OSCAR

UNIVERSITY OF OXFORD

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牛津大学高等研究院（苏州）
OXFORD SUZHOU CENTRE FOR ADVANCED RESEARCH

June 2018

NEWSLETTER 011

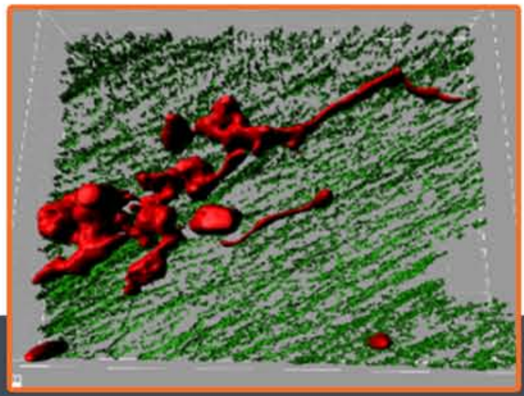
HEADLINES

Introduction to the CRMI Technology Centre at the University of Oxford

The CRMI Technology Centre at the University of Oxford in the UK is an industry-sponsored research centre developing novel devices, technology and systems for healthcare benefit and translation into clinical practice. The centre is located within the Institute of Biomedical Engineering, a world-class centre of excellence in research at the forefront of innovation in medical technology. Since December 2013, research at the centre has been sponsored by China Regenerative Medicine International Limited, China's first world-leading enterprise in industrialisation and commercialisation of tissue engineering.

IBME The Institute of Biomedical Engineering

The main aim of the Technology Centre is to address many challenges that are currently limiting widespread delivery of cell therapies and regenerative medicine and, by doing so, to bridge the gap between the laboratory and the clinic.



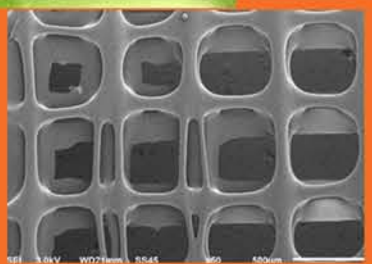
Directed by Professors Zhanfeng Cui and Cathy Ye, the centre has the laboratory space and equipment required to carry out work being undertaken in the fields of tissue culture, multi-photon microscopy, fabrication, and characterization by experts in the fields of tissue engineering and bio-product design, biomaterials and biochemistry, membrane and biomedical engineering and bioreactor and scaffold biotechnology.

The research team, composed of 11 post-doctoral scientists and 10 DPhil students is undertaking an ambitious research programme in the field of stem cell therapy and tissue engineering. More than twenty research projects are which cover areas including stem cell expansion, cell storage and transport, soft tissue and skin regeneration and neural regeneration are on-going.

To meet the need for bioreactors that can cope with more diverse requirements and methodologies that can improve cell purity, for example, the centre is developing novel bioreactors, micro-carriers and macro-carriers, better transport and storage media, and improved cell viability following cryopreservation.

A number of support systems are also being developed including functional hydrogels for neural network formation and vascularisation, 3D bio-printed membranes suitable for guided tissue regeneration and bio-intelligent biomaterial scaffolds that can be used in tissue reconstruction to treat chronic wounds. The centre is also developing quality control and quality assurance protocols and exploring the use of Next Generation Sequencing as a novel way to test for cell safety.

This cutting edge scientific research and novel technology development has, so far, led to four patent applications being filed in the UK and a utility model in China. Researchers in the centre have published eight peer-reviewed papers and three book chapters, received three awards and presented their work at numerous international conferences. At the heart of innovation in medical technology, this translational research will enable rapid application of therapies to target major unmet clinical needs.

