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PEPTIDE SYMPOSIUM 2010

SEPT 14 – 16, 2010

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Roche Colorado's Fourth Peptide Symposium continues the tradition of bringing the best minds in peptide drug development for three days of scientific presentations and networking opportunities.

FEATURING

> **PEPTIDE INNOVATION SHOWCASE**
Company presentations from biotech innovators on the newest therapeutic programs and technologies related to peptides.

> **NETWORKING EVENTS**
Meet and Greet – Sept 14
Gala Dinner – Sept 15
Farewell Reception and Dinner – Sept 16
Meet with Roche Pharma Partnering – Sept 16

> **REGISTRATION COST**
Registration fee includes round trip airport transportation, two breakfasts, lunches and dinners, and admission to all sessions.

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The Roche Colorado Corporation Peptide Symposium (RCCPS) is the industry leading event dedicated exclusively to a focus on the development of peptide therapeutics. While peptide therapeutics can have the advantage of being potent and highly selective, their development into effective treatments can be challenged by: limited delivery routes, product stability, manufacturing challenges, and an ever-evolving regulatory landscape. Despite these hurdles the number of novel peptides entering clinical trials continues to grow. RCCPS brings together peptide leaders from across the globe to address these challenges with open and honest dialog. A few abstracts are presented in the following pages.

Shk Peptides For The Treatment Of Autoimmune Disease

Shawn Iadonato, Chief Scientific Officer, Kineta, Inc.

Kineta is developing derivatives of the Stichodactyla helianthus toxin (ShK) for the treatment of autoimmune disease, with a focus on multiple sclerosis (MS) and Type 1 diabetes mellitus (T1DM). The lead product candidate ShK-186 is a 39 amino acid cyclic peptide that is a specific and potent inhibitor of the mammalian Kv1.3 potassium channel. The peptide's size and compactly folded structure permit stable, potent and highly specific interactions with the target channel that are typically not achieved using conventional small molecule approaches. ShK-186 specifically targets the effector memory T cell population, which is dependent on the Kv1.3 channel for proliferation. Effector T cells are primary mediators of inflammation and tissue damage in numerous autoimmune diseases. Nonclinical evaluation of the peptide has demonstrated that ShK-186 is effective in the treatment of animal models of autoimmune disease (e.g. RA, MS/EAE, DTH) and is well tolerated and nontoxic in repeat-dose toxicology studies. Treatment with ShK-186 does not compromise the protective immune response to model viral or bacterial pathogens. Kineta plans to initiate a first-in-human clinical study of the drug in late 2010.

Dr. Iadonato is a Founder, Executive Vice President and Chief Scientific Officer of Kineta. Prior to founding Kineta, Dr. Iadonato founded Illumigen Biosciences Inc. (sold to Cubist Pharmaceuticals in 2007) – a genetics-driven drug discovery company with lead development programs in HCV and influenza. Dr. Iadonato received his B.A. in Biology from the University of Pennsylvania and a Ph.D. in Genetics from the University of Washington.

Development Of A Nonapeptide (Syn1002) For The Treatment Of Autoimmune Diseases And Neuropathic Pain

Jamal Temsamani, Vice-President R&D, CLL Pharma

SYN1002 or pat (peptide analog of thymulin) is a peptide drug that is currently under development for the treatment of autoimmune diseases and neuropathic pain. The pharmacological activity of syn1002 has been investigated in various animal models. In the arthritis model (adjuvant-induced arthritis model), syn1002 inhibited the clinical manifestations at low doses and was more potent than indomethacin. In the crohn model (tnbs model), syn1002 reduced significantly the colon inflammation and the production of pro-inflammatory cytokines. In the mononeuropathy models (cci and sni models), syn1002 reduced significantly neuropathic manifestations, while morphine and a cox-2 inhibitor failed to do so. The mechanism by which syn1002 exerts its effects indicates that syn1002 reduces the pro-inflammatory cytokines (tnf-alpha, il-1b and il-6) and acts via the tnf-signalization pathway. Recently, we have carried out a phase i, single-centre, double-blind, placebo-controlled, randomized study with sequential ascending single dose groups. The study was designed to assess safety, tolerability and pharmacokinetics of syn1002 across 5 doses. This study has shown that syn1002 is very well tolerated in human volunteers and that the maximum tolerated dose was not reached.

