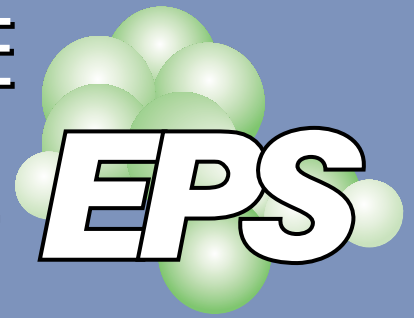
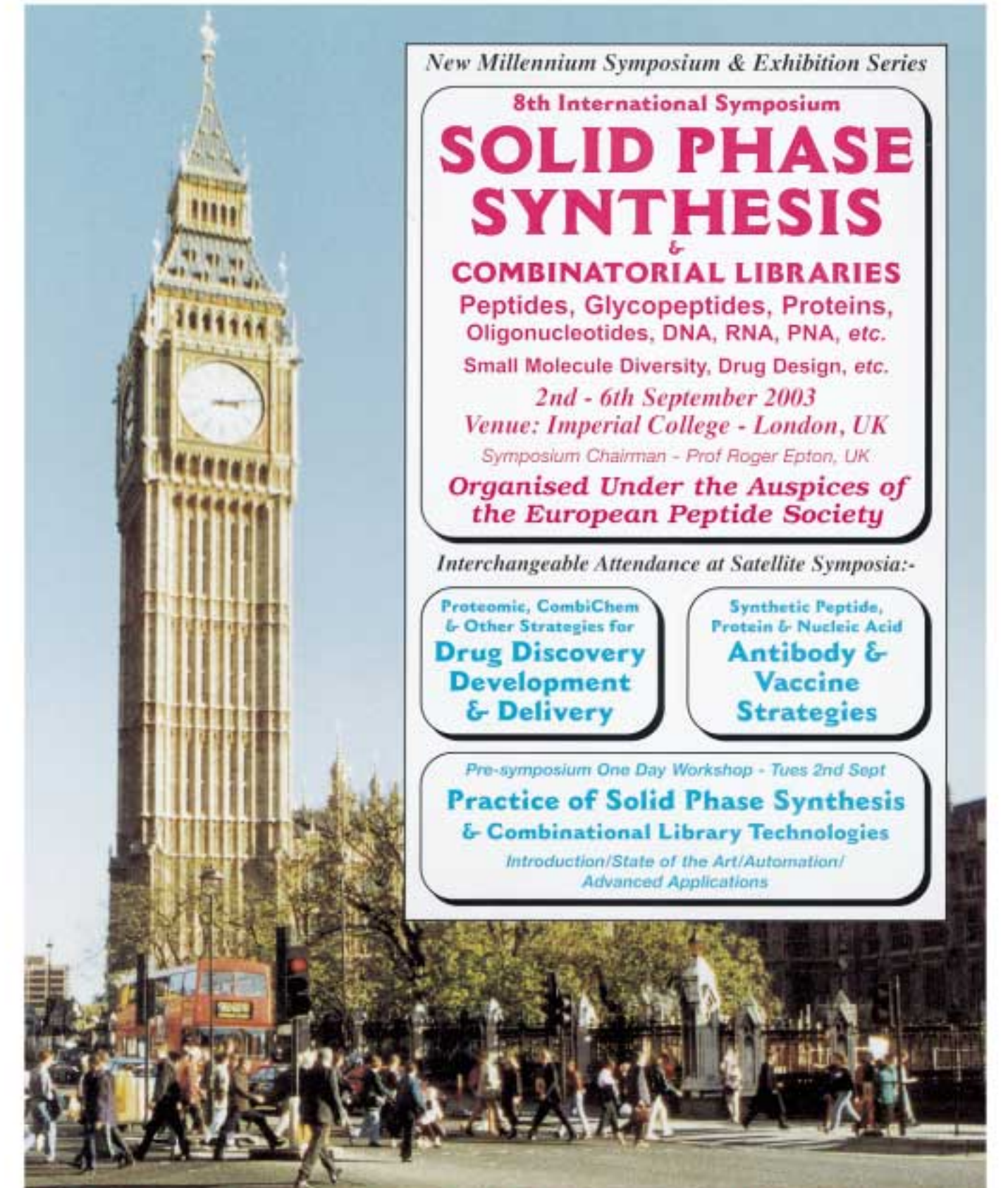


THE EUROPEAN PEPTIDE SOCIETY NEWSLETTER

ISSUE NUMBER 29, 1 JULY 2003





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A message from the editor



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SOCIETY WEBSITE

<http://www.eps.chem.elte.hu/>

The above is correct as at present but quite soon a new Society Website will be accessible, technically organised and serviced by John Wiley & Sons.



