The University of Nottingham

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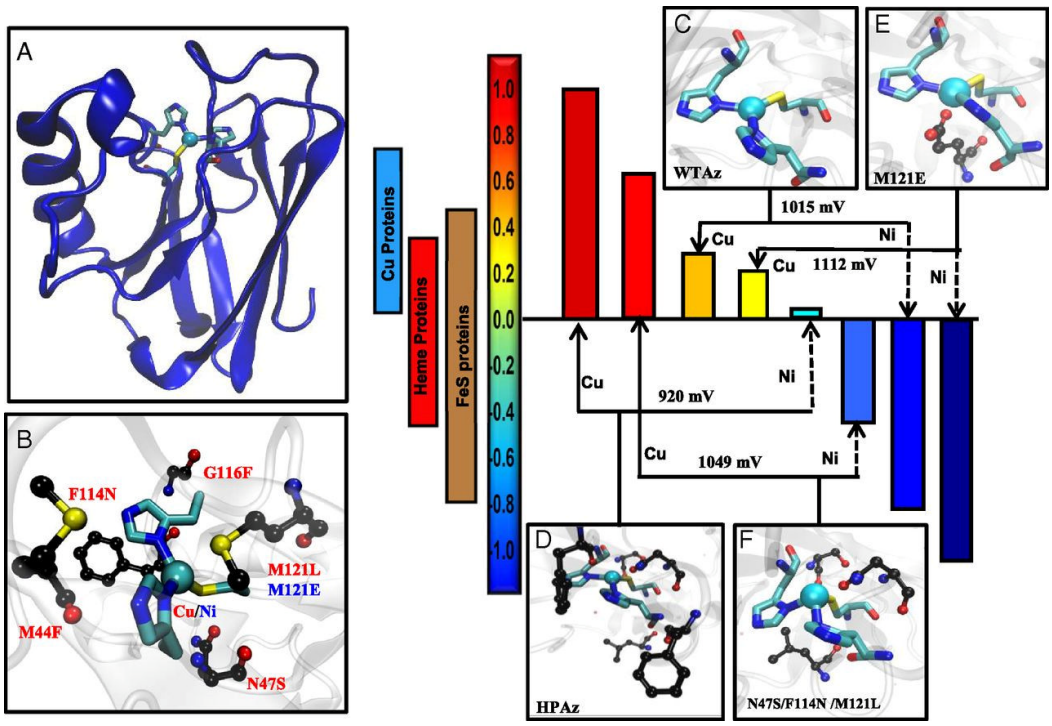
The School of Pharmacy Journal



November 2015-January 2016

Foreword

Welcome to our latest edition of the School of Pharmacy Journal, a quarterly collection of publications and press releases from November 2015 to January 2016.

As evident in this report the School at both UNUK and UNMC continues to produce many high quality research articles propelling the impact of our work on the health and wealth of society. The UNMC School has maintained a healthy research portfolio over 2015 with several successful grant capture and publications. There has also been an increase in postgraduate student numbers at UNMC. Five PhD students from UNMC graduated in February 2016 graduation ceremony. In Nottingham, we congratulated 52 students who graduated on December 10th, including the first cohort from the Masters in Drug Discovery and Pharmaceutical Sciences programme. The School was also pleased to see one of our Honorary Professors, David Needham, receive an honorary Doctor of Science degree during the ceremony.

Professor David Needham (left), Honorary Professor to the School, received an Honorary Doctor of Science Degree at the graduation ceremony in December. The oration was given by Phil Williams (right) and is copied below.

David came to Nottingham in 1972 to study for a degree in Chemistry at Trent Polytechnic. His colourful research career followed working in a pigment factory. David recounts of getting the blues, literally, and found himself looking for other opportunities. David replied to an advert for a "Graduate Student Demonstratorship" of Professor Daniel Eley F.R.S., head of Physical Chemistry here at Nottingham. David studied gas/solid catalysis maintaining the experiments each and every day for three years. Each month David wrote a report of progress and plans, which formed a growing pile at the side of Professor Eley's desk.