Jamal Temsamani, Ph.D, joined CLL Pharma in 2006 following the acquisition of the biotech Company Syntem. Previously, as Director Discovery Group of Hybridon USA and later as Scientific Director of Hybridon Europe he led internal discovery efforts and managed external collaborations. A graduate of The University of Montpellier in France he has published more than 61 scientific articles and 6 book chapters and is co-inventor of 40 patents.

Pepducins: Novel Lipopeptide Allosteric Modulators Of Gpcr Signaling

Steve Hunt, Chief Scientific Officer, Anchor Therapeutics

Pepducins are a breakthrough approach to targeting g-protein coupled receptors (gpcrs) on the inside surface of the cell membrane, dramatically expanding the gpcr frontier. Pepducins are comprised of a short peptide derived from the sequence of a gpcr intracellular loop linked to a hydrophobic moiety that anchor in membrane and modulate gpcr activity via a unique intracellular allosteric mechanism. Pepducin technology represents an exciting new area of research directed towards a well-validated class of drug targets and will be the focus of this presentation.

Dr. Hunt is currently Chief Scientific Officer and SVP of Research and Development at Anchor Therapeutics. Dr. Hunt joined Anchor in October 2008 with over 15 years of drug discovery and development experience in Pfizer Global Research and Development and Parke-Davis Pharmaceuticals. Before assuming this role, Dr. Hunt held a series of positions of increasing responsibility in exploratory biology and pharmacology within the Parke-Davis and later, Pfizer R&D organizations. Prior to joining industry, Dr. Hunt was a member of the faculty at the University of North Carolina Chapel Hill. Dr. Hunt received his Ph.D. from the University of Pittsburgh and was a Postdoctoral Fellow in the laboratory of Dr. Leroy Hood at the California Institute of Technology.

Ensemblins: A New Class Of Therapeutic Macrocycles

Nicholas Terrett, Chief Scientific Officer, Ensemble Therapeutics Corporation

Macrocycles are found widely in nature where they fulfill numerous specific biological functions. However they have been generally underexploited as drug molecules as they are larger than more conventional 'Rule of 5'-compliant molecules and their synthesis and screening has been considered a challenge. In order to permit the further investigation of macrocyclic compounds, Ensemble Therapeutics has developed two complementary platforms for the rapid synthesis and screening of Ensemblins and are currently using these macrocycles for the discovery of lead molecules for challenging protein-protein interaction targets. The platform incorporates both a DNA-programmed chemistry (DPC) approach to compound libraries as well as more conventional synthetic and medicinal chemistry. DPC permits the synthesis of hundreds of thousands of macrocyclic molecules using predefined DNA sequences to control individual synthetic steps. The process allows for the step by step purification and analysis of complex mixtures of intermediates and final macrocyclic products. The macrocycle collections have been used successfully for the discovery of compounds that interact with a number of important drug discovery targets, including the oncology target BCL-XL. Ensemble Therapeutics has shown that these small molecule macrocycles have good drug-like properties including solubility, membrane permeability and oral bioavailability.

Nick Terrett was born in London and educated at Cambridge University (BA, PhD). During his career Nick has worked at both GSK and Pfizer as a medicinal and technology chemist and is an inventor on patents for candoxatrilat and sildenafil (Viagra, Revatio). Nick established Pfizer's combinatorial chemistry group, and directed high throughput screening and materials management groups. From 2003 Nick was Head of Chemical Sciences at Pfizer, Cambridge MA. Nick is currently Chief Scientific Officer for Ensemble Therapeutics, a biotech company exploring macrocycles for drug discovery.