Dear Colleagues and Friends,

It was an honour for me to have been proposed (during the 27th European Peptide Symposium in Sorrento) as the new Editor of the EPS–Newsletter. Accordingly, I would like to thank past and present Executive Committees of the European Peptide Society for this privilege.

This is the first Newsletter issued after January 2003, the date when John Jones, in his Editorial Farewell, made known that *the time has come to step aside after many years and 28 issues*. The cover of this issue is a token of recognition and appreciation of the excellent job Dr. Jones and his team have performed.

The Newsletter is a very important vehicle for the dissemination of information about European Peptide Society activities. The long mailing list shows an increasing number of interested readers and an obligation for us to make it useful and pleasant to read. The editorial project will follow the lines set up by the previous Editor. Needless to say that suggestions and contributions are not only welcomed but rather sought and requested. From my part I would like to assure the European peptide community that I shall do my best to stand up to the job's requirements.

Paul Cordopatis

Cellular Transport Strategies for Targeting Epitopes, Drugs and Reporter Molecules

Budapest, 6–9 March 2003

An International Workshop

During the 3–days meeting 29 invited and 8 short lectures and 43 posters were presented. Uptake mechanisms involving macrophage receptors (L. Martinez–Pomares, Oxford, UK), Rab proteins (A.T. Jones, Cardiff, Wales, UK) and lysosomal cathepsins (C. Isidoro, Novara, Italy) were comprehensively discussed from different points of views. Scavenger receptors of macrophages were also considered as a new class of surface structure suitable for novel drug–targeting (P. Lehtolainen, Kuopio, Finland, F. Hudecz, Budapest, Hungary) or immunomodulating approaches (S. Rath, Delhi, India).

A great deal of new results were demonstrated by lectures covering various natural cell penetrating / transporter peptides and their cargo–derivatives. These included communications from leading laboratories from the field on Tat (E. Vives, Montpellier, France, M.J. Gait, Cambridge, UK), arginin rich peptides (S. Futaki, Kyoto, Japan), transportans (Ü. Langel, Stockholm Sweden), penetratins (B. Penke, Szeged, Hungary). In addition several new approaches using tailor–made constructs (M. Bienert, Berlin, Germany, J. Gariépy, Toronto, Canada, H. Grass–Masse, Loos, France, A. Pipkorn, Heidelberg, Germany, L. Chaloin, Montpellier, France) or nature derived calcitonin (A. Beck–Sickinger, Leipzig, Germany) and melanocortin–1 receptor ligand (A. N. Eberle, Basel, Switzerland) widened our knowledge about approaches to deliver drugs, peptides, DNA, reporter molecules intracellularly.

A special session was dedicated to review various strategies for drug–targeting tumour vasculature (G. Molema, Groningen, The Netherlands) including antibody–based targeting of angiogenesis (C. Ebbinghaus, Zürich, Switzerland). Antibodies as molec-

ular tools could play a crucial role in targeted imaging and radiotherapy of cancer as emphasised (C.F. Meares, Davis, USA, S.M. Deyev, Moscow, Russia) and also in modulation the immune responses by complement receptor–targeted constructs (J. Prechl, Budapest, Hungary).

After outlining the new MS–based strategies for the identification of epitopes (M. Przybylski, Konstanz, Germany) exciting new results were presented on several MHC–I and/or MHC–II related epitope uptake, processing and presentation events (P. van Endert, Paris, France, M. Del Val, Madrid, Spain, H. Kalbacher, Tübingen, Germany). In the light of these reports findings in relation to vaccine/diagnostics design were specially appreciated (Y. Reiter, Haifa, Israel, É. Rajnavölgyi Debrecen, Hungary, and F. Koning, Leiden, The Netherlands).

