

CONGRESS REPORT

11-14 April 2010, Zermatt, Switzerland

Improving on Nature or Relying on Nature?



This fourth edition of the international Natural Peptides to Drugs (NP2D) congress took place as previously, in Zermatt, in the heart of the Swiss Alps. NP2D is devoted to the development and commercialization of peptide-based drugs and was therefore established as an interdisciplinary exchange platform for specialists and decision makers involved in major overlapping areas of pharmaceutical research and development, such as: peptidic hormones, antimicrobial peptides, toxins, immunomodulators. A scientific steering committee formed of Prof. Paul Alewood (University of Queensland, Australia), Prof. Richard DiMarchi (Indiana State University, USA), Dr Peter Hoffmann (VP at Genzyme Pharmaceuticals, Cambridge, USA), Dr John P. Mayer (Senior Research Advisor, Eli Lilly and Co., Indianapolis, USA), Dr George Miljanich (CEO of Airmid LLC, Redwood City, USA), Dr Les Miranda (Director Research at Amgen Inc., Thousand Oaks, USA), Prof. Robin Offord (Executive Director of Mintaka Medical Research Foundation, Geneva, Switzerland), Dr Michael Pennington (President and COO at Bachem Biosciences Inc., King of Prussia, USA), Dr Reto Stöcklin (President and CEO of Atheris Laboratories and NP2D organizer, Geneva, Switzerland) and Dr Timothy Wells (CSO of Medicine for Malaria Venture, Geneva, Switzerland) is guarantor of a high quality and state-of-the-art scientific level.

This congress was sponsored by Debiopharm, Lilly, Genzyme Pharmaceuticals and Peptisyntha. Petides & Elephants and Quality Assistance were present as exhibitors.

The program included 10 invited lectures, 25 selected oral presentations and 15 selected short presentations, divided in ten sessions covering all steps from natural peptides to drugs, such as bioactivity guided drug discovery, structure-function and modeling, lead validation, early development, production and validation, delivery and membrane interaction and drug development. Some of the high quality lectures are summarized below.

Prof. Kurt Hostettmann (Universities of Geneva and Lausanne, Switzerland) opened the meeting by describing how Nature is a wonderful reservoir of drugs for the future. He talked about the plant kingdom which is already well studied in drug discovery, but is an endless source of new compound due to the large diversity of plant species. He also mentioned the potential of animals and bacteria as sources of new drugs.

Dr Richard Houghten (Torrey Pines Institute for Molecular Studies, USA) proposed an approach to enhance, at a preliminary stage, hits with desired biological profiles using phenotypic *in vivo* models. He illustrated his purpose by showing tetra-peptide and classic small compound libraries tested on a mouse tail flick assay that resulted in individual compounds having enhanced desired activity.

Prof. Amos Bairoch (Swiss Institute of Bioinformatics, Switzerland) presented his new project CALIPHO, for Computer Analysis and Laboratory Investigation of Proteins of Human Origin, with the global aim to increase the knowledge on human proteins by a combination of bioinformatics and experimental procedures. He also discussed general considerations on human secretome and uncharacterized secreted human peptides.

Dr Steffen Reedtz-Runge (Novo Nordisk, Denmark) exposed results on the structure of the extracellular domain of glucagon-like peptide-1 (GLP-1) receptor in complex with different ligands. By comparing the resolved crystal structure of the GLP-1 receptor extracellular domain bound to the exendin-4(9-39) antagonists and GLP-1, he showed that important hydrophobic ligand–receptor interactions are conserved in agonist- and antagonist-bound form, with specific residues in the ligand binding site adopting a GLP-1 specific conformation.

Dr Derek Maclean (Kai Pharmaceuticals, USA) described a novel approach using ‘modular’ peptides to alter the activity of intracellular protein targets by selectively inhibiting or enhancing intracellular protein-protein interactions. He demonstrated the potential of modular peptides to protect heart tissue during and after ischemia and to target ‘undruggable’ proteins and also illustrated his presentation with different identified lead products.

Dr Christophe Bonny (Xigen SA, Switzerland) presented the lead product XG-102, a cell penetrating kinase inhibitor peptide that entered Phase 1 clinical trials this year. He showed its applications as an inhibitor of secretion of various pro-inflammatory cytokines *ex vivo* and *in vivo*, in models of inflammatory disorders.

Dr Andrea Leon-Bay (Mannkind Corporation, USA) talked about Technosphere[®] particles for inhalation, containing the glucagon-like peptide-1 (GLP-1) an endogenous incretin hormone produced in the intestinal tract that is secreted at mealtime and reduces blood glucose, postprandial glucose excursions and food intake, and enhances satiety. She explained this technology was developed to be ideally administered at mealtime with exposure limited to postprandial period. She detailed the results obtained *in vivo* showing that pulmonary insufflation of GLP-1 Technosphere[®] in rats results in high level of circulating GLP-1, released insulin and reduced glucose concentrations. She also mentioned that initial clinical studies using GLP-1 Technosphere[®] inhalation produced similar results without side effects.

Dr Gregor Cevc (Pamet AG, Germany) reviewed non-invasive and targeted transcutaneous therapeutic peptides delivery. He discussed the development of different technologies facilitating peptide transport through the skin barrier, i.e. perforators, microneedles, mechanical abraders and porators. He also talked about the use of ultradeformable and stable nano-sized drug carriers that when properly designed and applied, opens spontaneously and transport peptides through pores in the skin barrier.

Dr Abdellah Sentissi (Transmolecular Inc, USA) presented the potential applications of chlorotoxin, a peptide originally isolated from the venom of the giant yellow Israeli scorpion. He showed this peptide has unique properties of highly specific tumor cells binding, uptake and internalization, with no effect on normal cells and has also an inhibitory effect on new blood vessel growth in tumor surrounding. He discussed the development of this peptide as a targeting vector to directly deliver an anti-tumor compound to cancer cells and also talked about other potential applications.

Prof. Janice Reichert (Tufts University and Peptide Therapeutics Foundation, USA) closed this meeting by exposing trends in the development and approval of peptide therapeutics based on a dataset of over 400 peptide therapeutics, vaccines and diagnostics issued from information available in the public domain. She showed for example, the number of therapeutic peptides entering clinical study each year nearly doubled between the 1990s and 2000-2007 periods. Approval and success rate have remained though steady over time, the limiting factor for approval success being Phase 2 to Phase 3 transition. She also demonstrated a total of 51 peptide therapeutics are now approved for marketing worldwide, with promising near-term prospects for additional approval, at least in the USA, with four peptide candidates (mifamurtide, sinapultide, liraglutide and tesamorelin) being under review by the Food and Drug Administration (FDA).

This NP2D 2010 edition was a great success again with outstanding scientific presentations and a nice mixture of people from academy and industry allowing interesting exchanges and business opportunities. The organizers are already very pleased to announce the fifth NP2D meeting that will be held in Zermatt on December 4-7 2011. The registration to this meeting is a full accommodation package, including the registration, nights in a five stars hotel, meals and recreational activities. Please, save already the dates!

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