Dr Simon Kolstoe appointed as Senior Research Fellow

Dr Simon Kolstoe has been recruited as Senior Fellow in Structural Biology, with a remit to apply structural biology methods to biomedical problems. Simon joins us from Prof. Steve Wood's group at The Royal Free Hospital (University College, London), where he worked on the structural and molecular basis of amyloidosis and related diseases.

Personnel

Two PhD students have left IBBS for postdoctoral jobs in top Institutes. Emily Newman has moved to the European Molecular Biology Laboratory (EMBL) in Grenoble (in the lab of Dr Daniel Panne). Neil Ball has moved to the National Institute for Medical Research (NIMR, Mill Hill) in the lab of Dr Ian Taylor.

Ms Valeria Runfola and Mr Manfredi Ponente are returning to Sicily after completion of their RA contracts. Valeria will be returning in the new year to start a new contract, again in the Biomolecular Structure division and under the supervision Dr Garry Scarlett.

Dr Steve Prior is leaving to join Professor Steve van Doren's NMR group at the University of Missouri in January 2012.

Francesca Pieropan has joined Professor Arthur Butt's group to work on a collaborative project with Drs Paul Cox, Asmita Sautreau and Roz Gibbs on novel effects of flavonoids **funded by a small grant from IBBS.**

Conferences

- **Dr Steve Prior** was invited speaker at the 2011 Gordon Research Conference on Matrix Metalloproteinases at Bryant University, Rhode Island, USA.
- **Professor Arthur Butt** was invited speaker at the 2011 Euroglia Conference in Prague, Czech Republic
- **Louise Butt** was awarded the prize for the best poster presentation at the 2011 South West Structural Biology Consortium (SWSBC) meeting in Reading.

Roads to Impact

- **Swarm Intelligence NMR technology** was applied to protein structure determination of pharmaceutically-relevant targets in two collaborations with colleagues at Pfizer, Sandwich.
- **Nebulisation of intravenous (IV) drugs for the treatment of Cystic Fibrosis in children,** by Marisa van der Merwe and colleagues was highlighted as one of Impact Posters presented at the recent UoP Research Day.

Recent Publications

Arnold LH, Butt LE, Prior SH, Read CM, Fields GB & Pickford AR (2012) The interface between catalytic and hemopexin domains in matrix metalloproteinase-1 conceals a collagen binding exosite. J BiolChem (in press).

Butt AM (2011). ATP: a ubiquitous gliotransmitter integrating neuron-glial networks. Seminars in Cell and Developmental Biology 22:205-213.

McGeehan,JE, Ball NJ, Streeter SD, Thresh SJ, Kneale GG. (2011) Recognition of dual symmetry by the Controller protein C.Esp1396I based on the structure of the transcriptional activation complex Nucleic Acids Research. (in press) Available on-line :doi: 10.1093/nar/gkr1250

Kennaway C, Taylor JE, Song C, Potrzebowski W, Nicholson W, White J, Swiderska A, Obarska-Kosinska A, Callow P, Cooper L, Roberts G, Artero J-B, Bujnicki J, Trinick J, Kneale G, Dryden D (2011) Structure and operation of the DNA-translocating Type I DNA restriction enzymes. Genes and Development (in press)

MacGregor HJ, Kato Y, Marshall LJ, Nevell TG, Shute JK. A copper-hydrogen peroxide redox system induces dityrosine cross-links and chemokine oligomerisation. Cytokine. 2011 Dec;56(3):669-75.

Message from the Editor

IBBS is one of the most successful research groupings in the University of Portsmouth, with recognised international excellence in each of our research divisions. The aim of the *IBBS Newsletter* is to provide a vehicle for communicating our achievements and increasing the exchange of information between our research divisions. In this first issue, I have tried to highlight some of our recent accomplishments, based on the information you kindly provided. I apologise if I have omitted something important. Please keep me up-to-date with your research activities so that I can include them in the May issue.

Thanks Arthur

IBBS
University of Portsmouth

ISSUE 01
January 2012

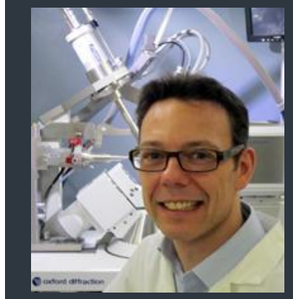
NEWSLETTER

IBBS

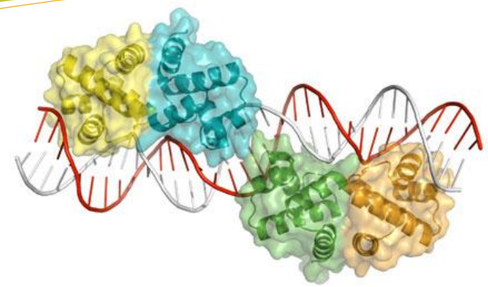
Institute of Biomedical and Biomolecular Science