As briefly outlined, the Workshop organized in collaboration with the Scientific Committee, D. Andreu, (Barcelona, Spain),

M. Bienert, A. Erdei (Budapest, Hungary), S. Gordon (Oxford, UK), H. Grass–Masse and S. Welling–Wester (Groningen, The Netherlands) and supporting staff in Budapest (G. Mezö, Gy. Kóczán, A. Magyar, J. Prechl, Sz. Bószé, K. Uray) provided a platform for scientists working in the various research fields ranging from basic chemistry to applied pharmacology, a vivid discussion on potentials and limitations of cellular delivery existed throughout the conference.

The Workshop was made possible by the generous support of the EU–5FP by a grant to FH (QLK2–CT–2002–30585) which provided financial assistance not only for invited speakers but also 40 Ph.D. students and post–doctoral fellows.

Contributed by Ferenc Hudecz



The Scientific Committee of the Workshop

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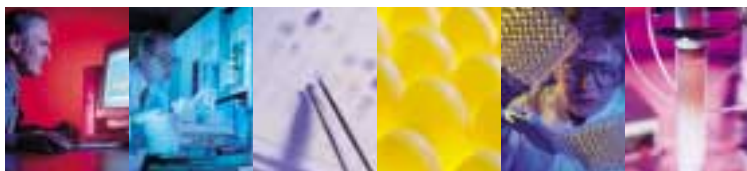
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6th GERMAN Peptide Symposium

Berlin, 23–26 March 2003



The entrance of the main building of the Humboldt University, Berlin, Unter den Linden

The Humboldt–University of Berlin, located in the famous street Unter den Linden, was the venue of the 6th German Peptide Symposium (GPS), 23–26 March 2003. The symposium was organised by Michael Bienert and his staff from the Department of Peptide Chemistry of the Research Institute of Molecular Pharmacology, Berlin–Buch. The conference was attended by about 250 participants, including 25 colleges from Switzerland, US, UK, Netherlands, Sweden, Poland and Czech Republic. English was chosen as the conference language. The meeting was supported by the Research Institute of Molecular Pharmacology, the Deutsche Forschungsgemeinschaft (DFG–FOR 299), the European Peptide Society, and 18 generous industrial sponsors. 17 Companies were present as exhibitors during the symposium, thus also helping in the financing of the 6th GPS.

The 42 lectures (11 main lectures, 31 short

lectures) were presented in 11 sessions. Following the custom of previous German Peptide Meetings, the symposium was started by a Sunday evening Opening Lecture, this year presented by Stephen Kent, Chicago, on recent developments in the field of chemical protein synthesis. Also the Monday morning session was devoted to methods in chemical protein synthesis and protein engineering, with contributions of Arne Skerra, München (Engineering of binding proteins), Raffaele Ingenito, Berlin (Effect of copper salts on thioester–mediated amide bond formation), Wolfgang Haehnel, Freiburg (Combinatorial synthesis of four–helix bundle proteins), and Jutta Eichler, Braunschweig (Engineering of discontinuous protein binding sites). In the session “Peptide Synthesis” Ananth Srinivasan, Londonderry, reviewed the impact of the Metathesis Reaction for the synthesis of cyclic peptides and presented applications in the somatostatin field. Horst

Kunz reported on the development of a novel, silyl–derived anchor for the solid–phase synthesis of glycopeptides, and Christian Birr, Heidelberg, summarised the advantages of Ddz–amino acid derivatives for peptide synthesis in solution. Jörg Rademann, Tübingen, presented improved strategies to synthesise peptide isosteres on solid phase, and the group of Norbert Sewald, Bielefeld, summarised in the lecture of Micha Jost its progress in synthesising Aib–containing, naturally occurring peptides by means of azido amino acid chlorides. Frank Bordusa, Halle, demonstrated the utility of enzyme–mediated coupling reactions on the basis of the Substrate Mimetic Strategy. In the session Peptide Assembly, Neville Boden, Leeds, reported on the engineering of self–assembling peptides, thus bridging amyloid research and material sciences (EPS lecture), whereas Erich Wanker, Berlin, and Aphrodite Kapurniotu, Aachen, gave insights into strate-