Towards the end of his time here David attended a talk at the Cancer Research Laboratories and decided that this is the area in which he would like to work. David was introduced to Professor Dennis Haydon F.R.S. in Cambridge, where he started the day after finishing at Nottingham. Whilst working in Cambridge David turned the 42 reports he had written for

Professor Eley into his PhD thesis. He submitted three copies; not in the normal loosely-bound state, but in velour-covered hard-bound books with gold embossed lettering. Such is his incredible attention to detail and scientific rigour David was awarded his PhD with not one correction required to his thesis.

David studied black lipid films and how other molecules interacted with them. A chance observation led David to develop a new technique using micropipettes. For David this was a relief; it permitted him to study these molecules and make important discoveries, and it meant that he didn't have to move to use equipment in Liverpool – something a Manchester United supporter would never willingly do.

It is testament to David's talents as a researcher and skills in presentation that in 1982 he was awarded the Oppenheimer Research Fellowship: David had been asked by Professor Haydon to go to a 'meeting' on his behalf. It was only afterwards when he was congratulated on being awarded a Fellowship that he realized this meeting was actually a presentation to and interview with the selection panel.

David's mastery of using micropipettes led him to be awarded a NATO/SERC Fellowship to work with Professor Evan Evans at the University of British Columbia. There, David studied the mechanics of liposomes using the techniques they pioneered. The combination of experimental skill, tenacious thirst for knowledge, and the Vancouver weather enabled David to make ground-breaking measurements of lipids across a wide-range of temperatures. His paper describing this work has been cited over 600 times.

Evan Evans wrote:

> *"David is a brilliant, intuitive scientist who runs to the lab and quickly assembles a simple experiment to reveal deep insights into the unknown complexity of whatever chemical concoction or colloidal soup that interests him! Moreover, he then senses the hidden opportunity to engineer some new advance in material science that aides human health and well being (e.g. from "sighting devices" to aid downtrodden dart throwers in a pub to nano-drug delivery systems to cure cancer patients)."*

David's first research talk, in 1986, was his successful interview for the position at Duke University in North Carolina. At Duke, David expanded his research into the temperature dependent biophysics of membranes, building collaborations in many areas of endeavour, doing this whilst teaching materials science, and in what free time there was, playing darts. David maintained the desire to treat cancer. In the early 1990s, through a meeting with a postdoctoral researcher (whilst playing darts) and crashing a Black Tie party held by the Duke Fund Raising Development Campaign David met Dr. Mark Dewhirst, a Radiation Oncologist.

Mark explained to David that neither current medicines nor hyperthermal treatment were working. David had the idea that if he could trap a drug in a liposome membrane below its solid-liquid phase transition, and then heat the tumour, then maybe the encapsulated drug would leak out faster into the tumour and kill the cancer. The "Low Temperature Sensitive Liposome" was realized. David's first two *Cancer Research* papers showing the enhanced anti-tumour effect of this formulation have been cited over 670 times.

Through a number of animal studies and clinical trials David's cancer drug delivery system was demonstrated to successfully inhibit tumour growth. The licensed formulation, "ThermoDox", is currently undergoing phase III clinical trials for liver cancer, and pre-clinical development is ongoing for RCW breast cancer, liver metastases, brain, pancreatic, and breast cancers.

