WHEN SPECTROSCOPY MEETS LIFE SCIENCES AND DRUG DISCOVERY

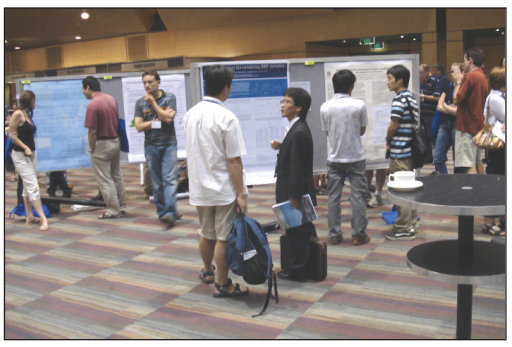
4th International Peptide Symposium in conjunction with the 7th Australian Peptide Symposium and the 2nd Asia-Pacific International Peptide Symposium

The 4th International Peptide Symposium was held at The Cairns Convention Centre in far north tropical Queensland from 21st to 25th October, 2007. The meeting, which had the overall theme "Discovery to Drugs: The Peptide Pipeline" was organised by the Australian Peptide Association and Profs. John Wade (Howard Florey Institute) and Ian Smith (Monash University) co-chaired the meeting. There were over 420 delegates from all parts of the world, with excellent support from the Japanese, Korean, Chinese, US and European peptide communities. In addition, three very successful specialist satellite meetings were held immediately prior to the Symposium. These focussed on Advances in Solid Phase Peptide Synthesis (Port Douglas, Chair John Wade), Chemical Protein Synthesis and Ligation (Heron Island, Chair, Paul Alewood) and Protein Misfolding (Dunk Island, Chair Kevin Barnham). These satellite meetings each attracted from 35 – 75 delegates.

The co-chairs, Ian Smith (left) and John Wade (right)

Spectroscopy Focus

Using the successful format of previous Australian Peptide Symposia, the conference focussed heavily on the role of emerging peptide and protein technologies in modern biological discovery, with a particular emphasis on proteomics and peptidomics. The techniques were applied to a number of different disease states including cancer, diabetes, rheumatoid arthritis and Alzheimers. In total there were 74 oral and 212 poster presentations. Student poster prizes were awarded for each poster session. Specialist workshops were organised by ABI, Agilent, Beckman Coulter, Bruker and Thermo Scientific, and there was an excellent trade display with 30 companies presenting their latest products.



The Poster Sessions

The meeting opened on the Sunday evening with a stimulating plenary lecture by Brian Chait (Rockefeller University, New York, USA) entitled Proteomic Approaches for Analysing Complex Biological Machines. Brian presented a focused proteomics approach for dissecting Nuclear Pore Complexes, leading to a detailed architectural map of the assembly. These data have recently been published in back to back articles in Nature (Nov 29th 2007 edition).

The remaining oral presentations were divided into individual morning sessions with 2 or 3 parallel sessions running in the afternoons. The following areas were addressed: Protein Misfolding and Disease; Peptidomimetics and Drug Design; New Developments in Peptide Drug Delivery; Chemical Peptide Synthesis: Innovations and Applications; Peptidomics: Towards Therapeutics; Peptides-to-Clinic; Clinical Proteomics; Toxins and Targets: New Therapetic and GMO leads; Molecular Interactions- Exploring Affinity and Specificity; Emerging Technologies for Studying peptide Structure and Function; New Concepts in Bioactive Peptide Design; Peptidomics; Biomarker Analysis and Characterisation; Peptide and Protein Engineering; Peptides as Drugs in Infectious Diseases and Neuropeptides and Pain. It is not possible in this report to cover all the many excellent presentations that were made at the meeting. Instead I have selected personal highlights from a number of sessions that I hope will be of interest to readers of this journal.

PROTEIN MISFOLDING AND DISEASE

This session included several of the invited speakers who had attended the Protein Misfolding satellite meeting. Colin Masters (University of Melbourne, Australia) gave an excellent overview of the potential of Aβ-ameloid as a molecular and therapeutic diagnostic target. Sheena Radford (University of Leeds, UK) described the detailed exploration of protein folding landscapes using ultra-rapid (sub-microsecond) mixing experiments.