gies to develop inhibitors for polyglutamine aggregation in Huntington's Disease and β A4 peptide-mediated amyloid formation, respectively. Photomodulation in azabenzene-containing peptides (Christian Renner, München), a review on β - and γ - peptides (Magnus Rueping, Zürich), the structural organisation of β - peptide-derived nucleopeptides (Ulf Diederichsen, Göttingen), and the synthesis of novel norbornene-type β -sheet mimetics (Christian Hackenberger, Aachen) were the topics of the session "Conformational Studies". Two sessions were devoted to studies on peptide-protein and peptide-lipid interactions. Annette Beck-Sickinger (Leipzig) reviewed strategies applied in order to identify binding sites of peptide ligands at G-protein-coupled receptors and presented examples for the successful design of receptor subtype-specific analogs, and Sven Rothmund (Berlin/Leipzig) reported on the expression and peptide binding of N-terminal CRF receptor domains. Insights into the molecular recognition between rhodopsin and transducin/arrestin were presented by Oliver Ernst, Berlin. In very interesting lectures Wolfgang Höhne, Berlin, and Ulrich Schwarz-Linek, Oxford, provided structural data for the polyspecific recognition by antibodies and for the specific interaction of an unfolded bacterial polypeptide with human fibronectin, respectively. Semi-synthetic methods as well as ligation chemistry improved the accessibility of lipidated Ras-proteins, allowing studies of their interaction with model membranes and living cells (Jürgen Kuhlmann, Dortmund, Daniel Huster, Leipzig). The significance of membrane-bound conformations for the recognition of NPY peptides by their receptors was considered in the lecture of Oliver Zerbe, Zürich. The influence of structural modifications in gramicidin on the ion selectivity of gramicidin channels was studied by Ulrich Koert, Marburg, and Peter Pohl, Berlin, reported that desformylation of gramicidin increases dramatically the water permeability. In the session "Studies in Drug and Diagnostics Development", Horst Kessler, München, characterised the way from proteins over peptides to non-peptidic drug candidates, summarising his work about integrin ligands. Karl-Heinz Wiesmüller, Tübingen,



John M. Stewart (left) and Horst Kessler (right) in the "Audimax", the lecture hall of the 6th German Peptide Symposium

and John M. Stewart, Denver, reviewed the status in the development of MHC II ligands for prevention of experimental CNS autoimmunity, and of bradykinin antagonists as potential drugs for lung and prostate cancer, respectively. Remarkable progress was made in the group of Roderich Süßmuth, Tübingen, in elucidating biosynthetic pathways of glycopeptide antibiotics and the application of this knowledge for the synthesis of novel vancomycins. SAR studies on inhibitors of serine proteinases were reviewed by Krzysztof Rolka, Gdansk. Oliver Seitz, Darmstadt, and Niels Metzler-Nolte, Heidelberg, presented novel approaches for DNA detection on the basis of PNA-dye conjugates and the synthesis and characterisation of organometallic complexes for the detection of bioactive peptides. The synthesis of complexes of peptides with transition metals in order to mimic the catalytic center of enzymes was reported by Siegmund Reissmann, Jena. In the session "Peptide Libraries and Arrays" Roland Frank, Braunschweig, and Ulf Reimer, Berlin, presented summaries on their work to develop and to use peptide arrays for the epitope-targeted proteom analysis and for kinase profiling. A new method for the discovering of low-molecular compounds with catalytic activity was presented by Helma Wennemers, Basel. The final session was devoted to mechanisms of cellular uptake of peptides. Liam Good, Stockholm, reported on successful ap-

proaches to kill micro-organisms by peptide-mediated delivery of PNA-based antisense compounds, and Roland Brock, Tübingen, compared the uptake efficiency of fluorescently labelled cell-permeable peptides. Iris Thondorf, Halle, studied structural requirements of the transport of di- and tripeptides by PEPT1 transporter and determined the pharmacophore structure by molecular modelling.

