Foreword

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

Caterpillar fungus could hold the key to relieving the pain of osteoarthritis

Dr Cornelia de Moor and her team have a three-year grant of £260,000 from Arthritis Research UK to investigate cordycepin as a new type of drug that has potential to relieve the symptoms of osteoarthritis, a common joint condition that affects more than eight million people in the UK. They will test the effectiveness of the compound, given as food pellets to rats and mice, to find out if cordycepin can prevent pain occurring after an injury to a joint, and also whether it relieves existing pain. Dr de Moor said that although their research was in its early stages they were excited about cordycepin’s prospects as a completely new type of painkiller. “When we first started investigating this compound it was frankly a bit of a long-shot and there was much scepticism from the scientific community,” she said. “But we were stunned by the response from the pilot study, which showed that it was as effective as conventional painkillers in rats."To the best of our knowledge, cordycepin has never been tested as a lead compound for osteoarthritis pain." “This study is the first step in a potential drug development for a new class of drugs for osteoarthritis, although there are a number of hurdles we have to go through – necessarily so – before it gets nearer patients. To the best of our knowledge, cordycepin has never been tested as a lead compound for osteoarthritis pain.”Dr de Moor said that provided the safety and effectiveness of the compound could be proven, clinical trials could begin within six to ten years. This research has also featured on BBC local television.

Youtube video of EPSRC Rise leader Kevin Shakesheff on tissue engineering

RISE Leader Professor Kevin Shakesheff, Nottingham University and Rising Star Dr Marianne Ellis, University of Bath meet with Professor Jeremy Farrar, Director Wellcome Trust.

https://www.youtube.com/watch?v=gGTrxDMc0Ww

Kevin Shakesheff's tissue engineering group also published a paper in Nature family journal Scientific Reports (2015) 5, 8577. This shows the ability to build and manipulate multicellular microscopic structures will facilitate a more detailed understanding of cellular function in fields such as developmental and stem cell biology. A holographic optical tweezers based technology accurately generates bespoke cellular micro-architectures.

A second paper in Advanced Materials describes a dual thermo-responsive and magnetic colloidal gel matrix for enhanced stem-cell culture (Advanced Materials (2015) 27, 662-558)
Nature Structural and Molecular Biology publication in RNA biology.

Catherine Jopling has published an exciting study of micro-RNAs in the journal Nature structural and Molecular Biology (22, 319–327 (2015)) showing the mechanisms of how they contribute to the regulation of genes. This project was a collaboration with the group of Nick Proudfoot at Oxford University.

The Guardian

There is a new article in The Guardian 04/02/2015 which highlights a study which was published by Rachel Elliott in the Pharmaceutical Journal. This article showed that pharmacist intervention via the New Medicine Service (NMS) increases patient adherence in new medications by around 10%. Such awareness would lead to new approaches in compliance

Structural Biology of the protease coagulation Factor XII resolved

The original model of the waterfall coagulation cascade describing how proteases regulate blood coagulation was published in 1964. Crystal structures have been important for understanding the molecular mechanisms underlying blood coagulation and to date crystal structures are available for all the coagulation protases except for factor XII (FXII) which lies at the top as initiator of the intrinsic pathway.

There has been a resurgence of interest in the FXII protease of late as knockout studies in mice reveals it is essential for formation of pathological thrombi is mouse mouse systems of cardiovascular disease and stroke. In addition there is a broad interest in FXII as it is involved not only in blood coagulation but also innate immunity and blood pressure regulation. In humans it has been shown to cause hereditary angiodema and has been linked to cardiovascular disease and alzheimers. FXII is clinically significant since over 200 million activated partial thromboplastin times (APTT), a routine screening test for bleeding disorders, are performed annually in United States requires its presence to be normal. Despite all this interest there was no structure for the FXII protease domain which is critical to observe the shape of the active site and understand mechanisms of zymogen activation, substrate recognition and inhibitor binding. For the first time the Emsley group at the University of Nottingham presents two crystal structures defining a zymogenic form of the FXII protease domain. This data describes the unique structural features of this important coagulation factor and provides a scaffold to develop novel anti-coagulants with a reduced bleeding side effect. (J. Thromb. Haemost. (2015) 13, 580-591)
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Allergy (2015) 70, 1-5  DOI: 10.1111/all.12517

