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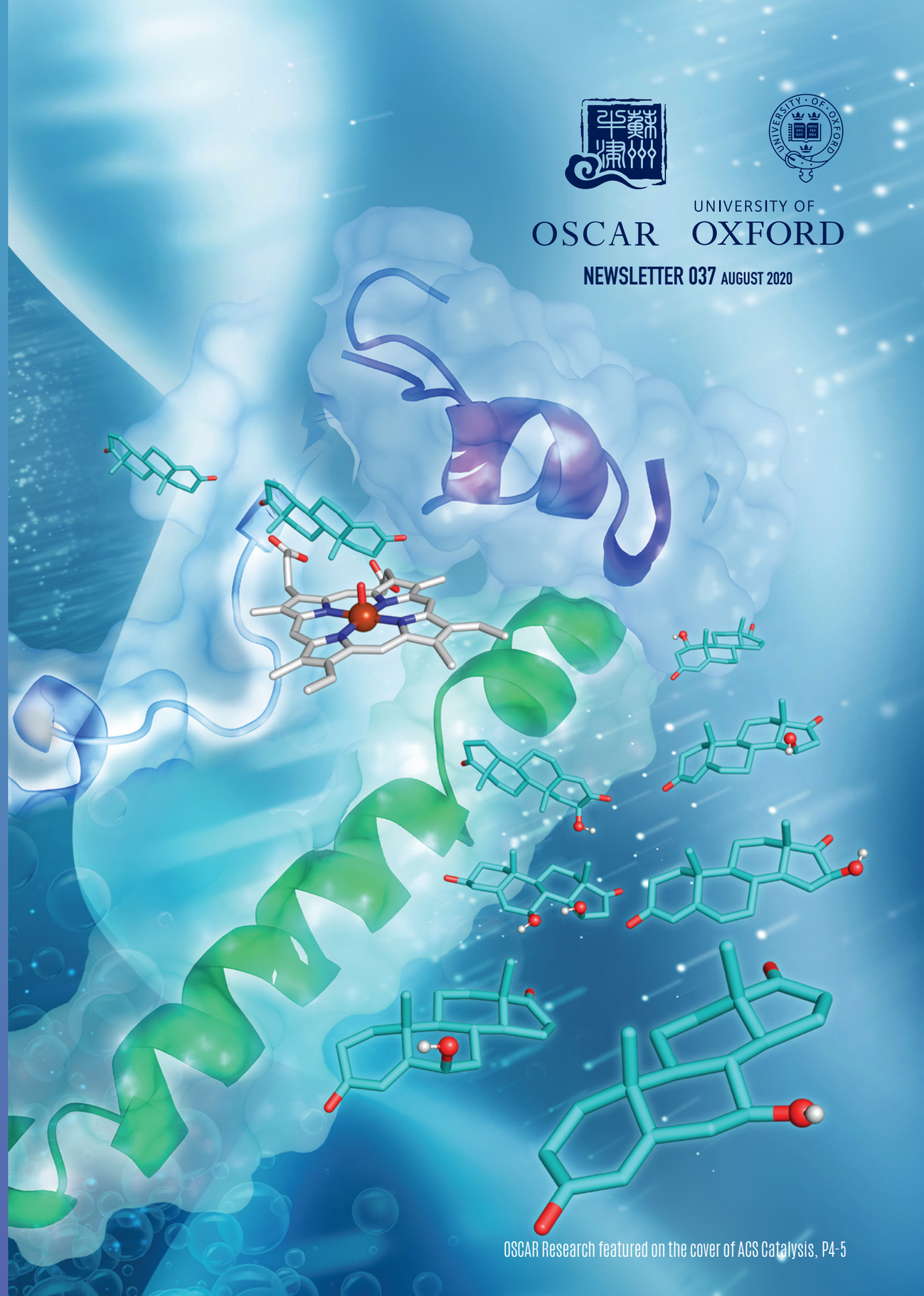