In addition to the lectures, there were two poster sessions with nearly 100 posters, most of them of remarkable quality. Prizes for three outstanding poster contributions of PhD students were awarded to Ines Heinemann, Dortmund, Manja Lang, Leipzig, and Thomas Henning, Berlin.

Fortunately, in spite of the extensive scientific program, there was also time to meet colleges outside the lecture hall and to discuss non-scientific subjects: The Welcome Reception took place Sunday evening in the Senatssaal of the Humboldt University, and the Symposiums Dinner was organised in the Opernpalais, a building also located in the street Unter den Linden, constructed 1733 by Friedrich Wilhelm Dietrichs.

The 7th German Peptide Symposium will be organised by Ronald Frank and Jutta Eichler in Braunschweig.

Contributed by Michael Bienert

Biologically Active Peptides VIII

Prague, 23–25 April 2003



Participants of the Conference in front of the Institute

In beautiful spring weather on April 23rd, the renovated lecture hall of the Institute of Organic Chemistry and Biochemistry of the Academy of Sciences of the Czech Republic welcome more than 50 Czech and Slovak peptide researchers together with 8 invited distinguished guests from abroad who participated at the national peptide conference called Biologically Active Peptides VIII (these conferences take place biannually, the official language being Czech and English). The Conference was opened by the contemporary director of the Institute, Dr. Z. Havlas, DrSc, and the national representative of Czech peptide researchers in EPS, Dr. Jiřina Slaninova, Ph.D.

In the following days (23rd – 25th April) altogether 18 lectures and 20 posters were presented. Plenary lectures were delivered by Dr. M.Flegel (PolyPeptide Lab., Prague, Czech Rep.) concerning peptides as bulk pharmaceutical chemicals, Dr. V. Kašička (Inst.Org. Chem.Biochem., Acad.Sci.Czech

Rep., Prague, Czech Rep.) on recent advances in high-performance capillary electrophoresis of peptides, Dr. L.Vezenkov (Dept.Org.Chem. Univ.Chem.Technology, Sofia, Bulgaria) on new analogues of anti-coagulant peptide TIC, Dr. T. Pajpanova (Inst.Mol.Biol., Bulg.Acad.Sci, Sofia, Bulgaria) on design and synthesis of new N-containing building blocks, Dr. B.Penke (Dept. Med.Chem. A.Szent-Gyorgy Med. Univ, Szeged, Hungary) on protein aggregation, neurodegeneration and neuroprotection, Dr. M. Ellmerer (Inst.Med. Technol. Health Manag., Graz, Austria) on long-acting insulin analogues and integrated physiology and Dr. D.Kodřík (Inst.Entomology, Acad. Sci Czech.Rep., České Budějovice, Czech Rep.) on characterization and function of adipokinetic peptide from the bug *Dysdercus cingulatus*. From other lectures the participants appreciated contributions of Mgr. O.Šedo (MALDI time of flight mass spectrometry analysis of humanin-like peptides),

Ing. J.Šebestík (May bis-intercalator peptides influence prion aggregation?), Bc. A. Cencialová (Synthesis and qualities of fluorescent labelled derivatives of human insulin), Mgr. L. Klasová (Truncated analogues of insulin modified in position B26) and Dr. P. Jelínková (Characterization of peptide proteinase inhibitors isolated from boar seminal plasma). In the poster section, many young peptide chemists and biochemists presented their work. Let us mention the contributions of the Greek students from Patras, M. Fragiadaki and E. Bissyris (New oxytocin analogues), A. Galanis (ACE active sites) and A. Zompra (New Leuprolide analogues), which belonged to the best ones. The competition was however strong – very nice work was presented as posters also by P. Tábořský and O. Šedo (Masaryk Univ., Brno), V. Šolínová and J. Maixnerová (IOCB, Prague). All the contributions will be published in English as short communications (2–3pp) in the Proceedings in Col-

Active Peptides

lection Symposium Series. At the end of the Conference, the previous and the present Czech national representatives in EPS (M. Flegel and J. Slaninová) informed the participants about the state of art of the most important upcoming event in the year 2004 – the 28th EPS and 3rd IPS which will take place in Prague under joint organisation of Czech and Israeli peptide groups (Co-chairs: M. Flegel, M. Fridkin, C. Gilon, J. Slaninová). They also mentioned the European Peptide Society and the decisions made in Sorrento concerning the Executive committee, the membership etc.