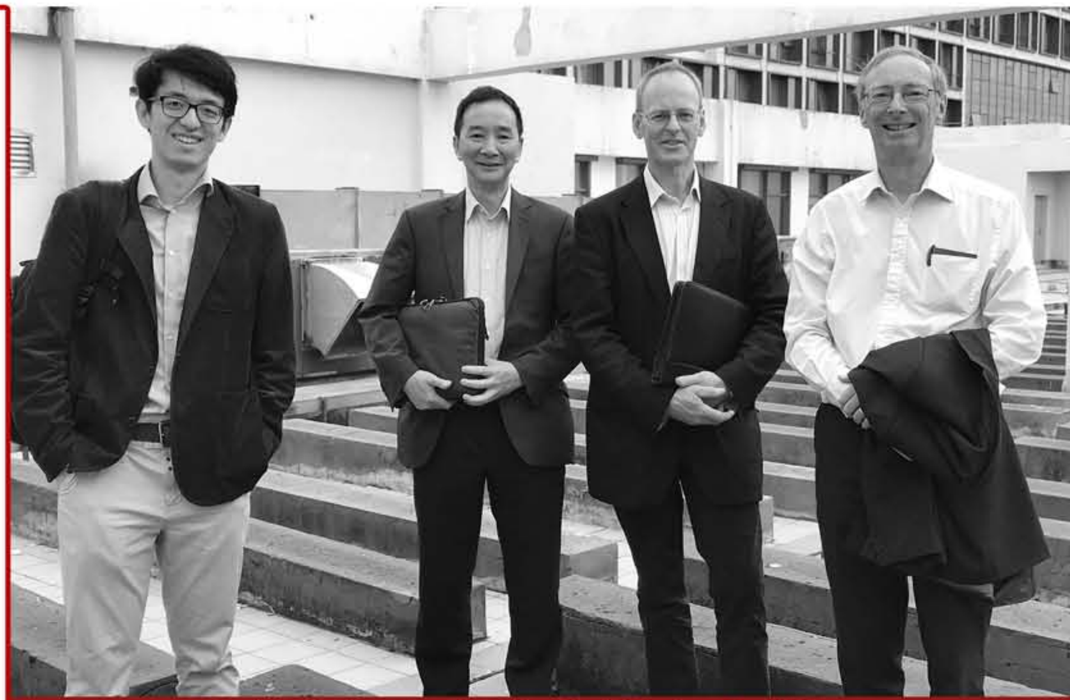


UNIVERSITY OF OXFORD

TISSUE ENGINEERING GROUP OXFORD

For more information about the CRMI Technology Centre at the University of Oxford, please go to:
http://www.ibme.ox.ac.uk/research/regenerative-medicine/tissue-engineering

Introduction to the Research of Professor Luet Wong and Professor Jeremy Robertson -Bio-hydroxylation in Fine Chemical Synthesis and Drug Discovery



From left: Dr. Yang Cao, Prof. Wong, Prof. Robertson, Prof. Moloney

Both Professor Wong and Professor Robertson obtained their Bachelors and D.Phil degrees in Chemistry at the University of Oxford. After post-doctoral work in the US they took up their Professor of Chemistry positions at the Department of Chemistry at Oxford in the 1990s.

Professor Wong has worked for over 20 years in the discovery and engineering of cytochrome P450 (CYP) enzymes. CYP enzymes catalyse the oxidation of chemically inert carbon-hydrogen bonds using oxygen from the atmosphere as the oxidising agent, often with exquisite selectivity for one alcohol product. CYP enzymes are involved in the biosynthesis of hormones and plant secondary metabolites. Examples include the anti-malarial drug artemisinin, which was discovered in China, the anti-cancer drug taxol, and numerous desirable plant flavour and aroma compounds such as the sandalwood aroma compound santalol and the grapefruit flavour nootkatone. CYP enzymes are of great importance in the pharmaceutical and agrochemical industry because they are responsible for the metabolism of the majority of drugs and other biologically active compounds by C–H bond activation. The metabolites may be the actual active drug or toxic. The synthesis and testing of metabolite is a key part of drug discovery and development.

Direct oxy-functionalisation of C–H bonds is difficult to accomplish by classical chemical synthesis methods. These require excesses of high-energy oxidising reagents such as peroxides and heavy metal compounds, which can be hazardous at large scale, and generate toxic wastes. Where catalytic reactions are possible, little control can be exercised over product selectivity. By contrast, biohydroxylations by CYP enzymes are catalytic, selective and the processes are friendly to the environment because of the benign nature of the reagents, the ambient conditions of the reactions and the absence of toxic waste. Regulatory agencies and the general public increasingly demand greener, less energy intensive processes that also generate the minimum amount of waste. Bio hydroxylation can play an important part in replacing existing, often polluted processes with green alternatives.

