RSC Advancing the Chemical Sciences
Protein & Peptide Science Group

The University of Nottingham

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Novabiochem Merck Chemicals sponsored mini-symposium
Thursday 09 July 2009
New Biochemistry Building, University of Oxford

# Chemistry and Biology of Peptides 2009

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| **10.00 a.m.** | **Registration** | Tea, coffee & biscuits |
| **10.25 a.m.** | **Introduction** | Dr Weng C Chan (School of Pharmacy, University of Nottingham) weng.chan@nottingham.ac.uk<br>Dr John Offer (National Institute for Medical Research, Mill Hill) joffer@nimr.mrc.ac.uk |
| | ***CS Bio Speaker*** | |
| 10.30 a.m. | **Professor Samuel Gellman**<br>Department of Chemistry, University of Wisconsin, Madison, USA.<br>gellman@chem.wisc.edu | **Structure and function in peptidic foldamers**<br>Over the past decade there has been a great deal of interest in developing unnatural oligomers that display peptide-like conformational and functional behaviour. We will describe efforts to establish folding rules for oligomers of β-amino acids and oligomers that contain both α- and β-amino acid residues. In addition, we will show how such foldamers can be used to block biomedically important protein-protein interactions. |
| 11.10 a.m. | **Dr Derek MacMillan**<br>Department of Chemistry, University College London, UK<br>d.macmillan@ucl.ac.uk | **Polypeptide synthesis through N- to S-acyl transfer and native chemical ligation**<br>Recently we observed that peptides undergo N- to S-acyl transfer at His-Cys, Gly-Cys, and Cys-Cys motifs in aqueous solution, at pH 2-5 and temperatures ranging from 40–60 °C. The thioesters formed when the S-peptide is intercepted by a small molecular weight thiol are isolable and can be used in native chemical ligation reactions. We will discuss the potential for this method to be applied more widely and obstacles that remain to be overcome. |
| **11.30 a.m.** | **Tea, coffee & biscuits (Poster presentations)** | |
| | ***RSC Protein & Peptide Science Group Speaker*** | |
| 11.50 p.m. | **Professor Chris Schofield**<br>Department of Chemistry, University of Oxford, UK<br>christopher.schofield@chem.ox.ac.uk | **Oxidative modifications to peptides and proteins: From antibiotics to oxygen sensing**<br>Many peptide antibiotics and proteins are modified by oxidation reactions involving inactivated C-H bonds that occur subsequent to formation of the peptide framework. Many of these reactions are catalysed by 2-oxoglutarate dependent oxygenases and are involved in physiologically important roles such as oxygen sensing. Although to date the post-translational modifications of animal proteins are limited to hydroxylation and demethylation the range of 2-oxygenase reactions in peptide antibiotic biosynthesis is much wider. The lecture will give an overview of 2-oxoglutarate oxygenase catalysed modifications of peptides / proteins and highlight the role of synthetic chemistry. |
| 12.30 a.m. | **Professor Garth Cooper**<br>School of Biological Sciences, University of Auckland, Auckland, New Zealand<br>g.cooper@auckland.ac.nz | **Is islet β-cell degeneration elicited via an amylin-activated intrinsic Fas/FasL/FADD pathway: route to new first-in-class therapeutic molecules for suppression of type-2 diabetes?**<br>Aggregation of the islet β-cell peptide hormone, human amylin (hA) into beta-sheet-containing oligomers is linked to islet β-cell degeneration and the pathogenesis of type-2 diabetes. We have now linked hA-evoked induction and activation of an intrinsic β-cell Fas/FasL/FADD/caspase 8 pathway to the initiation of β-cell apoptosis, and have also identified a Fas/FasL antagonist as a potent inhibitor of hA-evoked β-cell death. These studies provide substantive evidence to support a role for the Fas-associated signaling pathway in the induction of hA-mediated apoptosis, and indicate that molecules which can target this pathway could be of therapeutic value in preventing hA-induction of type 2 diabetes. |
| **12.50 p.m.** | **Lunch** | **Poster presentations** |

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***Merck Chemicals Speaker***

2.00 p.m.

**Dr Andrea J. Vernall**
Professor Paul Alewood
Institute of Molecular Bioscience, University of Queensland, Australia
p.alewood@imb.uq.edu.au

**Synthesis of α-helix mimetics via hydrogen-bond replacement**

2.40 p.m.

**Dr Mark Howarth**
Department of Biochemistry, University of Oxford, UK
mark.howarth@bioch.ox.ac.uk

**Towards covalent antibodies for imaging and sensing**

Using the principle of proximity-enhanced ligation, we are generating minimal proteins that react covalently with their endogenous protein targets. The generality, speed and specificity of these reactions are being explored and the potential applications for single molecule imaging of receptor trafficking and for cancer diagnosis will be discussed.

**3.00 p.m.** **Tea, coffee & biscuits (Poster presentations)**

3.30 p.m.

**Dr Jason Moss**
Polypeptide Laboratories San Diego, USA
jmoss@ppl-sd.com

**A new chemistry for solid-phase methylation in Fmoc/tBu SPPS**

Backbone methylation is a modification of critical importance in naturally-occurring peptides, with wide-ranging effects on structure and function. In recent years, backbone methylation has been exploited in a 'biomimetic' approach to enhance of the pharmacokinetic performance of peptide-based therapeutics. The presentation will describe a new chemistry for backbone methylation compatible with standard protocols in Fmoc/tBu SPPS.

3.50 p.m.

**Dr Peter White**
Novabiochem Merck Chemicals, Nottingham, UK
peter.white@merckbiosciences.co.uk

**Novel efficient coupling methods which eliminate the use of HOBt**

**4.10 p.m.** **Meeting closes**