UNIVERSITY OF OXFORD

OSCAR

NEWSLETTER 037 AUGUST 2020

OSCAR Research featured on the cover of ACS Catalysis, P4-5

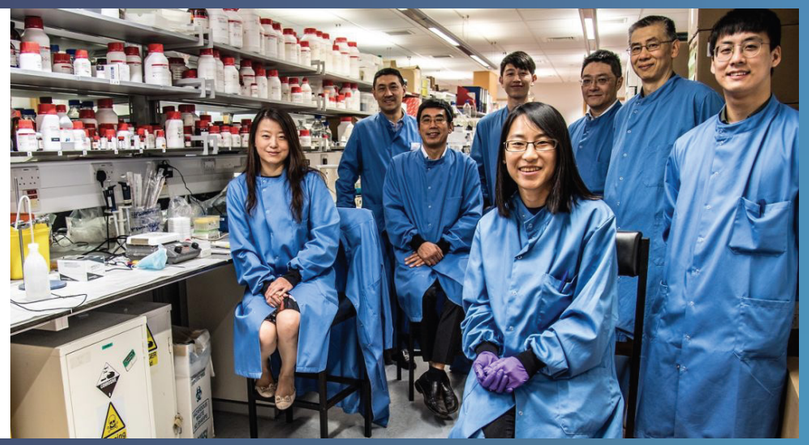
CONTENTS

OSCAR AND OXFORD RESEARCHERS AWARDED RAENG PRESIDENT'S SPECIAL AWARD FOR THEIR RAPID COVID-19 TEST

When China began lockdown in January, a joint research team of OSCAR and University of Oxford researchers, led by PI Prof. Wei Huang and Director Prof. Zhanfeng Cui, began work on a rapid test to identify carriers of Covid-19.

Pooling resources and expertise, they quickly established a working prototype capable of providing a result within 30 minutes. In less than six months, they developed the rapid test kit from first principles through to spinout. This achievement is even more remarkable given the limitations in both China and the UK at that time. They have shown great dedication to the project since its inception, working long hours and persevering through the uncertainty of a rapidly evolving situation.

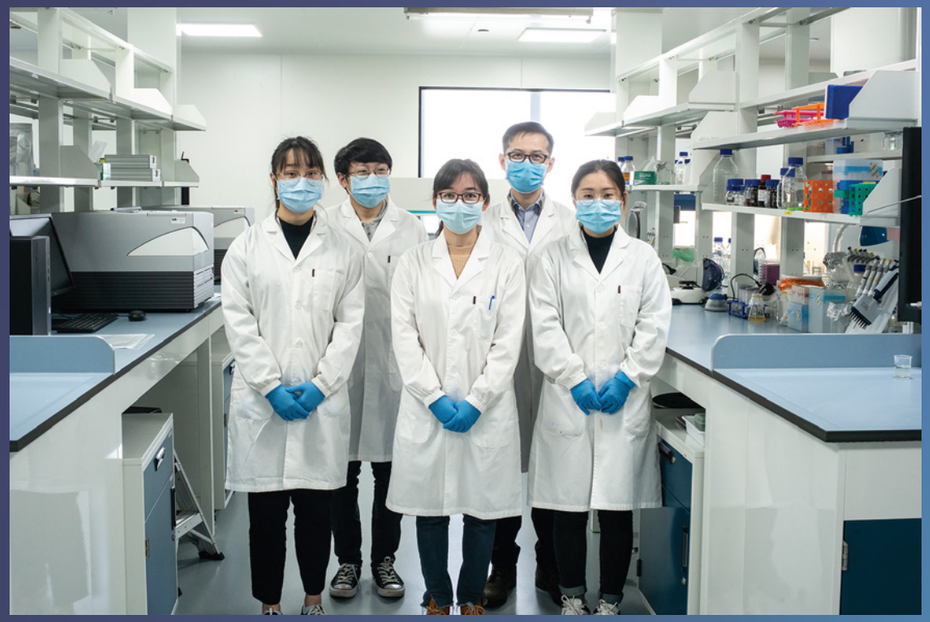
The team behind the extraordinary research have been recognised for their achievements as one of the 19 winners of the Royal Academy of Engineering President's Special Awards for Pandemic Service. These awards were presented for exceptional engineering achievements in tackling Covid-19 throughout the UK.



L-R: Dr. Hong Chang (Visiting Industrial Fellow at OSCAR), Dr. Huidong Jia (Senior Research Scientist, OSCAR), Prof. Zhanfeng Cui, Boon Lim (DPhil student, Oxford University), Dr. Chia-Chen Hsu (postdoctoral researcher, Oxford University), Prof. Wei Huang, Dr. Hui Wang (Senior Research Scientist, OSCAR) and Yejiong Yu (DPhil student, Oxford University).

