, the candidate student will efficiently evaluate the antibiofilm activities of designated agents, easing the process of discovering new antibiofilm agents. Prof Baofu Xu works at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences (SIMM, CAS), where established with state-of-the-art facilities and core technology platforms. Prof Xu's current work is focusing on discovery and biosynthesis of bioactive natural products from marine resources. This project, funded by both supervisors, focuses on discovering active peptides with similar antibiofilm characteristics to LL-37 or AS10 and on building an efficient biosynthesis platform producing the targeted peptides. The candidate student will work with two supervisors (B.X. and E.M.) to identify new peptides or toxin-like proteins from marine organisms, such as sea cucumber, Asteroidea, marine fungi, and marine bacteria, perform biosynthesis-related experiments, and evaluate the antimicrobial and antibiofilm activities. A pre-clinical trial could also be envisioned if the project goes very smoothly.
Contact points	Informal inquiries may be addressed to Assoc Prof Enrico Marsili (enrico.marsili@nottingham.edu.cn) and Prof. Baofu Xu (bfxu@simm.ac.cn)
PhD topic	**Discovery of new marine-derived antibiofilm agents**
SIMM Supervisor	Baofu Xu
UNNC Supervisor	Enrico Marsili
Short introduction & description of PhD project	The quest for novel antimicrobial compounds primarily relies on the bioprospecting of terrestrial and marine organisms capable of producing potent antimicrobials with low cytotoxicity. When these putative antimicrobial agents are screened for their activities, the screening is carried out mostly on planktonic cells in microwell plates. However, planktonic cells are rarely encountered in real-world conditions (e.g., clinical settings), where biofilm is the dominant mode of life for pathogens. Biofilms are microstructured communities of microorganisms living at solid interfaces. In biofilms, microorganisms are encased in a microbially-produced extracellular polymeric matrix composed on carbohydrates, protein, and extracellular DNA. The biofilm matrix provides a mechanical and chemical barrier to antimicrobial compounds, which must penetrate the matrix before reaching

	the viable cells and exerting their antimicrobial effect. Biofilms are responsible for approximately 60% of all infections and 80% of the chronic infections. The minimum inhibitory concentration for antimicrobials is much higher (10-100 times) in the presence of biofilms than with planktonic cells, thus the conventional antimicrobial screening might not provide reliable results. While biofilm testing is highly desirable, there are technical difficulties associated with growth and maintenance of reproducible biofilms. Enrico Marsili has developed an easy-to-use biofilm testing platform based on bioelectrochemical analysis, which can be used on single species and polymicrobial biofilms, the most relevant for clinical applications. The platform allows the characterization of both lethal and non-lethal (e.g., biofilm dispersing) antibiofilm agents. In this project, the student will work with both supervisors to isolate novel compounds from marine fungi or bacteria, perform biosynthesis-related experiments, and characterize the antimicrobial and antibiofilm activity of the newly isolated compounds using bioelectrochemical methods. If the lab-scale characterization is successful, the opportunity for pre-clinical trials in collaboration with a local research hospital might be considered. Both supervisors will fund the research expenses for this project. The Ph.D. candidate will have access to high-end equipment and receive excellent training, which will help in securing a position in the Antimicrobial Agents industry at the end of the Ph.D. or engage in an academic career. The prospective supervisors have 20 years of combined research experience in antimicrobial compounds, and they have supervised to completion 6 Ph.D. students. Shanghai Institute of Materia Medica, Chinese Academy of Sciences (SIMM, CAS) was founded in 1932, focusing on drug discovery and development against cancer, cardio-cerebrovascular disease, neuropsychiatric disease, metabolic disease, autoimmune disease, infectious disease, etc. Over 100 new drugs have been developed thus far. SIMM-CAS has been established with state-of-the-art facilities and core technology platforms. The University of Nottingham Ningbo is the first Sino-foreign University in China and comprises both international and Chinese scholars with strong research experience. China Beacons Institute is a newly opened research centre focused on ecological transition and sustainable technology.
Contact points	Informal inquiries may be addressed to Assoc Prof Enrico Marsili (enrico.marsili@nottingham.edu.cn) and Prof. Baofu Xu (bfxu@simm.ac.cn)
PhD topic	**Enabling Physiological Tissue Mimicry Devices through High-Precision 3D Printing Techniques**
SIMM Supervisor	Dongxin Zhao
UNNC Supervisor(s)	Yinfeng He
Short introduction & description of PhD	Physiological tissue mimicry devices can be achieved through the integration of bioengineering and high-precision 3D printing techniques. These devices, carefully designed with microscale features, enable users to replicate the geometries of real tissues, thereby mimicking tissue-specific functions. This approach serves as an effective model for human physiology and disease, offering a more relevant alternative to traditional 2D cell cultures and animal models. Driven by the