University of Portsmouth

Dr John McGeehan appointed Reader



John first joined Professor Geoff Kneales' Biomolecular Structure group in 2000, before leaving for a Postdoctoral Fellowship in 2005 with the European Molecular Biology Laboratory, Grenoble, France. John led the implementation of a new instrument at the world-leading European Synchrotron Radiation Facility, before returning to IBBS in 2007 to take up a prestigious RCUK Senior Research Fellowship. John now runs the new X-ray crystallography facility that complements many of the techniques available within the Biomolecular Structure Group in IBBS. John is involved in a number of projects including a new exciting project in collaboration with Dr Rhiannon Lloyd on the 'Structural analysis of mitochondrial-encoded proteins in human disease'.



this issue

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Dr Tony Lewis awarded major BBSRC grant

Tony Lewis has been awarded a BBSRC New Investigator Award which will begin Spring 2012. The award for over £400,000 is to understand the biophysics, regulation, and physiology of the fungal ion channel TOK1 - a potential anti-fungal therapeutic target.

Opportunistic fungal pathogens are a major cause of life-threatening infections in individuals with a compromised immune system, including HIV/AIDS patients and those receiving chemotherapy. Classical anti-fungal therapies are complicated by biological similarities between fungi and humans, and resistance to traditional interventions such as fluconazole is a growing problem. So the need for fungal specific antifungal targets is a priority.

TOK1 channels are **only** found in fungi and no similar protein exists in humans, animals or plants, making them ideal anti-fungal targets. Tony proposes that TOK1 channels control the growth and function of fungal cells by managing the movement of potassium ions in and out of the cell. Therefore, drugs which induce unregulated ion flow would lead to fungal cell death. With this in mind, Tony's research aims to determine how these channels work.

Data from Tony's research will allow the design of compounds specifically targeting TOK1 channels, providing a unique strategy for combating fungal infections in humans.

TOK1 are also expressed in fungi that infect plants. Tony hopes his research will ultimately impact on strategies for managing agricultural fungal pathogens, which are responsible for significant agricultural and economic losses worldwide. With this in mind, Tony has recently set up a collaboration with the world's largest agrochemical company, Syngenta, to begin to develop TOK1 targeted fungicides for agricultural use.

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Nebulisation of intravenous drugs for the treatment of Cystic Fibrosis

Dr Marisa van der Merwe has established a successful collaboration with Drs Amanda Bevan and Gary Connett of University Hospital Southampton NHS Foundation Trust. A grant from the Charlotte Francis May Foundation allowed Marisa to investigate the nebulisation profiles of intravenous drugs used in the treatment of Cystic fibrosis (CF). **Marisa's work was highlighted as one of the Impact Posters presented at the 2012 UoP Research Day.**

Most CF patients die as a result of lung disease, caused by infection and inflammation. More clinicians are administering drugs by nebulisation in order to increase the local concentration in the lung and drug efficacy. This requires a device that provides suitable particle sizes (between 1 and 5 μm) for effective delivery to the small airways, to achieve therapeutic concentrations.

Marisa's group have shown that the Pari eFlow Rapid® nebuliser produces more effective nebulisation of a number of intravenous drugs used to treat CF, however not for unfractionated heparin. The group is now focusing on other heparin formulations to determine the most effective treatment for CF and the most effective nebulisation system.

Improving links with the NHS in Portsmouth

Professor Arthur Butt (Director of IBBS) has begun to work closely with **Professor Anoop Chauhan** (Research Director of the Portsmouth NHS Trust) to improve research links between IBBS and the NHS in Portsmouth and build on existing successful research collaborations.

Alan Thorne (ADR, Science) is supervising a new MD student with **Professor Amjad Parvais (QAH)**, to assess the value of Sentinel Lymph Node in predicting prognosis of Colorectal Cancer.

James Brown has been working closely with **Consultant Professor Pradeep Bhandari (QAH).** Pradeep was recently on South Today describing their innovative discovery that vinegar to help diagnose Barrett's oesophagus. As part of this ongoing project, Dr Gaius Longcroft-Wheaton received his MD in November 2011 for "Novel endoscopic techniques in early gastrointestinal neoplasia', while Dr Peter Basford started a project in October 2011 investigating 'Advanced endoscopic imaging in the gastrointestinal tract: improving the view of neoplasia.'

In other collaborations involving Pradeep and James, **Jerome Swinny** is investigating 'GABA-A receptors as novel therapeutic targets for irritable bowel syndrome', In addition, with Dr Vitaly Zinkevitch and Professor Arthur Butt, they are investigating 'Bacterial flora and IBD' and 'Bacteria:glial cell interactions'.