Specially commissioned silver medals will be presented to all 19 winners later this year.

Professor Cui says: “I am extremely proud of our team, who have demonstrated R&D competence, engineering innovation, great dedication and social responsibility. We are grateful to the University of Oxford, OSCAR and Oxford University Innovation for their support, with which we were able to develop a unique product within six months and contribute to the fight against Covid-19.”



The team’s rapid viral RNA test, now marketed as Oxsed RaViD Direct, can detect whether a person is infected with the SARS-CoV-2 virus and is still infectious. It does not require the use of specialist equipment and can be used by anyone. Users need only transfer samples from mouth or nose swabs, or saliva, into a test tube supplied with the test, containing all the necessary reagents. The kits are formulated so they can be stored and supplied without being refrigerated and in a product format that is economical and readily deployable in quantity.

The accessible nature of the test means it has the potential to make a big impact in the fight against Covid-19. As no specialists are needed to operate it and results are easy to interpret, testing can be performed at GP clinics, schools, airport and community centres, for example, and could even be used for self-testing at home.

Oxsed RaViD Direct has received a CE Mark and is now commercially available. Licensing and manufacturing partnership opportunities with large pharmaceutical and medical device companies are in discussion, to roll out the products in large quantity.

Both the product patent and establishment of Oxsed Limited as a social venture spinout were a first for OSCAR. This award recognises many months of hard work by the research teams working in partnership in Oxford and Suzhou in forging new ground for OSCAR under uniquely challenging circumstances.

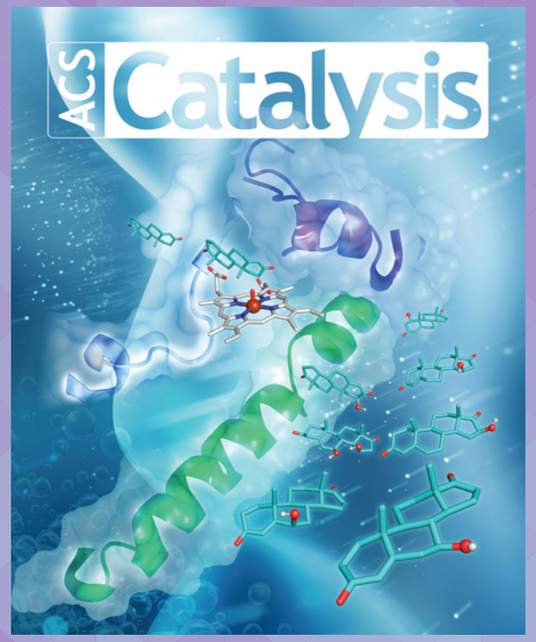
https://www.raeng.org.uk/grants-prizes/prizes/prizes-and-medals/awards/presidents-special-awards-pandemic-service/test-infectious.

RECENT OSCAR ACADEMIC PUBLISHING

Research Article from Professor Luet Wong's Group Published in **ACS Catalysis** Featured on Journal Cover

Professor Luet Wong's research team at Oxford and OSCAR have reported a new approach to engineer the active site of a cytochrome P450 monooxygenase enzyme to oxidise steroids to multiple products with high selectivity in the August issue of ACS Catalysis.

In the paper the research team used enzyme engineering to control the introduction of one or two oxygens at different positions of the steroidal core framework by direct oxidation of chemically inert carbon-hydrogen bonds. The high selectivity for oxidation at multiple positions, featured in a journal cover image, provides one-step routes to existing drugs and key intermediates for synthesising new steroidal agents for drug discovery.



ACS Catal, 2020, 10, 8334-8343; DOI:10.1021/acscatal.0c02077

ACS Catalysis

pubs.asc.org/acscatalysis

Research Article

Oxidative Diversification of Steroids by Nature-Inspired Scanning Glycine Mutagenesis of P450BM3(CYP102A1)