PEGylation: A Successful Strategy In Parenteral Drug Delivery

Francesco M. Veronese , Professor, Applied Pharmaceutical Chemistry, Padua University

Bioconjugation, the covalent linking of non toxic, non immunogenic polymers to drugs, is an established procedure in drug delivery. The conjugation of drugs with poly(ethylene glycol), known as PEGylation, represents the most successful procedure for peptides and proteins because it allows for long lasting residence time in circulation, decreases the in vitro and in vivo chemical and enzymatic degradation and prevents or reduces immunogenicity.

Several PEGylated proteins of different structure, and oligonucleotides also, already reached the market and rapidly became of great therapeutic success while many other are on the pipeline. In the case of small organic drugs, although the extensive research in academia and industry, so far no conjugate reached the market even if several products are much promising and at an advanced state of clinical experimentation. The greatest limit for these drugs resides in the intrinsic low loading capacity of the polymer.

Years of research allowed to develop a number of chemical strategies for the stable or reversible chemical and enzymatic linking of PEG to drugs, to find suitable strategies for the purification and evaluation of these new chemical entities, but also to discover limits of the method, as an eventual immunogenicity and toxicity. The research in bioconjugation is nowadays still active in improving the strategies of PEGylation but also to discover alternatives, on one side to overcome the physical and chemical limitations of this polymer and on the other to escape the huge number of patents regarding PEG that is making difficult the patenting of new products.

The description of successful PEGylated products will offer the opportunity to discuss the old and new chemical strategies employed, the advantages and the problems of PEGylation, and will give the chance to introduce promising alternatives such as the those based on polysaccharides, poly(oxazoline), and poly(dextrin).

Francesco M. Veronese, obtained the degree in Pharmacy at Padua University. Researcher at the Italian CNR (1960-79), research assistant' at UCLA Los Angeles (1979-81) assistant professor at the Ferrara and Padua University (1981-84). Full professor' of applied pharmaceutical chemistry, School of Pharmacy, at the University of Padova (1984-2007). Presently visiting professor. His past research activities have included: tryptophan metabolism, specific modification of peptides and proteins for structure-activity relationships, purification, enzymatic, and structural properties of enzymes from different sources including thermophiles, covalent modification by amphiphylic polymers of polypeptides and proteins for therapy and organic biocatalysis; entrapment of drugs in non-biodegradable or biodegradable polymers for controlled release. Present work is in the area of covalent binding of polymers to small organic drugs, peptides, and proteins for improved delivery and targeting. He was Chairman of the PHD program in Pharmaceutical Sciences at Padua University and organized the Italian Advanced School of Pharmaceutical Chemistry (1983-2003). President of the CRS Italian Chapter (2000-2005), program co-chairman of the 2001 Bostom CRS Meeting and since 2008 member of the BSA. He is author of over 230 research papers in peer journals, of 33 review articles or book chapters, of 22 EU or US patents, theme editor of three issues of ADDR and of a new book on PEGylation.

TPE, A Unique Formulation Based Technology Enabling Oral Delivery Of Macromolecules

Roni Mamluk , Chief Operating Officer, Chiasma

Chiasma develops new drug products based on a proprietary technology called TPE ("Transient Permeability Enhancer"), which enables oral delivery of macromolecules (up-to 20 kDa) and poorly-absorbed small molecules into the blood. The TPE facilitates paracellular transit across the intestinal wall and allows intact drug molecules to be absorbed via the portal system into the systemic circulation. TPE permeation activity is the result of a unique combination of excipients (all listed as GRAS); no chemical modification is introduced to the drug molecule. Pre-clinical studies in various animal models have demonstrated TPE's safety and efficacy. The TPE-induced permeation enhancement is transient and was demonstrated on various molecules, including peptides and small proteins. TPE technology allows only molecules smaller than 70 kDa to permeate the intestine; excluding as a result, potentially pathogenic elements penetrating through the GI. Chiasma's 1st product is a TPE-formulated peptide (currently an approved injectable peptide drug). The product was evaluated for safety in a 28-day BID dosing toxicology study in monkeys. It appears safe and no TPE-related findings were detected. In a Phase 1 study in humans, Chiasma's 1st product was well tolerated and showed therapeutically relevant dose dependant exposure. The conclusions of the study support advancing clinical development.