Professor Wong's research on the fundamental science of CYP enzyme structure and function has led to the generation of a collection of enzyme variants with high activity and product selectivity for the biohydroxylation of a wide range of organic compounds. He has a long-standing interest in biologically active compounds including flavour and aroma fine chemicals, drugs and drug fragment molecules. The CYP enzymes were engineered by artificial evolution to develop new routes to these compounds. One such reaction was the oxidation of valencene, a compound found naturally in orange essential oil, to nootkatone, the high-value grapefruit flavour compound. Oxford Biotrans Ltd. (http://oxfordbiotrans.com), a University spin out company, was founded with venture capital funding in 2013 to commercialise the process. Based in Didcot, just outside Oxford, the company has successfully scaled the fermentation and biotransformation steps to production volumes. Commercial sales of nootkatone produced by bio hydroxylation began in 2017. Professor Wong has ongoing projects to develop new CYP enzymes and processes to produce flavour and aroma compounds, in particular those currently obtained from rare plants. Over-harvesting has caused many such biological sources to become endangered in the wild. Biotechnology offers simple and green processes to provide alternative and secure supplies.

CYP enzymes convert a chemically inert carbon-hydrogen bond to an alcohol group. Alcohols are chemically reactive, and the entire arsenal of chemical and biological reactions used in synthesis can be applied. We only need to think of how little chemistry we can do with methane (CH4) and the multitude of products made with methanol (CH3OH). CYP enzymes can be used to oxidise chemically inert, persistent organic contaminants in the environment to more reactive compounds that are readily degraded by microorganisms. Professor Wong has shown that engineered CYP enzymes can oxidise polyaromatic hydrocarbons such as benzo[a]pyrene and polychlorinated compounds such as hexachlorobenzene, providing possible routes to degrade these carcinogenic compounds. At OSCAR Professor Wong will work with scientists in China to develop applications in environmental biotechnology.

The alcohol group formed by CYP bio hydroxylation offers an ideal synthetic handle to elaborate the structure to increase molecular complexity by varying the shape and property of newly attached fragments. This approach can be applied to every step of the drug discovery process, from small molecule collections used in screening against drug targets to initial hits and candidate drug compounds. Natural products with biological activity can be elaborated by this approach, potentially providing derivatives with higher efficacy and less side effects. Pathways for the total synthesis of natural product candidate drugs can be designed to introduce diversity at key intermediates using bio hydroxylation by CYP enzymes. These approaches are more efficient since it is unnecessary to repeat multi-step synthesis for each analogue/derivative for testing.

The groups of Professor Wong and Professor Robertson will collaborate in the synthesis efforts at OSCAR. Professor Robertson has a 20-year track record in total synthesis of natural products with medicinal properties. He has a long-standing interest in the application of novel radical reactions and oxidation chemistry including electrochemical oxidation. The two research teams will work closely together to deliver innovative solutions for all steps in the drug discovery process. There are exciting opportunities in working with the pharmaceutical industry in China.

Brief Introduction to the
"Supporting Universities and Institutions Recruitment of High-Level Talents" of Suzhou City

The Suzhou policy "Supporting Universities and Institutions Recruitment of High-Level Talents" offers funding for researchers of between 0.5m CNY and 5m CNY, depending on their career stage and markers of esteem. The Talents scheme is divided into 3 Levels:

Level 1

Noble prize winner, Fellow of Royal Academy of Sciences, Fellow of the Royal Academy of Engineering and the equivalent to the above levels.
No more than 55 years old (Case by case).

Level 2

1000 Talents Plan, CAS Hundred-Talent Program, Ten-thousand talents program, Scholar of the Yangtze River, National Natural Science Funds for Distinguished Young Scholar or the equivalent to the above levels.
No more than 50 years old.

Level 3

1000 Youth Talents Plan, Young Top-notch Talent of Ten-thousand talents program, Associate Professor, Outstanding Achievements in the Discipline or the equivalent to the above levels.
No more than 40 years old.

General requirements:
-Full time labor contract for at least 3 years;
-Started working in Suzhou between 2015 to 2018;
-Payed tax or social insurance in Suzhou.

Subsidy (CNY):
The annual subsidy is 50% of the annual salary, and the total amount of three years' subsidy is 150% of the annual salary.
-Talents of Level 1, up to 5 million.
-Talents of Level 2, up to 1 million.
-Talents of Level 3, up to half million.