Mark Dewhirst remarks:

> *"He has never taken a single piece of data at face value. He has always pushed to understand how an experiment was done – how to interpret results in light of his knowledge of biophysics. We were fortunate to have been able to license the technology. David has been tenacious in pushing the company to fulfill its obligations. David was the lone soldier doing battle. There is no doubt that his reluctance to accept defeat has contributed to their successes. We are still some years away from the results of the definitive trial for use of the drug with thermal ablation for primary liver cancer. But we are all very hopeful for a positive result."*

In 2013 David was awarded the 5-year Niels Bohr Visiting Professorship to the Southern University of Denmark where he continues to innovate cancer treatment. His work has been cited nearly 10,000 times. David accepted the invitation to help our research into new treatments and discovery of new biomaterials, and develop teaching in our courses. I haven't the time to describe the innovations in education that David has pioneered, nor the sports science technology he has developed for darts throwers. David's intuition, innovation and rigour in research, passion for education, and commitment to improve the health and wellbeing of society is something that we all look forward to benefitting from in the future.

Professor Phil Williams
Phil.Williams@nottingham.ac.uk
Director of Research
(Nottingham)

Professor Nashiru Billa
Nashiru.Billa@nottingham.edu.my
Associate Dean (Research)
(Malaysia)

Contents

Study of the effect of dipole interactions on hyperthermia heating the cluster composed of superparamagnetic nanoparticles

R. Fu, Y. Y. Yan and C. Roberts

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S. Van Nuffel, C. Parmenter, D. J. Scurr, N. A. Russell and M. Zelzer

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Phosphonium Polymethacrylates for Short Interfering RNA Delivery: Effect of Polymer and RNA Structural Parameters on Polyplex Assembly and Gene Knockdown

Vanessa Loczenski Rose, Saif Shubber, S. Sajeesh, Sebastian G. Spain, Sanyogitta Puri, Stephanie Allen, Dong-Ki Lee, G. Sebastiaan Winkler and Giuseppe Mantovani

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Christopher M. Humphreys, Samantha McLean, Sarah Schatschneider, Thomas Millat, Anne M. Henstra, Florence J. Annan, Ronja Breitkopf, Bart Pander, Pawel Piatek, Peter Rowe, Alexander T. Wichlacz, Craig Woods, Rupert Norman, Jochen Blom, Alexander Goesman, Charlie Hodgman, David Barrett, Neil R. Thomas, Klaus Winzer and Nigel P. Minton

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Erica L. Stone, Francesca Citossi, Rajinder Singh, Balvinder Kaur, Margaret Gaskell, Peter B. Farmer, Anne Monks, Curtis Hose, Malcolm F. G. Stevens, Chee-Onn Leong, Michael Stocks, Barrie Kellam, Maria Marlow and Tracey D. Bradshaw

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Claire Anderson, Susan Kirkpatrick, Damien Ridge, Renata Kokanovic and Claire Tanner
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Supporting adherence for people starting a new medication for a long-term condition through community pharmacies: a pragmatic randomised controlled trial of the New Medicine Service

Rachel Ann Elliott, Matthew J Boyd, Nde-Eshimuni Salema, James Davies, Nicholas Barber, Rajnikant Laxmishanker Mehta, Lukasz Tanajewski, Justin Waring, Asam Latif, Georgios Gkountouras, A J Avery, Antony Chuter and Christopher Craig
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ME Qazzaz, VJ Raja, K-H Lim, T-S Kam, JB Lee, P Gershkovich and TD Bradshaw.
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Alex Stephenson-Brown, Sue Yong, Muhammad H. Mansor, Zarrar Hussein, Nga-Chi Yip, Paula M. Mendes, John S. Fossey and Frankie J. Rawson
Chemical Communications (2015) 51, 17213-17216
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Hui Wen Ng, Stephen W. Doughty, Heng Luo, Hao Ye, Weigong Ge, Weida Tong and Huixiao Hong
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Weina Meng, Martin C Garnett, David A Walker and Terence L Parker
Experimental Biology and Medicine (2015) 0, 1-12
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Magdalena Montowska, Morgan R. Alexander, Gregory A. Tucker and David A. Barrett

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3D printing of tablets containing multiple drugs with defined release profiles

Shaban A. Khaled, Jonathan C. Burley, Morgan R. Alexander, Jing Yang and Clive J. Roberts