Dr. Mamluk joined Chiasma in 2006 as director of preclinical development and since that time, took the leading role in establishing Chiasma's TPE oral delivery platform and is one of the primary inventors of this technology. Dr. Mamluk joined Chiasma from Adnexus Therapeutics, where she established and headed up preclinical research and development. Dr. Mamluk received a BA and a PhD (summa cum laude) from the Hebrew University and she held a post doctoral fellowship at Children's Hospital/Harvard Medical School in the field of angiogenesis.

Cyclotides, A Novel Natural Peptide Scaffold For Drug Discovery

Julio Camarero, Associate Professor for Pharmacology, University of Southern California

Cyclotides are a new emerging family of large plant-derived backbone-cyclized polypeptides (˜28-37 amino acids long) that share a disulfide-stabilized core (3 disulfide bonds) characterized by an unusual knot. Cyclotides contrast with other circular poylpeptides in that they have a well-defined three-dimensional structure, and despite their small size, can be considered as miniproteins. The main features of cyclotides are therefore a remarkable stability due to the cysteine knot, a small size making them readily accessible to chemical synthesis, and an excellent tolerance to sequence variations. For example, the first cyclotide to be discovered, kalata b1, is an orally effective uterotonic, and other cyclotides have been shown to cross the cell membrane through macro-pinocytosis, cyclotides thus appear as promising leads or frameworks for peptide drug design.

We report for the first time the in vivo biosynthesis of natively-folded MCOTI-II based libraries inside live E. Coli cells. Biosynthesis of genetically encoded cyclotide-based libraries opens the possibility of using single cells as microfactories where the biosynthesis and screening of particular inhibitor can take place in a single process within the same cellular cytoplasm. We will also report the design and biosynthesis of a mcoti-grafted cyclotide with the ability to specifically induce programmed cell-death in-cell assays using different tumor cell lines.

Guanylate Cyclase-C Agonists As A New Class Of Drug Candidates For GI Disorders And Inflammatory Bowel Disease

Kunwar Shailubhai, Chief Scientific Officer
Synergy Pharmaceuticals

Uroguanylin (UG), Guanylin (GN), and bacterial heat stable enterotoxin (ST) are structurally related peptides that activate common guanylate cyclase-C (GC-C) receptors and stimulate intracellular production of cyclic guanosine monophosphate (cGMP), resulting in activation of cystic fibrosis transmembrane conductance regulator (CFTR) and also in enhancement of the transepithelial efflux of sodium (Na+), potassium (K+), chloride and water. Another physiological role for GC-C agonists appears to be in the maintenance of the proliferative index of the epithelial cells lining the GI mucosa. The cGMP pathway also mediates anti-inflammatory effects of cellular molecules such as nitric oxide and hemeoxygenase-1. Hence, therapies that upregulate cGMP and cAMP levels or inhibit their degradation (e.g., phosphodiesterase inhibitors) demonstrate good efficacy in murine models of ulcerative colitis. We previously reported that the expression of UG is dramatically reduced in human colon polyps and in cancerous tissues and that this deficiency might be one of the primary reasons for colon carcinogenesis. Moreover, treatment with UG inhibited proliferation, induced apoptosis in colon carcinoma cells (T84), and also inhibited polyp formation in Apc min/+ mice (Shailubhai et al., Cancer Res, 60:5151-5157, 2000).

We recently completed a Phase I double-blind, placebo-controlled, randomized single, oral, ascending dose study of SP-304, a novel analog of UG, in 71 healthy volunteers. The subjects were evaluated for safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) effects of SP-304. SP-304 was well-tolerated across all doses studied and it also exhibited PD activity in healthy volunteers with no detectable systemic absorption. Further clinical development to evaluate SP-304 as a treatment option for patients with CC and IBS-C is continuing and the phase II clinical trials are ongoing. In addition, recent preclinical data also demonstrated anti-inflammatory effects of SP-304 in TNBS- and DSS-induced colitis in mice. Importantly, the amelioration of colitis was also associated with downregulation of cytokines such as IL-4, IL-5, IL-23, and TNF. These results suggest that the GC-C receptor-mediated enhancement of cGMP production ameliorates GI inflammation via downregulation of certain pro-inflammatory cytokines. Subsequently, we have also discovered a more potent and a highly stable GC-C agonist SP-333, which we believe is more suitable as a drug candidate for treatment of ulcerative colitis. Thus, the seminar will discuss potentials therapeutic applications of GC-C agonists in GI diseases.