Progress of OSCAR's Fit-out and Construction in June

Updates on fit-out construction tendering process:

Fit-out construction is now undergoing the process of government regulated public tendering, which includes the following 6 sections.

- Section 1. Construction engineering supervision（Stage 5 completed, contract signed）
- Section 2. Non-lab space construction (Stage 5 completed, contract signed)
- Section 3. Lab space construction (Stage 1 in process)
- Section 4. Air-conditioning construction (Stage 5 completed, contract signed)
- Section 5. IT construction (Stage 1 in process)
- Section 6. Exhibition construction (to be announced in early July)

On-site construction:

On-site preparations for non-lab space in the OSCAR building has started. Construction of an on-site temporary office has been completed. Electricity, water and the freight elevator have been connected on-site, ready for wider construction to begin.

Description of the OSCAR Logo

Oxford Suzhou Centre for Advanced Research (OSCAR) is the first overseas research centre of the University of Oxford. OSCAR follows the rules of the University of Oxford for the use of logo. The colour and shape of the logo are based on the University's standard, such as the colour is Oxford Blue (C100, M80, Y0, K60), and the shape is designed in white colour on the blue square background. The upper right corner is the ancient seal form representing authority and credit.

The interior is the ancient script "Suzhou" and "Oxford". The bottom left corner of the water ripple shape means that OSCAR is located in Suzhou which is well known as an ancient oriental water city with more than 2,500 years' history. At the same time, it is like the shape of "lucky cloud", which means good luck in Chinses traditional culture. Below the logo is the English abbreviation "OSCAR" of the Oxford Suzhou Centre for Advanced Research in the University's font. The logo has a unique Chinese style and is consistent with the style of the other University companies'. According to the University rules, the OSCAR logo is to be used aside with the logo of the University's in parallel. When used with the name of OSCAR, it must be used both in Chinese and English at the same time.

Neighbours of OSCAR

Research Institute for Environmental Innovation (Suzhou), Tsinghua (RIET)

The Research Institute for Environmental Innovation (Suzhou), Tsinghua (hereinafter referred to as 'RIET') is a secondary institute affiliated to Tsinghua University. It is mainly engaged in environmental science and innovation activities, with its overall objective to build a comprehensive research and technology service institute with international influences. RIET plays a key role - in Tsinghua University's development ambitions of "building a world-class environment science centre, driven by institutional innovation" and scientific research, with a focus on industrial innovation.

Address: Building 16, 101 Business Park, No. 158 Jinfeng Road, New District, Suzhou, Jiangsu Province.

http://www.tsinghua-riet.com/page/home

News Links in June

Workshop on nanotech held in SIP

A workshop on nanotech was held at Suzhou Institute of Nano-tech and Nano-bionics (SINANO), SIP from June 28 to 29. More than 100 professionals in the field, including those from research institutes, schools, enterprises and investment companies, participated to grasp a better understanding of the current development and future prospects of the nanotech industry.

Jiangsu Department of Human Resources and Social Security sponsored the event, in the hope of offering the participants an opportunity to share information about the industry.

The event included several lectures given by experts engaged in micro and nano fabrication, new carbon materials, GaN materials and equipment, ink-jet printing, micro-electro mechanical systems (MEMS), magnetic materials and printing electronics, and a tour around SINANO's laboratories and discussions on related hot issues.

SIP showcases its ability to attract and retain talented individuals

Suzhou Science and Technology Bureau has released this year's first list of Candidate Innovation and Business Start-up Projects Initiated by Leading Talents. 22 leading business founders in SIP are on the list, another testimony to SIP's strong ability to attract and retain talents.

The report shows that SIP's Jinji Lake Talents Program, under which nearly 3 billion CNY in rewards and subsidies are earmarked for high-calibre talents each year, plays a big part in SIP's ability to recruit and retain talented individuals. SIP currently ranks top among domestic development zones in terms of the size of local talent pool, with over 600 people under national and local talent development programs, 45 teams led by academicians and tens of thousands of overseas returnees and expatriates.

Building A,388 Ruo Shui Road, Suzhou Industrial Park, Jiangsu, 215123, P.R. China

+86-512-62869088

info@oxford-oscar.cn