Wenyu Chen, Matthew J.Fisher, Aaron Leung, Yang Cao, and Luet L, Wong*

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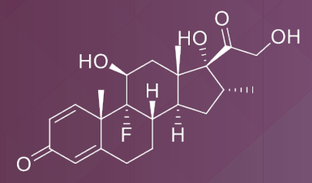
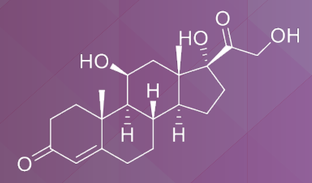
Steroids are some of the most prescribed medicines. Over 100 steroidal drugs are in clinical use for the treatment of cancer, inflammation and heart disease, amongst other conditions, including the recent discovery at Oxford of the use of dexamethasone in Covid-19 patient care. Many people have used hydrocortisone, sold over the counter in pharmacies, for skin irritation and inflammation. The biological activity of steroids depends on the position and number of oxygens and other groups attached to the periphery of the iconic four-ring steroidal core structure. These variations enable steroidal compounds to bind to a wide range of drug targets. As a result, the steroidal core is regarded as one the most privileged structures in drug discovery. There is a continuing need to synthesise new, richly functionalised steroid derivatives in the search for new therapies.



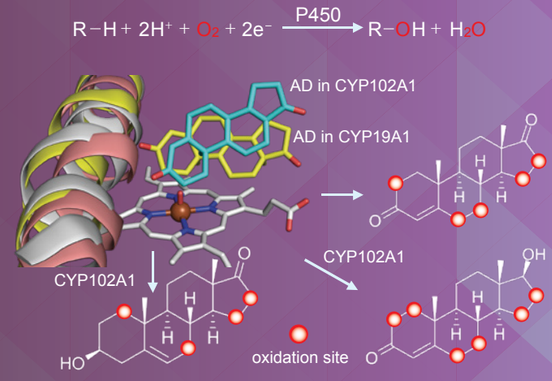
Dexamethasone



Hydrocortisone

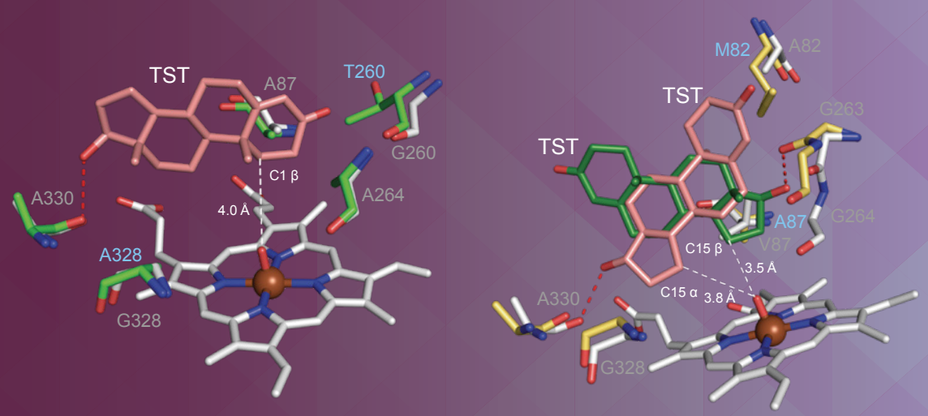
Dexamethasone and hydrocortisone differ by modification of the 4-ring steroidal core structure and attached functional groups.

Total chemical synthesis of the complex steroidal core is impractical; instead, plant steroids are converted chemically to common medicinal steroids which are the starting materials for steroidal drugs in use today. The simplest pathway to new derivatives is to oxidise C–H bonds on the periphery of the steroidal core followed by functional group elaboration. However, steroidal C–H bonds are inert to classical synthesis methods. On the other hand, direct insertion of an oxygen atom from oxygen in the atmosphere into inert C–H bond is the signature reaction of cytochrome P450 enzymes.



The signature C–H bond oxidation reaction of cytochrome P450 enzymes and the hydroxylation positions on screened steroidal cores in this paper.

Application of the unique activity of P450 enzymes requires control over the position and number of C–H bonds oxidised. The research team used computational methods and comparison of the structures of cytochrome P450BM3 and human steroid-oxidising enzymes to design a small library of P450BM3 variants. This nature-inspired approach led to selective oxidation of 3 steroids (androstenedione, dehydroepiandrosterone and testosterone) to 17 products which included compounds with anti-hypertension, anti-inflammation and neuro-protective properties. Most reactions showed higher than 90% product selectivity. Five products are new compounds from P450-catalysed steroid oxidation.