Kunwar Shailubhai, Ph.D., M.B.A has served as our Chief Scientific Officer since July 2008. Dr. Shailubhai also holds joint appointment as professor at the Institute of hepatitis Virus Research (IHVR). From 2003 until July 2008, Dr. Shailubhai served as Senior Vice President, Drug Discovery, of Synergy Pharmaceuticals Inc. From 2001 to 2003, Dr. Shailubhai held the position of Vice President, Drug Discovery at Synergy Pharmaceuticals Inc where he was responsible for the preclinical development of Synergy's GC-C agonist program for drugs to treat colon cancer and GI disorders and diseases. Between 1993 and 2000, he was with Monsanto Company, serving as Group Leader of the cancer chemoprevention group. Dr. Shailubhai previously served as a Senior Staff Fellow at the National Institutes of Health, and as an Research Assistant Professor at the University of Maryland. Dr. Shailubhai received his Ph.D. in microbiology from the University of Baroda, India, and his M.B.A. from the University of Missouri, St. Louis. Dr. Shailubhai has more than 50 publication and several patents.

Oral Delivery of Peptides Using GIPET® Technology

Tom Leonard,Vice President & Chief Scientific Officer
Merrion Pharmaceuticals

GIPET® technology is focused on oral delivery of various types of poorly absorbed compounds. The technology has been validated in humans with successful clinical trials for several products, including peptides. Efficacy, safety, and side effect profiles of drugs can be improved substantially using this delivery technology. GIPET uses specifically designed formulations of GRAS absorption enhancers which form mixed micelles with the drug of interest to facilitate transcellular absorption of peptides with good reproducibility and a strong safety profile. Case studies of clinical studies of GIPET formulations of MER-104 (acyline) and desmopressin in man will be presented. For MER-104, the physical/chemical characteristics of GNRH antagonists in general, and acyline in particular, have limited clinical evaluation to sustained release dosage forms which have relatively short duration, and have prohibited development in more novel indications where sub-castration doses are of interest. Oral delivery overcomes some of these issues wile maintaining flexibility in designing appropriate therapeutic regimens. Current desmopressin tablets have very poor bioavailability and substantial inter subject variability associated with them. GIPET-enhanced tablets give a large improvement in variability with intersubject variability similar to SC injections. The demonstrated power of GIPET to deliver peptides has resulted in initiation of human clinical programs of several additional peptides.

Thomas W. Leonard, PhD, CSO, Merrion Pharmaceuticals. Merrion is developing oral products using proprietary technology. A pharmacist (USC) with 28 years of pharmaceutical industry experience, Dr. Leonard holds a Ph.D. in Pharmaceutics/Clinical Pharmacokinetics from VCU. He has authored numerous publications, and holds inventions on 38 issued and in-process drug delivery patents.

The Role Of Peptide Properties During Microencapsulation And Extended-Release From Bioresorbable Polymers

Tom Tice, Vice-President Research, Surmodics Inc

Several extended-release, parenteral peptide formulations are on the market today. And, many more are being developed for systemic and local delivery for a variety of therapeutic indications. One successful formulation approach is to place peptides within resorbable polymers, like lactide/glycolide polymers, to form injectable microparticles and implants. A single administration of these formulations can deliver peptide at efficacious levels for days, weeks, and months. Interestingly, the production process and in vivo release characteristics of these polymeric formulations are highly influenced by the physical and chemical properties of the peptide. Consequently, one can use peptide properties to their advantage in this regard. Or, on the other hand, peptide properties can cause difficulties and create formulation challenges. The relationships between peptide properties, polymer properties, formulation processes and peptide release kinetics will be a central theme of this presentation.