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Hollie Ryder, Trudi Aspden and Janie Sheridan

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3D printing of five-in-one dose combination polypill with defined immediate and sustained release profiles

Shaban A. Khaled, Jonathan C. Burley, Morgan R. Alexander, Jing Yang and Clive J. Roberts

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Thermoresponsive magnetic colloidal gels via surface-initiated polymerisation from functional microparticles

S. A. Braim, K. M. Shakesheff, B. R. Saunders and C. Alexander

Journal of Materials Chemistry B (2016) 4, 962-972

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Synthesis, Biological Evaluation, and Utility of Fluorescent Ligands Targeting the μ-Opioid Receptor

Luke S. Schembri, Leigh A. Stoddart, Stephen J. Briddon, Barrie Kellam⊥ Meritxell Canals, Bim Graham and Peter J. Scammells

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Shailesh N. Mistry, Manuela Jörg, Herman Lim, Natalie B. Vinh, Patrick M. Sexton, Ben Capuano, Arthur Christopoulos, J. Robert Lane and Peter J. Scammells

Journal of Medicinal Chemistry (2016) 59, 388-409

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The metabolic network of Clostridium acetobutylicum: Comparison of the approximate Bayesian computation via sequential Monte Carlo (ABC-SMC) and profile likelihood estimation (PLE) methods for determinability analysis

Graeme J. Thorn and John R. King

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Srinivasarao Ravipati, David R. Baldwin, Helen L. Barr, Andrew W. Fogarty and David A. Barrett

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DOI: 10.1007/s11306-015-0811-x

Enantiopure titanocene complexes – direct evidence for paraptosis in cancer cells

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Metallomics, available online

DOI: 10.1039/c5mt00297d

Receptor Crosslinking: A General Method to Trigger Internalization and Lysosomal Targeting of Therapeutic Receptor: Ligand Complexes

Paul R Moody, Edward J Sayers, Johannes P Magnusson, Cameron Alexander, Paola Borri, Peter Watson and Arwyn T Jones

Molecular Therapy (2015) 23, 1888-1898

DOI: 10.1038/mt.2015.178

Antibacterial alkaloids from Artabotrys crassifolius Hook.f. & Thomson

Tan, Kok Kwan; Khoo, Teng Jing; Rajagopal, Mogana and Wiart, Christophe

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A non-proteolytic role for ubiquitin in deadenylation of MHC-I mRNA by the RNA-binding E3-ligase MEX-3C

Florencia Cano, Radu Rapiteanu, G. Sebastiaan Winkler and Paul J. Lehner

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Direct visualisation of internalization of the adenosine A3 receptor and localization with arrestin3 using a fluorescent agonist

Leigh A. Stoddart , Andrea J. Vernall, Stephen J. Briddon, Barrie Kellam and Stephen J. Hill

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DOI: 10.1016/j.neuropharm.2015.04.013

Fistulopsines A and B antiproliferative septicine-type alkaloids from Ficus fistulosa

Veronica Alicia Yap, Mohannad E. Qazzaz, Vijay J. Raja, Tracey D. Bradshaw, Hwei-San Loh, Kae-Shin Sim, Kien-Thai Yong, Yun-Yee Low and Kuan-Hon Lim

Phytochemistry Letters (2016) 15, 136-141

DOI: 10.1016/j.phytol.2015.12.007

In Vivo Assessment of Bone Regeneration in Alginate/Bone ECM Hydrogels with Incorporated Skeletal Stem Cells and Single Growth Factors

David Gothard, Emma L. Smith, Janos M. Kanczler, Cameron R. Black, Julia A. Wells, Carol A. Roberts, Lisa J. White, Omar Qutachi, Heather Peto, Hassan Rashidi, Luis Rojo, Molly M. Stevens, Alicia J. El Haj, Felicity R.A.J. Rose, Kevin M. Shakesheff and Richard O.C. Oreffo