	demand for human-like testing systems and advancements in tissue engineering, the trend is increasingly shifting from academic research to industrial applications, such as in the pharmaceutical and cosmetic industries. However, challenges remain, including designing devices that take into account experimental needs and processing limitations, and selecting materials that offer both high printability and biocompatibility, as well as cell instructive functions. This project aims to tackle these challenges with an interdisciplinary team, bringing together expertise in materials science, high-precision 3D printing, and bioengineering. Ph.D. students joining our team will have the opportunity to work in this interdisciplinary environment, exploring the application of the latest 3D printing technology and its potential to enhance physiological tissue mimicry devices for future industrial applications
Contact points	Informal inquiries may be addressed to Dr Yinfeng He (Yinfeng.he@nottingham.edu.cn) and Dr Dongxin Zhao (zhaodongxin@simm.ac.cn).
PhD topic	**New design of antibody-based conjugates and biomaterials for therapeutic applications**
SIMM Supervisor	Prof. Wei Huang, Prof. Feng Tang
UNNC Supervisor	Dr. Yinfeng He, Prof. Zheying Zhu
Short introduction & description of PhD project	Antibody-drug conjugates (ADCs) utilize the specific recognition of antibodies against antigens to offer an efficient targeted drug delivery system and attract great research enthusiasm in the past decades. The payloads used in ADCs include a range of diverse molecules such as toxin, oligonucleotide, hormone, radionuclide, peptide, etc. New design of antibody-based conjugates has been an important direction of biotherapeutics. This project will focus on two major objectives: (i) design and development of new antibody-based biomaterials compatible with Additive Manufacturing technology to expand the application of biotherapeutics in treatment of cancer or neurodegenerative diseases; (ii) construction of novel antibody-oligonucleotide conjugates (AOC) as targeted gene therapy for Alzheimer's disease and/or other biological applications.
Contact points	Informal inquiries may be addressed to Dr Yinfeng He (yinfeng.He@nottingham.edu.cn), Dr. Zheying Zhu (zheying.zhu@nottingham.ac.uk), and Dr. Wei Huang (huangwei@simm.ac.cn).
PhD topic	**Rebalancing inflammation in bacterial infections as immune intervention in the aging mice**
SIMM Supervisor	Jia Li
UNNC Supervisor	Enrico Marsili
Short introduction & description of PhD project	Age-associated alterations in host immune cell functions may play a role in the occurrence of infections even with less virulent bacteria. The innate immune response is impaired in older individuals. Given the varied efficacy of conventional antibiotics between young and old subjects, it's important to develop new strategies. The minimum inhibitory concentration for antimicrobials is much higher (10-100 times) in the presence of biofilms than with planktonic cells, thus the conventional antimicrobial screening might not provide reliable results. While biofilm testing is

	highly desirable, there are technical difficulties associated with growth and maintenance of reproducible biofilms. Enrico Marsili has developed an easy-to-use biofilm testing platform based on bioelectrochemical analysis, which can be used on single species and polymicrobial biofilms, the most relevant for clinical applications. The platform allows the characterization of both lethal and non-lethal (e.g., biofilm dispersing) antibiofilm agents. Jia Li is committed to the research of molecular mechanisms of metabolic diseases and innovative drugs. Prof Li focuses on the pathogenesis and development of aging associated metabolic diseases such as diabetes and cancer, and combines high-throughput screening to discover new molecular entities to carry out research on mechanisms and innovative drugs. In this project, the student will work with both supervisors to discover novel compounds which display antimicrobial and antibiofilm activity using bioelectrochemical methods. Then the student will apply this compound in cellular and mice model between young and aging group for further phenotype and mechanism study.
Contact points	Informal inquiries may be addressed to Assoc Prof Enrico Marsili (enrico.marsili@nottingham.edu.cn) and Prof. Jia Li (jli@simm.ac.cn)
PhD topic	**Targeting macrophage infectivity potentiator (Mip) in *Enterococcus faecalis* biofilms catalyse the folding of proline-containing proteins through their peptidyl prolyl cis-trans isomerase (PPIase) activity and have been shown to play an important role in the virulence of several pathogenic bacteria.**
SIMM Supervisor	Dehua Yang
UNNC Supervisor(s)	Enrico Marsili
Short introduction & description of PhD	The macrophage infectivity potentiators (Mips) belong to the ubiquitous FK506 binding protein (FKBPs) family of peptidyl-prolyl cis/trans isomerases (PPIases). FKBPs are found in all bacteria serving as general house-keeping proteins involved in protein folding and chaperoning. However, a small subset has been identified as virulence proteins, particularly in Gram-negative pathogens. In fact, the PPIase activity renders the extracellular matrix sensitive to, serine protease, which allows the invasion of pathogens through the epithelial barrier. In Gram-positive bacteria, PPIases were also involved in bacterial virulence and host colonization. However, there is little information on MIPs role as virulence factor in *Enterococcus faecalis*, a leading Gram-positive pathogen responsible for difficult-to-treat urinary tract infections (UTI) and gastrointestinal (GI) infections. Mips are particularly important in biofilm infections, as they favor attachment to the extracellular matrix of the host. Due to the presence of chemical gradients and the high concentration of pathogens, biofilm infections are resilient to conventional antibiotic and antimicrobial treatments. Thus, novel non-lethal approach that target biofilm formation and virulence are preferred. In this project, the PhD student will review the current literature to identify possible MIPs that serve as virulence factors for *E. faecalis* biofilm infections. Following experiments in biofilm models in vitro to determine the effect of specific MIPs in biofilm formation, the PhD candidate will carry out an in-silico screen of the compound library at SIMM to identify possible compounds that target MIPs as virulence factors. The most promising candidates will be hen tested