Dr. Tice, Vice President Research, SurModics, is internationally recognized for his research/product development in drug delivery. He has been a leader (31 years) in the advancement of injectable, extended-release resorbable microparticles and implants. He holds 30 US patents. One patent led to the first commercial, injectable microparticle product - 1-month LHRH peptide delivery to treat prostate cancer. He attended Syracuse University, receiving a BS degree (chemistry) and a PhD degree (biophysics).

Targeted Delivery Of Bioactive Cell Penetrating Peptides: Implications For Anti-Cancer Therapy

John Howl, Professor of Molecular Pharmacology
University of Wolverhampton

Numerous cell penetrating peptides (CPPs) have been utilised as vectors for the intracellular delivery of diverse bioactive cargoes. The utility of this strategy requires highly efficient CPP with minimal toxicity and negligible biological activity. However, general consideration of the multi-domain architecture of many human proteins indicates that cell penetrant cryptic sequences could mimic and/or modulate their functions. This strategy has enabled the study of cryptic CPPs in which multiple pharmacophores for cellular penetration and biological activities are discontinuously organised within the primary sequence. The term rhegnylogic is used to distinguish this class of CPP, also termed biportide [1], from the more usual sychnologic combination of CPP and cargo.

Cryptic CPP sequences are located within both amino and carboxyl helical domains of cytochrome c (Cyt c), a signalling protein integral to apoptotic events. Detailed characterisation of these peptides [1,2], has identified a series of efficient CPP vectors that differentially target intracellular organelles. These molecular properties mimic the propensity of Cyt c to translocate biological membranes as a mediator of both mitochondrial apoptosis and inflammation. Moreover, chimeric combination of Cyt c-derived CPPs and a peptide mimetic of the conserved FXFG motif of nucleoporins disrupts nuclear pore function to potently induce apoptosis in tumour cells. Related studies have identified nosangiotide (eNOS492-507), a cryptic CPP within nitric oxide synthase. Significantly, this CPP potently inhibits the proliferation, migration and tube-forming capacity of primary endothelial cells and displays potent anti-angiogenic properties in vivo.

The development of methodologies to target bioactive CPPs to therapeutic sites include the application of receptor ligands and homing sequences as cell- and tissue-selective motifs [3,4]. Such strategies enable CPPs to preferentially localize within various therapeutic sites, including breast and brain cancers, and indicate that CPPs are indeed a viable emerging technology for both diagnostic and therapeutic applications.

Professor of Molecular Pharmacology, the Research Institute in Healthcare Science, University of Wolverhampton, U.K. Honorary Research Fellow, School of Biosciences, University of Birmingham. Director of Pantechnia PLC.

Analytical Challenges On PEGylated Peptide API

Ping Zhuang , Research Fellow, Merck and Co.

The analysis and characterization of PEGylated peptide API are quite challenging due to the large molecular mass and polymeric feature of the PEG moiety of the molecule. In this talk, analytical method development and characterization of pegylated peptide API is presented, early stage regulatory filing strategy is discussed.

Ping Zhuang joined Merck & Co. Inc. after she obtained her Ph.D. in Chemistry from New York University in 2001. She is a Research Fellow in Early Development Analytical Research Department in Process Research. She and her group are responsible for analytical support for small molecule drug candidates & outsourced peptides, including method development, API release, and CMC source documentation preparation supporting regulatory filings.

Are Today's Medicinal Chemists Better Prepared To Design Therapeutic Peptides That Exhibit Good Oral Bioavailability?

Ronald T. Borchardt , Solon E. Summerfield Distinguished Professor, The University Of Kansas

During the past thirty years significant advances have been made in our basic knowledge concerning: (i) the structural features of peptides that afford optimal permeation of the intestinal mucosa via passive diffusion; and (ii) the biochemical machinery (e.g. enzymes, efflux transporters) in the intestinal mucosa and liver that limit systemic exposure of peptides after oral dosing. By integrating this new basic knowledge into drug design and by employing a drug discovery strategy that focuses on simultaneously optimizing a peptide's affinity and specificity for the macromolecular target and its drug-like properties (e.g. solubility, permeability, metabolism), today's medicinal chemists are much better prepared to design therapeutic peptides that exhibit good oral bioavailability than medicinal chemists who practiced in the 1980s and 1990s. In his lecture, Professor Borchardt will detail the reasoning behind his optimistic view for the discovery of therapeutic peptides that are clinically efficacious after oral administration to humans.