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DOI: 10.1371/journal.pone.0145080

Economic Evaluation of a General Hospital Unit for Older People with Delirium and Dementia (TEAM Randomised Controlled Trial)

Lukasz Tanajewski, Matthew Franklin, Georgios Gkountouras, Vladislav Berdunov, Rowan H. Harwood, Sarah E. Goldberg, Lucy E. Bradshaw, John R.F. Gladman and Rachel A. Elliott

PLOS One (2015) Available online

DOI: 10.1371/journal.pone.0140662

Highly efficient delivery of functional cargoes by the synergistic effect of GAG binding motifs and cell-penetrating peptides

James E. Dixon, Gizem Osman, Gavin E. Morris, Hareklea Markides, Michael Rotherham, Zahia Bayoussef, Alicia J. El Haj, Chris Denning and Kevin M. Shakesheff

PNAS (2015) 113, E291-E299

DOI: 10.1073/pnas.1518634113

Design of a Single Protein that Spans the Entire 2V Range of Physiological Redox Potentials

P. Hosseinzadeh, N. M. Marshall, K. N. Chacón, Y. Yu, M. J. Nilges, S. Y. New, N. J. Blackburn, Y. Lu

PNAS (2016) 113, 262-267

DOI: 10.1073/pnas.1515897112

Synthesis of ^{19}F nucleic acid–polymer conjugates as real-time MRI probes of biorecognition

Giovanna Sicilia, Adrienne L. Davis, Sebastian G. Spain, Johannes P. Magnusson, Nathan R. B. Boase, Kristofer J. Thurecht and Cameron Alexander

Polymer Chemistry (2016) Available online

DOI: 10.1039/c5py01883h

Investigating NF-κB signaling in lung fibroblasts in 2D and 3D culture systems

Su Su Htwe, Helen Harrington, Alan Knox, Felicity Rose, Jonathan Aylott, John W. Haycock and Amir M Ghaemmaghami

Respiratory Research (2015) 16, 144

DOI: 10.1186/s12931-015-0302-7

Pastoral power in the community pharmacy: A Foucauldian analysis of services to promote patient adherence to new medicine use

Justin Waring, Asam Latif, Matthew Boyd, Nick Barber and Rachel Elliott

Social Science & Medicine (2016) 148, 123-130

DOI: 10.1016/j.socscimed.2015.11.049

- **Reviews**

Use of Humanized Rat Basophilic Leukemia Reporter Cell Lines as a Diagnostic Tool for Detection of Allergen-Specific IgE in Allergic Patients: Time for a Reappraisal?

Franco H. Falcone, Marcos J. C. Alcocer, Yoshimi Okamoto-Uchida and Ryosuke Nakamura
Current Allergy Asthma Reports (2015) 15, 67
DOI: 10.1007/s11882-015-0568-3

Dental pulp stem cells: function, isolation and applications in regenerative medicine

Marco Tatullo, Massimo Marrelli, Kevin M. Shakesheff and Lisa J. White
Journal of Tissue Engineering and Regenerative Medicine (2015), 9, 1205-1216
DOI: 10.1002/term.1899

Staff Research News

- Professor Cameron Alexander has been invited to give talks at the following international meetings:
    - "Polymers for Bacterial Binding and Quorum Sensing Interference" – Nanomaterials as Antibiotics Symposium, French Embassy, London, 30 November-01 December 2015.
    - "Information-coded and responsive polymers for therapeutic detection and delivery" – International Conference on Nanoscience and Nanotechnology (ICONN) 2016, Canberra, Australia, 7-11 February 2016.

- Professor Nashiru Billa has been:
    - Appointed as an external examiner for the International Medical University BPharm Programme, 2015-2017
    - Invited to attend a planning/implementation workshop on research management and governance for the Ungku Omar Funding Program, organised by the Ministry of Science Technology and Innovation, Malaysia (MOSTI).