Dr Tim Trebble (Consultant Gastroenterologist, QAH) collaborates with **James Brown** and **Jan Shute** on a range of projects on inflammatory diseases of the GI tract. They are co-supervising the PhD studies of Dr Dan Pearl, who has now completed his laboratory-based studies on 'The relationship between mucosal n-3 PUFA bioavailability, inflammatory response and disease course in patients with active distal colitis.' **An IBBS pump-priming grant** supported the initial developmental stages of this very successful project. Dan has presented his findings at a number of National and International conferences and won 'Best Presentation' at the Regional 'Gut Club'.

IBBS laboratories provide research facilities and expertise for MD and PhD students from the Portsmouth Hospitals Trusts

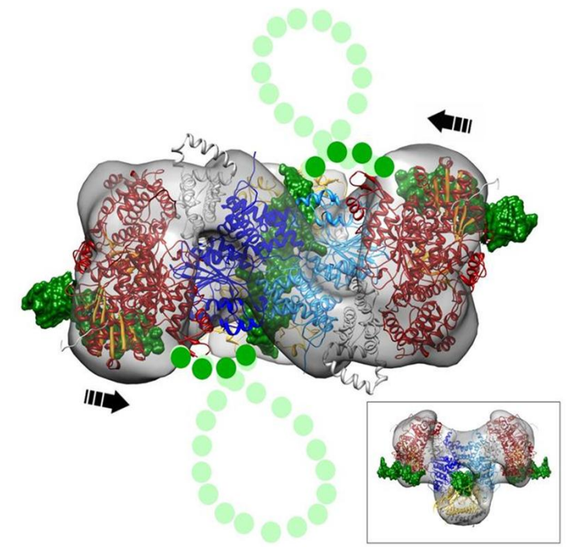
David Laight (IBBS) and **Professor Mike Cummings (Academic Unit of Diabetes & Endocrinology, QAH)** jointly supervise a number of MD students. In October 2011, Dr Marc Atkin was awarded his MD for a study on 'The effects of garlic upon endothelial function, vascular inflammation, oxidative stress and insulin resistance in patients with type 2 diabetes at high cardiovascular risk'. His findings showed that treatment with garlic extract does not improve endothelial function and were presented at UK Diabetes Conferences.

On-going projects in David's lab include those of Dr Georgina Page (Thiamine deficiency in diabetes mellitus), Dr Rajeev P Raghavan (Links between dysglycaemia, insulin resistance, endothelial function and oxidative stress: Aspirin use in Type 2 diabetes-I), and DrLina Chong (The impact of probiotics (VSL#3®) on cardiovascular risk and liver injury in patients with non alcoholic fatty liver disease).

Dr Jan Shute and **Professor Anoop Chauhan** are currently co-supervising the MD studies of Dr Jonathan Owen on 'Coagulation Factors and Exacerbations of Asthma', testing the hypothesis that markers of coagulation in the urine predict the onset of an asthma attack. An award from **Asthma UK** has funded the appointment of Suzanne Edgar as a research associate in Jan's lab for the analysis of the clinical samples. Scott Elliott, a Biomedical Scientist at QAH, is also joining the team and has registered for an MPhil. Scott will develop the technique of SELDI-TOF-MS for the quantitative proteomic analysis of urine samples, as part of a collaboration with Dr Peter Howarth (Respiratory Consultant, Southampton General Hospital.

Strong links between IBBS and the NHS will help us deliver Research with Impact.

Professor Geoff Kneale and colleagues prove the structure of large multisubunit molecular motor and proposed path of the DNA as it translocates



Geoff Kneale and colleagues at Portsmouth collaborating with groups at Universities of Leeds, Edinburgh and Warsaw, provide the structure of a large multisubunit molecular motor (a type I Restriction Enzyme / DNA methyltransferase) and the proposed path of the DNA as it translocates, based on small angle X-ray and neutron scattering and high resolution Electron Microscopy. Published in Kennaway et al. (Genes and Development, 2012)

Brain Tumour Alliance Launched in Portsmouth

Professor Geoff Pilkington launched the South of England Brain Tumour Alliance (SEBTA), which draws together seven neuro-oncology centres spread across universities and hospitals involved in brain tumour diagnosis, therapy and research.

South Coast RNA network

Portsmouth was home to the 2011 South Coast RNA Network meeting in November. The network promotes collaboration between groups in different Universities throughout the South of England who are involved in cutting edge research concerning all aspects of RNA. Delegates from Portsmouth, Southampton, Kings and Kent Universities presented topics ranging from NMR Structure Determination to the Role of Micro RNAs in Disease. The meeting was organized by **Anastasia Callaghan, Colin Sharpe and Garry Scarlett** from the Biomolecular Structure and Genes & Development divisions within IBBS. This year the meeting will be held at the University of Kent.

Other News

Dr John McGeehan has been appointed Secretary of the Biological Structures Group (BSG) and a council member of the British Crystallographic Association (BCA). He was also appointed treasurer of the European Crystallography Meeting ECM28.

Louise Butt was awarded the Best Poster Prize at the 2011 South West Structural Biology Consortium (SWSBC) meeting in Reading.