PEPTIDOMIMETICS AND DRUG DESIGN

Garland Marshall (Washington University Medical School, USA) discussed peptidomimetics of helical protein surfaces. He concluded that peptidomimetic design requires accurate mimicry of the side-chain orientations that generate the helical surface required for recognition. As he said in the title of his talk, the devils' in the details!! Bill Lubell (Universite de Montreal, Canada) presented work from his laboratory on aza-amino acid scanning to explore conformation-biological activity relationships: aza-peptide libraries, generated by replacing each of the native amino acids in a peptide sequence with its aza-amino acid counterpart, are screened for biological activity.

NEW DEVELOPMENTS IN PEPTIDE DRUG DELIVERY

This session addressed a number of alternative methods of presenting peptides for drug delivery. In particular, Vlademir Torchilin discussed the use of cell penetrating particles for the delivery of pharmaceutical nanocarriers (eg liposomes, lipoplexes or polymer-lipid micelles). Pavla Simerska (University of Queensland, Australia) showed the use of liposaccharides in peptide vaccine delivery and demonstrated their efficacy in an animal model of cancer.

PEPTIDOMICS: TOWARDS THERAPEUTICS

William Hildebrand ((University of Oklahoma Health Science Centre, USA), likening Class 1 HLA molecules to an in vivo peptide chip, presented his studies on the analysis of peptide epitopes unique to diseased cells to discriminate virus affected from cancerous cells. Michael Przybylski (University of Konstanz,

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The lecture theatre

Germany) showed how selective proteolytic epitope-excision and extraction of the immobilised immune complexes, in combination with high resolution Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) could be used for epitope identification. Christie Hunter (Applied Biosystems, Foster City, USA) described the use of multiple reaction monitoring (MRM) for targeted multiplexed MS analysis of plasma biomarkers.

PEPTIDES-TO-CLINIC

Pierre de Meyts (Hagedorn Research Institute, Denmark) gave an enlightening review of the structure, function and evolution of ligands and receptors of the insulin family. He presented models that explain the mechanism of receptor activation, the observed negative cooperativity, and the triggering of intracellular signalling pathways.

Anna Papini (University of Firenze, Italy) presented a "Chemical Reverse" approach, in which specific post translational modifications (PTMs) are introduced during solid phase synthesis to mimic conformational epitopes, to isolate autoantibodies as potential disease biomarkers. She showed that aberrant N-glucosylation is a fundamental determinant of autoAb recognition in Multiple Sclerosis (MS) and that a statistically significant number of sera from MS patients showed elevated titre to glycosylated peptides and that this correlated with disease activity.

CLINICAL PROTEOMICS

This session highlighted many of the challenges currently faced in biomarker discovery and analysis. Ralph Bradshaw (UCSF, USA) discussed the need to carefully characterise PTMs. He illustrated his talk with a number of practical situations showing that extreme care must be taken to ensure correct PTM identification (eg formylation versus dimethylation; double oxidation versus persulphide formation; sulphation versus phosphorylation), and highlighted the significant problem of distinguishing artifactual from true in vivo modifications.

Bill Hancock (Northeastern University, USA) used their multiple-lectin affinity chromatography as part of a multidimensional separation approach to detect low abundance proteins present in the plasma glycoproteome. This was applied to a number of clinical and mouse model situations.

The Protein Biosensing group from the Ludwig Institute in Melbourne, Australia, presented their proteomic approaches for identifying tumour-related proteins and peptides in faecal samples from colon cancer patients, which they humorously called "Turdomics". Alan Sawyer (Monash University, Australia) described the automated high throughput hybridoma platform for the generation and characterisation of large panels of monoclonal antibodies that he is currently establishing.

MOLECULAR INTERACTIONS-EXPLORING AFFINITY AND SPECIFICITY

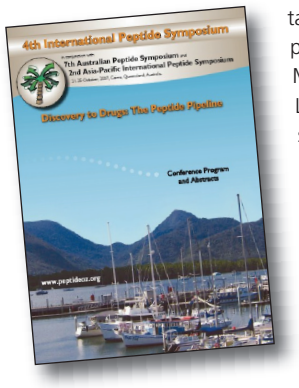
This session focussed on alternative technologies for detecting and analysing protein-protein interactions. Bill Gelb (Microcal LLC, Northampton, USA) gave an overview of modern microcalorimetric techniques. Gideon Schreiber (Weizmann Institute, Israel) described their recent studies on mutational analysis of a number of different protein complexes using the recently released Biorad ProteOn™ high throughput SPRi system which uses image analysis to simultaneously track optical changes at many different sites in an image (array) with high sensitivity and without the need for molecular labelling. Simultaneous measurement can be made of up to 36 samples using a 6 x 6 grid laid down on the sensor surface. Stefan Stahl (Royal Institute of Technology, Stockholm, Sweden) described the generation and use of affibody molecules for tumour targeting applications, and showed that an anti-Her2 affibody could be used clinically when patients were being treated with the anti-Her2 antibody Herceptin.