	in biofilm system, both in vitro and in animal model, aiming to develop a novel therapeutic approach for *E. faecalis* biofilms. The ideal candidate for this project has a background in Molecular Biology, in-vitro/in vivo pharmacology and a strong interest in developing non-lethal therapeutic approach against biofilm infections. **Enrico Marsili** has developed an easy-to-use biofilm testing platform based on bioelectrochemical analysis, which can be used on E. faecalis biofilm to test novel therapeutic approach. The platform allows the characterization of both lethal and non-lethal (e.g., virulence factors-based) antibiofilm agents. In this project, the student will work with both supervisors to characterize Mips and eventually discover novel compounds which target this group of virulence factors. **Dehua Yang** has 11 years' experience in high throughput screening, target discovery and validation for metabolic disease. The Chinese National Compound Library possesses two million compounds with diversified structures, which can potentiate the chance to find novel antibiofilm compounds.
Contact points	Informal inquiries may be addressed to Dr Enrico Marsili (enrico.marsili@nottingham.edu.cn) and Prof Dehua Yang (dhyang@simm.ac.cn)
PhD topic	**To explore the pathogenesis of cardiovascular diseases and find new therapeutic targets based on modern medical biotechnology. This will encompass, drug screening, developing novel drug delivery systems, and evaluating biological mechanisms for the treatment of cardiovascular diseases.**
SIMM Supervisor(s)	Prof. Hanbin Lin
UNNC Supervisor(s)	Prof. Yong Ren
Short introduction & description of PhD	Cardiovascular disease is a prevalent and progressively worsening condition, with its incidence and death rates consistently rising and affecting individuals at younger ages. Currently, cardiovascular disease has surpassed cancer as a leading cause of mortality globally. This underscores the importance of exploring the pathological mechanism and developing new therapeutic targets to aid the diagnosis, prognosis, and treatment of cardiovascular diseases. As such, our study will aim to investigate pathological mechanisms of cardiovascular disease and develop new therapeutic targets and drug delivery systems via technologies including microfluidics. This will encompass the utilization of multi-omics and molecular biotechnology to examine and validate novel targets and biological mechanisms of cardiovascular diseases. In vivo and in vitro models will be established to study the biological mechanisms of cardiovascular disease through cardiac function, including histopathological changes, and myocardial enzymes. Furthermore, novel therapeutic targets will used to evaluate the attenuation of cardiovascular disease in vitro and in vivo. In addition, our study will investigate novel drug delivery systems to improve drug bioavailability and achieve targeted treatment of cardiovascular diseases. This major involves pharmacodynamics, pharmacology, histopathology, materials science, nanomedicine pharmaceutics, and other disciplines. Candidates should be self-motivated and have a strong background in pharmacology, pathology, or materials science.

	This Ph.D. program is multi-disciplinary, which covers broad fields of pharmacology, pharmacodynamics, pharmaceutics, and histopathology and materials science. 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. Hanbin Lin (linhanbin@simm.ac.cn), and Dr. Yong Ren (Yong.ren@nottingham.edu.cn).