- Dr Matthew Boyd has been:
    - Asked to be an advisor to the General Pharmaceutical Council for the 2015 Student Fitness to Practise Review
    - Asked to be an external academic panel member for the University of Huddersfield's Revalidation/Subject Review Event for Pharmacy
    - Appointed as an Associate of the University of Nottingham's Peer Observation College.

- Dr Franco Falcone has been:
    - Invited to give a seminar at the Institute of Food Research in Norwich in January 2016.
    - Invited to give a seminar at the School of Pharmacy, University of East Anglia in March 2016
    - Appointed as External Examiner for the Medway School of Pharmacy, University of Kent
    - Asked to act as External PhD examiner for Anna University, Chennai, India
    - Selected as a peer reviewer for the French CNRS and Inserm.

- Invited as a peer reviewer by the Shota Rustabeli National Science Foundation, Georgia

- Professor Clive Roberts gave the following invited talks:
  - "3D Printing as a practical manufacturing method of pharmaceuticals" at the BPSA Science into Practice Conference, Nottingham, 21 November 2015
  - "3D Printing as a practical manufacturing method of pharmaceuticals" at the MediLink 3D Printing and Additive Manufacturing in Healthcare Conference held at the National College for Teaching & Leadership, Nottingham on 2 December 2015.
  - "3D printing a functional polypil: a practical manufacturing method?" at the 3D Medicine Printing Conference, Maastricht, the Netherlands on 27 January 2016.

- Dr Jing Yang has been:
  - Appointed an editorial member of a new journal called "Journal of 3D Printing in Medicine". The journal is published by Future Medicines Group and the Editor in Chief is Professor Dietmar Hutmacher, a renowned academic in tissue engineering and regenerative medicine. Dr Yang published an editorial piece in the first issue.
  - Invited to give a talk in March 2016 on 3D bioprinting at the Advanced Manufacturing and Functional Materials meeting organised by the Institution of Engineering and Technology.

Grants/Studentships Awarded

- Alliance Boots are funding a 3-year studentship on future models of care with Professor Claire Anderson.

- Dr Weng Chan has been awarded a University of Nottingham Hermes Fellowship "Proof of concept study using bromagyrin for the treatment of *C. difficile* infection.

- Dr Franco Falcone has been awarded a 3-year PhD studentship from the Rosetrees Trust.

- Dr Felicity Rose will be collaborating with Locate Therapeutics on an Innovate UK funded proof-of-concept grant on a new cell therapy.

Student News

- The School would like to congratulate the following students who graduated in December 2015:

  - **PhD**
    Mr Salah Mohammed Ahmed Abdelrazig
    Mrs Leigh-Anne Brace
    Miss Victoria Capel
    Miss Sivaneswary Genapathy
    Miss Alexandra Hughes
    Mr Yindong Liu
    Mr Vijay Raja
    Mr Charles Snart
    Mr Francesco Tres
    Miss Wahyu Utami

  - **MRes**
    Mr Navjot Singh

  - **MSc**
    Mr Alsulami Ali
    Mrs Bara M Ahmed D
    Mr Ramy El Masri
    Mr Kenneth Jackson
    Mr Suman Khan
    Miss Ruiling Liu
    Mr Stefan Milutinovic
    Miss Namrita Modgill
    Mr Shadrack Mutuku
    Mr Sean Saldanha
    Mr Oliver Sandy-Hindmarch
    Miss Ilda Qistina Sethw Hassan
    Miss Anna Sipitanou
    Ms Pragya Mehrotra
    Mr Abdullah Bader A Alreshaidan
    Miss Yogavalli Poobalan

- Congratulations to CDT PhD students Claire Lewis, Rosa Catania, Monica Mistry, Georgina Marsh and Gudrun Fridgeirsdottir who won the 20th national Biotechnology Yes competition. For more information please see the School's news website.