EMERGING TECHNOLOGIES FOR STUDYING PEPTIDE STRUCTURE AND FUNCTION

In this session several groups showed the potential of a range of technologies to probe peptide structure and function. Francis Separovic (University of Melbourne, Australia) showed the correlation of data generated using solid-state NMR, fluorescence, quartz crystal microbalance (QCM) and atomic force microscopy (AFM) from studies on membrane interactions on antimicrobial peptides from Australian tree frogs. John Lee (Monash University, Australia) used Surface Plasmon Resonance (BIAcore), Dual Polarisation Interferometry (Farfield) and atomic force microscopy (AFM) to probe geometrical changes of antimicrobial peptides in neutral and negatively charged membranes. Joseph Poduslo (Mayo Clinic College of Medicine, USA) showed a new peptide-based contrast agent for the non-invasive visualisation of ameloid plaques by Magnetic Resonance Imaging while Toshimasa Yamazaki (Protein Research Unit, Tsukuba, Japan) used NMR spectroscopy to address the structure and function of N-terminal domains of the ubiquitin related protein, SUMO.

NEW CONCEPTS IN BIOACTIVE PEPTIDE DESIGN

Motoyoshi Nomizu (Tokyo University of Pharmacy and Life Sciences, Japan) presented on the use of cell adhesive peptides identified in laminins, conjugated to chitosan membrane, for keratinocyte transfer to a wound bed. Bob Millar (Medical Research Council, Edinburgh, UK) presented their data on ligand-induced selective signalling at the GnRH receptor and identified a key residue as the main determinant which could provide the basis for the development of cancer therapeutics that directly target tumour cells or inhibit pituitary gonadotrophins. Morton Meldal (Carlsberg Laboratory, Denmark) showed a method for optical encoding of beads used for combinatorial chemistry libraries.



The Proceedings Programme

PEPTIDOMICS: BIOMARKER ANALYSIS AND CHARACTERISATION

Hidehito Mukai (Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan) described experiments to identify cryptides: functional peptides hidden within protein sequences. Tony Purcell (Bio 21 Institute, Melbourne, Australia) reported on an immunopeptidomic approach for the identification of new targets in autoimmune disease showing different T cell responses for patients with type 1 diabetes and rheumatoid arthritis. Peter Hoffman (University of Adelaide, Australia) showed the potential of IMAC, C8 and antibody enriched magnetic beads for biomarker discovery using downstream proteomics analysis. Rudi Grim (Agilent Technologies, Santa Clara, USA) showed their latest nanospray microfluidic HPLC chips for sample enrichment and separation prior to MS analysis.

PEPTIDES AS DRUGS IN INFECTIOUS DISEASES

Gyorgy Keri (Semmelweis University, Budapest, Hungary) discussed their approaches to the identification of new therapeutic kinase inhibitors using Nested Chemical Library™ technology where libraries focused around 108 core structures are used to generate novel pharmacophore models. He also presented their proteomics approach (KinaTor™) in which immobilised kinase inhibitors are used to fish for their protein binding partners in cell lines or tissue samples.

NEUROPEPTIDES AND PAIN

In the final session of the meeting a number of biological pathways involved in the understanding and treatment of pain were discussed. Catherine Rougeot (Institut Pasteur, Paris, France) described the discovery of rat sialorphin and human opiorphin, recently described modulators of opioid-dependent signalling pathways. Victor Hruby (University of Arizona, USA) discussed the specific problems of prolonged and neuropathic pain where tolerance and severe toxicity become major problems. He demonstrated the potential of multivalent ligands, with balanced mu and delta opioid activities, to address this. Richard Clark (University of Queensland, Australia) described their studies on an orally available cyclic conotoxin analogue for the treatment of neuropathic pain in a rat model.

In conclusion, this meeting provided a stimulating smorgasbord of technologies and applications applicable to a wide range of biochemical and biomedical studies. The friendly ambience of the meeting encouraged lengthy discussion and brain storming between many of the delegates which will surely result in many exciting new developments in the future.

> ***There were over 420 delegates from all parts of the world***