Ronald T. Borchardt is the Solon E. Summerfield Distinguished Professor of Pharmaceutical Chemistry at The University of Kansas (KU). He earned his B.S. degree in Pharmacy (University of Wisconsin, 1967) and his Ph.D. degree in Medicinal Chemistry (KU, 1970). From 1969-71, he served as a postdoctoral fellow at the NIH. He is the author of 500 scientific publications and 460 abstracts and the editor of 10 books. His research interests include drug design and drug delivery. His awards include: Fellow (1988), Research Achievement Awards in Biotechnology (1993) and Medicinal Chemistry (1994), and Distinguished Pharmaceutical Scientist Award (1997) from AAPS; Takeru and Aya Higuchi Memorial Lectureship Award from APSTJ-Japan (1993); Paul Dawson Biotechnology Award (1997) and Volwiler Research Achievement Award (1998) from AACP; Hoest-Madsen Medal (1999) from FIP; Takeru Higuchi Research Prize (2003) from APhA; Smissman-Bristol-Myers Squibb Award from ACS (2003); and the PolyPops Foundation Award (2007) from SBS. He also has received Honorary Doctorate Degrees from The Danish University of Pharmaceutical Sciences, Copenhagen, Denmark (2002), Katholieke University, Leuven, Belgium (2004) and Uppsala University, Uppsala, Sweden (2006).

Peptides On Synthetic Scaffolds For Mimicry Of Proteins Towards Synthetic Vaccines And Beyond

Rob M.J. Liskamp , Professor, Utrecht University

A tremendous challenge in the design and synthesis of protein mimics is replacement of the greater part of a protein by a relatively small synthetic scaffold. This scaffold may provide the right orientation and rigidity of peptide sequences, which are crucial for the biological activity. For this purpose we have developed CycloTriVeratrylene (CTV), TriAzaCyclophane (TAC) as well as multi-arm amino acid based dendrimeric scaffolds. CTV was used for the design and synthesis of collagen mimics. The selectively addressable synthetic TAC-scaffold was used for mimicry of discontinuous epitopes of whooping cough pertactin by confined presentation of several different peptide arms. This approach yielded protective antibodies. As such it will be employed to design and construct new synthetic vaccines that induce functional antibodies. The use of multi-arm scaffolds based on our amino acid based dendrimers has been very valuable in the design and exploration of protein mimics for tumor and infection imaging and/or treatment. Many significant chemical challenges are found in the construction of these protein mimics having different (peptide) loops on scaffolds or dendrimers and include "click" reactions and chemical ligation.

Rob Liskamp studied chemistry and did his Ph.D. Bio-organic Chemistry at the University of Nijmegen, The Netherlands (1982) working with Harry Ottenheijm. Post-doctoral research (1983-1986) was carried out in the group of I. Bernard Weinstein in The Institute of Cancer Research and in the group of W. Clark Still, Department of Chemistry, Columbia University, New York. In 1986 he moved to the University of Leiden working as an assistant professor in the group of Jacques van Boom. In 1991 he was a visiting professor at the University of California in Los Angeles in the group of François Diederich. In 1994 he became associate professor at Utrecht University and in 1996 professor of molecular medicinal chemistry. He is head of the group medicinal chemistry and chemical biology. He has a joint appointment at the departments of Pharmaceutical Sciences and Chemistry. He is coordinator of the Utrecht University research focus area "drug innovation". Dr Liskamp' s research interests include biologically active modified peptides and peptidomimetics, dendrimers, peptide folding, molecular recognition, synthetic receptors, protein mimics including synthetic antibodies and vaccines.