The oxidation position is controlled by manipulating the binding orientation of steroids, e.g. testosterone (TST, pink and dark green), in the P450 enzyme active site by designed combinations of amino acid substitutions.

This breakthrough in enzyme engineering reported by the Oxford-OSCAR team will speed up the synthesis of novel steroid derivatives for drug screening. Synthesis of derivatives with diverse functional group substituents is a key process in drug development. P450-catalysed oxidative diversification of drug lead compounds provides unique advantages and efficiency gains at all stages of this process.

RESEARCH SPOTLIGHT

Prof. Mark Moloney
Principal Investigator and Deputy Director, OSCAR
Professor of Chemistry, University of Oxford

Prof. Mark Moloney, Deputy Director and PI of the Surface Chemistry group at OSCAR, has a longstanding interest in surface modification and functionalisation, particularly to create antimicrobial materials (for example, to prevent biofouling in healthcare or environmental settings).

This research is especially pertinent in the current climate, as surface sterilisation is becoming commonplace in everyday life and antimicrobial materials are critical to protect users (i.e. both clinicians and patients).

Prof. Moloney recently published a research paper with colleagues at the School of Chemistry and Pharmaceutical Engineering, Qilu University of Technology (Shandong Academy of Sciences). This project is an example of OSCAR PIs' collaborative work with partners across China, something that is important to consolidating our position and reputation in the country.

The paper presents research into surface functionalisation of silver nanoparticles by a furyl-substituted carbene. These nanoparticles were subsequently crosslinked by a reversible Diels-Adler reaction mechanism. Silver has long been known as an antibacterial agent and is widely used in the health industry, particularly in sterile wound dressings. Silver nanoparticles offer a potent and more targeted delivery of silver, without oxidation which can cause dark staining. The strength of antibacterial activity is related to silver nanoparticle size. The method described in this paper allows controlled, tunable aggregation with different particle sizes, thereby allowing controlled dosage.

This approach opens a new horizon for the carbene chemistry to modify silver nanoparticles with variable size and give controlled antibacterial activity. The article, with joint OSCAR and Oxford affiliation for Prof. Moloney, is available to read online:

Jing, L., Moloney, M., Xu, H., Liu, L., Sun, W., Li, J. and Yang, P. (2020). Carbene modification and reversible crosslinking of silver nanoparticles for controlled antibacterial activity. Scientific Reports **10 (1):** 1-9.

Prof. Rama Cont
Principal Investigator, OSCAR Mathematics

Prof. Rama Cont joined OSCAR in April 2020 as one of four PIs at the new Mathematics Institute. His research focuses on stochastics analysis, stochastic processes and mathematical modelling in finance. He is particularly concerned with high-frequency modeling, quantitative risk management, regulation, financial stability and systemic risk.

He is scientific advisor to the International Monetary Fund (IMF) and the central bank of Norway and has previously worked as advisor to the European Central Bank, the Bank of England, the New York Federal Reserve, the Chicago Mercantile Exchange and the Hong Kong Exchange (HKEX) on matters related to stress testing, risk management and financial stability.

Many of OSCAR's PIs have directed research efforts to investigating the Covid-19 pandemic and leading mitigation efforts. While mathematics may seem unrelated to frontline healthcare, it is fundamental to understanding patterns and applying these to inform short-term responses and draw longer term conclusions.

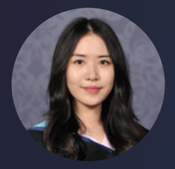
Prof. Cont presented the background to his Covid-19 monitoring research at OSCAR's most recent academic research seminar, in which PIs share their current research with OSCAR's research family across all disciplines. Prof. Cont discussed different epidemiology models to examine how epidemic behave in populations and how these can enable more accurate modelling in heterogenous populations.

Prof. Cont and his Oxford research students have used spatial epidemic modelling to study the regional dynamics of Covid-19 across England. Their model considered demographic and geographic heterogeneity, emphasising the role of variability across different age groups and regions. Importantly, it also provides a framework for assessing the impact of policies targeted at specific populations or sub-populations. This is useful in generating risk assessments and also creating targeted mitigation responses, for example in implementing more effective restrictions in local virus hotspots. Their data showed that both shielding vulnerable people and targeted local monitoring can reduce fatality forecasts. They also show that targeted local, as opposed to centralised, policies and monitoring can help prevent the emergence of 'second waves' and remove the need for a return to full-scale national lockdown.