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Dragos Lostun, Consuelo J. Perez, Peter Licence, David A. Barrett and Demian R. Ifa

Analytical Chemistry (2015) 87, 3286-3293  DOI: 10.1021/ac5042445

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**The malignant phenotype in breast cancer is driven by eIF4A1-mediated changes in the translational landscape**

A Modelska, E Turro, R Russell, J Beaton, T Sbarrato, K Spriggs, J Miller, S Gräf, E Provenzano, F Blows, P Pharoah, C Caldas and J Le Quesne

Cell Death and Disease (2015) 6, e1603  DOI: 10.1038/cddis.2014.542

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Maria Marlow, Mohammed Al-Ameedee, Thomas Smith, Simon Wheeler and Michael J. Stocks

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Colloids and Surfaces B: Biointerfaces (2015) 126, 169–177
DOI: 10.1016/j.colsurfb.2014.12.020

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DNA Repair (2015) 25, 104-115  DOI: 10.1016/j.dnarep.2014.10.009

**Characterisation of human saliva as a platform for oral dissolution medium development**
Sally Gittings, Neil Turnbull, Brian Henry, Clive J. Roberts and Pavel Gershkovich
DOI: 10.1016/j.ejpb.2015.01.007

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European Journal of Pharmaceutics and Biopharmaceuticals (2015)90, 22-29
DOI: 10.1016/j.ejpb.2014.11.009

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Magdalena Montowska, Morgan R. Alexander, Gregory A. Tucker and David A. Barrett

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Biomaterial modification of urinary catheters with antimicrobials to give long-term broadspectrum antibiofilm activity
Journal of Controlled Release (2015) 202, 57-64  DOI:10.1016/j.jconrel.2015.01.037

In vivo evaluation of different formulation strategies for sustained release injectables of a poorly soluble HIV protease inhibitor
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Journal of Immunological Methods (2015) 420, 50-55 DOI: 10.1016/j.jim.2015.03.005

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Microprocessor mediates transcriptional termination in genes encoding long noncoding microRNAs
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Nature Structural & Molecular Biology (2015) 22, 319-327  DOI:10.1038/nsmb.2982

Combination of (M)DSC and Surface Analysis to Study the Phase Behaviour and Drug Distribution of Ternary Solid Dispersions
Joke Meeus, David J. Scurr, Xinyong Chen, Katie Amssoms, Martyn C. Davies, Clive J. Roberts and Guy Van den Mooter
Pharm Res (2015) 32, 1407-1416  DOI: 10.1007/s11095-014-1543-8

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PLOS One (2015) 10, 30121653  DOI:10.1371/journal.pone.0121653

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Research in Social and Administrative Pharmacy (2015) 11, 216-227
DOI: 10.1016/j.sapharm.2014.06.005

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Scientific Reports (2015) 5, 8577  DOI: 10.1038/srep08577

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Staff Research News

- In the University Staff Oscars Professor Barrie Kellam won the ‘Personal Tutors: All Rounder’ category and Mr Gautam Paul was runner up in the ‘University Life: Prepare for the Future’ category and was also nominated for the ‘Teaching: Most Inspiring’ category.

- Professor Morgan Alexander has been invited to give a talk at the 16th European Conference on Applications of Surface and Interface Analysis, Granada, Spain.

- Dr Frankie Rawson has been invited to be a member of the Royal Society of Chemistry’s Analytical Bioscience Interest Group Committee.

- Dr Kok Thong Wong is a member of the Organising Committee for the 12th Malaysian Pharmaceutical Society Scientific Conference 2015.
Grant/Studentships Awarded

- **Dr Matthew Boyd** has been awarded £25k from the Nottingham City CCG Research Capability Fund “Pump priming funding to enable RfPB application workup”. The project is a collaboration with Professor AJ Avery, B Roe and L Hyland.

- **Professor Barrie Kellam** has been awarded a British Council Newton Fund for £144k and is also part of another Newton Fund award with Professor Steve Hill (School of Life Sciences, UoN).

- **Dr Beppe Mantovani** has been awarded a grant of £573k from the Medical Research Council for a project entitled “Targeting glycans for the treatment of ischemia-reperfusion injury”. The project is a collaboration with Luisa Martinez-Pomares (Faculty of Medicine & Health Sciences, UoN) and Alan Salama (Faculty of Medical Sciences, UCL).