- The School extends a big welcome to the first students on our joint UK-China Pharmacy course. The students, who are currently studying at Tianjin University of Traditional Chinese Medicine (TUTCM), will join us in Nottingham in 2017 for two years as part of the joint 5 year course between Nottingham and TUTCM. For more information please see the School's news website.

General News

- The School's Research Groups in Malaysia were recently:
    - Drug Delivery
        - Division Lead – Assistant Professor Dr Siu Yee New
        - Members – Professor Andrew Morris, Professor Nashiru Billa and Dr Wai Hau Tung
    - Drug Discovery
        - Division Lead – Associate Professor Chee Mun Fang
        - Members – Professor Stephen Doughty, Associate Professor Dr Teng Jin Khoo, Associate Professor Dr Christophe Wiart, Associate Professor Dr Kuan Hom Lim, Assistant Professor Dr Siu Yee New, Assistant Professor Dr Abigail Emtage
    - Social Pharmacy
        - Division Lead – Associate Professor Dr Bee Yean Low
        - Members – Associate Professor Mr Kok Thong Wong, Assistant Professor Dr Sharmini Balashanker, Assistant Professor Dr Abigail Emtage, Assistant Professor Dr Jim Chai

- Professor Clive Roberts, Head of School, recent celebrated 25 years of working in the School of Pharmacy at the University's Long Service Awards hosted by the Vice Chancellor, Professor Sir David Greenaway. Congratulations Clive!

Highlighted Papers

- **A General Method to Trigger Internalisation and Lysosomal Targeting of Therapeutic Receptor:Ligand Complexes**
  Paul R Moody, Edward J Sayers, Johannes P Magnusson, Cameron Alexander, Paola Borri, Peter Watson and Arwyn T Jones
  Molecular Therapy (2015) 23, 1888-1898
  DOI: 10.1038/mt.2015.178

  This paper, from work funded under EPSRC Grant EP/J021180/1, was featured on the front cover of Molecular Therapy, on the British Society of Nanomedicine homepage (http://www.britishsocietynanomedicine.org/) and was selected for a commentary by the journal (Receptor Crosslinking in Drug Delivery: Detour to the Lysosome? Manfred Ogris and Haider Sami. Mol Ther 23: 1802-1804; *DOI: 10.1038/mt.2015.207*).

- ***Cell and protein compatible 3D bioprinting of mechanically strong constructs for bone repair***
  M J Sawkins, P Mistry, B N Brown, KMShakesheff, L J Bonassar and J Yang
  Biofabrication (2015) 7, 035004
  DOI: 10.1088/1758-5090/7/3/035004

  This paper has been selected as one of the ten highlighted papers in 2015 by Biofabrication. In this paper the authors have developed a unique way of 3D printing strong scaffolds at cell-compatible conditions.

- ***3D printing of five-in-one dose combination polypill with defined immediate and sustained release profiles***
  Shaban A. Khaled, Jonathan C. Burley, Morgan R. Alexander, Jing Yang and Clive J. Roberts
  Journal of Controlled Release (2015) 217, 308-314
  DOI: 10.1016/j.jconrel.2015.09.028

  

  This paper made the front cover of the Journal of Controlled Release and featured in the Editorial
  DOI: 10.1016/j.jconrel.2015.10.014

- ***Electronic communication of cells with a surface mediated by boronic acid saccharide interactions***

  Alex Stephenson-Brown, Sue Yong, Muhammad H. Mansor, Zarrar Hussein, Nga-Chi Yip, Paula M. Mendes, John S. Fossey and Frankie J. Rawson

  Chemical Communications (2015) 51, 17213-17216

  DOI: 10.1039/c5cc04311e

  This journal was featured on the front cover of the Chemical Communications journal. Some of the data for the paper was generated by two 3rd year MPharm students who did a summer placement in Dr Frankie Rawson's group and are included as authors on the paper.