The article was published in August and, in the spirit of international collaborative COVID response, is free to view. The pre-print is available on the SSRN (Social Science Research Network) repository.

Cont, R., Kotlicki, A. and Xu, R. (2020). Modelling COVID-19 contagion: Risk assessment and targeted mitigation policies. Available at SSRN 3681507.
Learn more: https://oscar.web.ox.ac.uk/mathematical-modelling-and-data-analytics

MEET OSCAR'S VISITING STUDENTS



Rui Lei

Second year DPhil candidate in the Tissue Engineering group at the Institute of Biomedical Engineering (IBME), University of Oxford.

Rui is a visiting student in the Regenerative Medical Engineering group at OSCAR. Her research focuses on exosomes derived from human bone marrow MSCs.

"What appeals to me the most about OSCAR is its role as the first overseas research and innovation centre of the University of Oxford. Along with many other research institutes, universities and tech companies, OSCAR is situated in the Suzhou Industrial Park (SIP), which has been a keen advocate for technology transfer, making OSCAR a great place for good ideas, and a good platform for scientific research and collaboration."

Peng Tang

Second year DPhil candidate from the Department of Materials at the University of Oxford.

Peng is a visiting student in Prof. Pasta's Energy Storage and Conversion research group at OSCAR. His doctoral research involves applying electrochemical methods to the efficient conversion of clean energy. During his time in Suzhou, he is working on projects to synthesize efficient, inexpensive and stable single atomic catalysts and to conduct electrochemical characterization.

"OSCAR's location in the heart of the industrial park is ideal, especially for our research in the field of energy materials and our collaboration with neighbouring research institutes, such as the Gusu Laboratory of Materials and the Institute of Nano Science of the Chinese Academy of Sciences. OSCAR's management and operation model is efficient, with the PI being directly responsible for the research work and the administration team providing support to the research groups. There are several research groups with different research interests at OSCAR, which makes it easy and efficient to collaborate and communicate across disciplines. Also, OSCAR is a small, close-knit research centre that operates with latitude."

Xiaoyu Chen

DPhil candidate from the Department of Engineering Science at the University of Oxford.

Xiaoyu is a visiting student in Prof. Wei Huang's Environmental and Synthesis group at OSCAR. His doctoral research in synthetic biology focuses on development of SimCell-based biosensors for disease diagnosis and drug delivery. He is interested in how to detect and cure cancer using probiotic bacteria.

"The concept of bacteria therapy is not new; however, the ability to precisely edit and rationally re-design bacteria genome was not possible before. Now, with the novel genome editing and synthesis tools, we can create and programme micro bacteria bots to execute any pre-designed function. In medical practice, a vivid analogy would be similar to that of the famous sci-fiction 'The Fantastic Voyage': living bacteria act as micro-scale doctor that can swim inside our body for disease diagnosis and apply treatment on-site.

We can construct multiple logic functions that integrate, transmit and amplify various chemical signals according to different tumour microenvironments or specific biomarkers. Our work has two main aspects: to build a universal cell chassis, and to create a precise, accurate, integrated disease sensing system. The progress of experiments at OSCAR is very efficient, and the most attractive features of OSCAR are the office environment, the equipment, and the team!

I think, as an institute, OSCAR is pursuing tech transfer and efficiency. You'll find photonics experts, regenerative medicine experts, organic/inorganic synthesis experts, artificial intelligence experts, and so on, spread out on different floors. This has helped create a upstairs-downstairs work relationship, so it's a very smooth collaboration."

OUTREACH AND COLLABORATION

OSCAR's first Open Day in 2020

On 28th August, OSCAR welcomed nearly 100 guests from academia, industry, and the financial sector in the local region to attend its inaugural Open Day. This was one of the first such events in the area as Suzhou recovers from Covid-19 disruption.

The event was initiated by the Science & Technology Department of Suzhou Industrial Park (SIP) and the Administrative Committee of Suzhou Dushu Lake Science, Education & Innovation District (SEID), and hosted by OSCAR and SEID Entrepreneurship Office. Xiaoming Lin, Vice-Chairman of the Administrative Committee of SIP, opened the event with welcoming remarks and spoke about SIP's consistent role as a collaboration enabler between academia and industry. In her keynote speech, General Manager Leah He described OSCAR's unique status as a partnership between the University of Oxford and Suzhou Industrial Park, as well as introducing OSCAR's research themes and high-profile research teams.