- **Professor David Pritchard** has been awarded an NIH Clinical Trial Planning grant for $20k for hookworm production.

- **Professor Clive Roberts** has been awarded a Wellcome Trust Pathfinder grant for £102k for a project entitled “Nanoparticles for safer and efficient delivery of radionuclides for cancer diagnosis and therapy”.

Student News

- Yamina Boukari, a PhD student principally supervised by Professor Nashiru Billa, won the UNMC Research Showcase 2015 with her poster "Repair bones with one price of a needle". The competition was an opportunity for research students within UNMC to present their work in an easy to understand manner with appeal to the general public. The final round constituted the top 6 competitors from UNMC presenting to a panel of judges at the UK Graduate School via a video conference.

- Naim Hage, a PhD student principally supervised by Dr Franco Falcone, has been selected to receive a Postgraduate Prize for 2014/15 in recognition of his outstanding research progress and contribution to the postgraduate community. The Andrew Hendry Postgraduate Scholarship was founded in 1968 from subscriptions raised in memory of the late Mr Andrew Hendry, Bursar of the University, 1948-66. A small official ceremony was held on May 13th 2015.
Highlighted Papers

- **Label free imaging of drugs in cells with Time of Flight Secondary Ion Mass Spectrometry (ToF SIMS).**
  With colleagues in NPL and GSK, Nottingham PhD student Carla Newman has demonstrated for the first time three-dimensional secondary ion mass spectrometry (SIMS) images of the cellular uptake of the phospholipidosis inducing pharmaceutical compound, amiodarone in an article recently accepted for publication in the Journal of the American Chemical Society. Images from this work won the GSK **Global Beautiful Biology Award** for Carla Newman, Peter Marshall and Andrew West.

  *Single-cell Analysis: Visualizing Pharmaceutical Compounds in Cells with Label-free 3D Mass Spectrometry Imaging*

- **A novel polymer for cell manufacture**
  James Smith (Centre for Biomolecular Sciences) and Adam Celiz (currently at Wyss Institute, Harvard) jointly first authored a paper recently accepted for publication in Advanced Materials which is a major collaboration with colleagues from the Wolfson Centre for Stem Cells (CBS), MIT, CSIRO Manufacturing Flagship (Melbourne), Cardiff School of Biosciences and the MRC Centre for Regenerative Medicine (Edinburgh). This EPSRC funded work produced a new polymer which is attracting interest from the regenerative medicine industry for expansion and manufacture of cells from human pluripotent stem cell lines which can be used off the shelf, without the need to use pre adsorption of proteins.

  *Discovery of a novel polymer for human pluripotent stem cell expansion and multi-lineage differentiation*

- **Chain length affects pancreatic lipase activity and the extent and pH-time profile of triglyceride lipolysis**
  Paloma Benito-Gallo, Alessandro Franceschetto, Jonathan CM Wong, Maria Marlow, Vanessa Zann, Peter Scholes, and Pavel Gershkovich
The above article has been recently accepted for publication in Eur J Pharm Biopharm (IF 4.245), with Dr Gershkovich as a last and corresponding author, and is currently in press. The article describes an optimization of in vitro lipolysis model in order to assess a wider range of lipid-based formulations with diverse chain lengths of lipids. The in vitro lipolysis model is used to rank-order the performance of oral lipid-based drug delivery systems in fast and efficient manner without using laboratory animals for assessment. The model is currently established in a very few other laboratories in the world. Dr Gershkovich has previously established the lipolysis model in the University of British Columbia, and published in the past 3 research articles using that model (as first and corresponding, or as second author): Gershkovich et al., J Pharm Sci. 2012 Jan;101291-300; Ibrahim et al., Eur J Pharm Sci. 2012 Aug 15;46:323-8; Zhao et al., Int J Pharm. 2012 Oct 15;436:707-10. These works are recent, but have been already cited, in total, 19 times.

However, this new article in Eur J Pharm Biopharm demonstrates recognition of a significant optimization and improvement of the in vitro lipolysis model that has been achieved as a result of establishment of the model in the Dr Gershkovich’s laboratory in the University of Nottingham.