In a pre-taped video speech, OSCAR Director Prof. Cui joined Leah in thanking the audience for their interest in OSCAR and stressing OSCAR's firm commitment to research cooperation, particularly seeking expanded collaboration and partnership with industry. He commented on SIP's sound industrial foundation which made it an ideal situation for OSCAR-Oxford University's first overseas research centre in China. He also expressed his hope to establish broader and closer connections to industrial partners through further events such as this Open Day.

Industry Cooperation Manager Alex Yang showcased to the participants OSCAR's remarkable research capacity and exciting research outputs achieved since its official launch in November 2018. As PIs were unable to attend, researchers were represented by Senior Research Scientist Dr. Jingsong Huang. He introduced research from the Optoeletronic Technologies Lab (OeTL) group led by Profs. Paul Stavrinou and Donal Bradley and gave participants a tour of OSCAR's world-class Optoelectronic Technologies Laboratory.

Prior to this, OSCAR had actively reached out to the public through its "OSCAR Thinking" branding series and has successfully organized over 20 themed events. Physical networking and interactive visits have not been possible in recent months. This Open Day, and planned future events, demonstrate OSCAR's commitment to engaging with local partners across allied sectors.

AI group visits specialist institutes in Nanjing

OSCAR's AI for Healthcare research team were recently invited by Nanjing University to visit the city for a day of academic and industrial networking. They were accompanied by Ms. Jian Lu, Senior Official at British Consulate-General Shanghai, together with OSCAR General Manager Leah He and Industrial Cooperation Manager Alex Yang.

During their trip, the OSCAR delegation visited the National Health and Medical Big Data Centre (Nanjing), the Yangtze Industrial and Economic Institute, the School of Artificial Intelligence, Nanjing University, the AI Research Institute in Nanjing AI Valley, and the Cambridge University-Nanjing Centre of Technology and Innovation. The trip is expected to enhance OSCAR's connections to academia in the region and open channels for academic cooperation and tech commercialization in clinical AI.

Chancellor of Nanjing University of Aeronautics and Astronautics visits OSCAR

A delegation led by Mr. Zhongde Shan, President of Nanjing University of Aeronautics and Astronautics and Academician of the Chinese Academy of Engineering, visited OSCAR on 14th August.

Mr. Shan and his colleagues were accompanied by Qingwen Wu, CPC Secretary of SIP, and Xiaoming, Vice-Chairman of the Administrative Committee of SIP. The visit laid the groundwork for cooperation between OSCAR and academic institutions in Nanjing, the capital and largest city of Jiangsu province.

SIP NEWS FOR AUGUST

Suzhou hosts Global AI Product & Application Expo 2020

Bringing over 1,000 AI products and innovative solutions, the **Global AI Product & Application Expo** (AI Expo 2020) was held in Suzhou International Expo Centre between 14th and 16th August.

A grand annual gathering for the global AI community, the first AI Expo was held in Suzhou two years ago. It is a large event covering a huge range of applicants for AI, including intelligent education, payment, security screening and data backup.

This year's expo offered a range of exhibitions, conferences, contests, professional forums and interactive AI performances. The event was attended by industry and academic representatives from the artificial intelligence field, including popular AI companies. It saw the debut of innovation platforms and several new product launches.

The 2020 Expo had 12 themed exhibition areas, including three new areas "Suzhou AI Innovative Experiment Exhibition", "Anti-COVID-19 Innovative Product Exhibition", "AI Popularization Exhibition" and "Creative Cultural Product Exhibition".

Celebrated scientists and guests delivered keynotes during the forum, including Gao Wen, Xu Yangsheng, and Li Lanjuan, members of the Chinese Academy of Engineering, and Sethu Vijayakumar, Professor of Robotics at the University of Edinburgh and Programme Co-Director for Artificial Intelligence at the Alan Turing Institute.

In addition, representatives from world-leading technology companies such as Huawei, Baidu, Alibaba Cloud, and Microsoft gave topical talks about facets and applications of AI including big data, cloud platforms, and intelligent internet.

https://mp.weixin.qq.com/s/yY3isEr8mF_gwhFUjkN3JQ