Thanks to the sponsor contributions (INGOS Ltd., IRIS Biochem. GmbH, MERCK Ltd.,

IntracoMicro Ltd., PolyPeptide Labs Ltd., Schoeller Ltd., Sigma Aldrich Ltd.), the get-together party could take place in the nearby Masaryk Colleague on Wednesday and the participants could enjoy the W. Tennessee's play in the theatre Viola on Thursday evening.

We can conclude that the meeting fulfilled our expectations. The peptide research in Czechia and Slovakia is living, the interest in peptides is even increasing (there were namely many informal participants of the Conference coming only for special sections). We hope that the interest in peptides will survive and that our probable joining the European Community will not mean

their exodus. Nowadays our main effort will be devoted to the organisation of the 28th EPS and 3rd IPS which will take place in Prague, in the Congress Centre, in September 5–10, 2004. We hope many members of the European Peptide Society will come to Prague next year.

Contributed by Jiřina Slaninová



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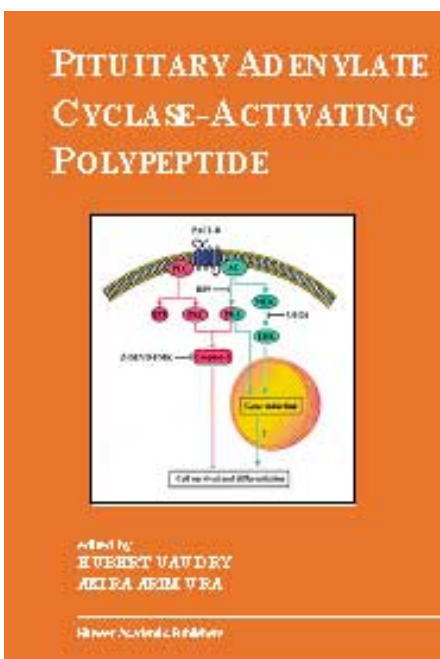
H. Vaudry and A. Arimura (Eds.)

Kluwer Academic Publishers.

Norwell, MA, USA and Dordrecht,

The Netherlands, xiii + 406pp. 2002.

ISBN 1–4020–7306–2



Pituitary adenylate cyclase-activating polypeptide (PACAP) is undoubtedly one of the most fascinating neuropeptides ever identified. PACAP belongs to the largest family of regulatory peptides, which comprises several other prominent neuroendocrine peptides including vasoactive intestinal polypeptide, secretin, glucagon, and growth hormone-releasing hormone. The structural and physiological relationships of these paralogues, as well as their receptors, provide a unique model for investigating the processes of molecular evolution leading to the diversification of multigene families. The primary structure of PACAP has been remarkably well conserved from the sea squirt to hu-

mans, suggesting that this peptide must be involved in vital functions throughout the animal kingdom. Indeed, PACAP appears to be implicated in a large array of physiological processes such as development, growth, endocrine, cardiovascular, respiratory, reproductive and digestive functions, immune responses, and circadian rhythms. There is also clear evidence that PACAP exerts both trophic and antiproliferative effects on normal and tumor cells. The beneficial influence of PACAP agonists and antagonists in various pathological states including heart failure, ischemia, asthma, impotence and cancer has motivated the development of novel selective PACAP ligands that could potentially be used as antihypertensive, neuroprotective, bronchodilatory, vasodilatory and/or antiproliferative drugs. The occurrence of multiple PACAP receptor subtypes and spliced isoforms that exhibit tissue-specific expression and possess differential affinity for various ligands, generates hopes for the development of new therapeutic agents acting selectively on the desired target cells. This textbook will undoubtedly be the reference book on PACAP for the years to come.

The different chapters of this book cover the current knowledge about this fascinating neuropeptide, from the molecular characterization of the PACAP gene and PACAP receptors to the elucidation of the physiological activities and possible therapeutic value of the peptide. The table of contents comprises: PACAP, discovery, gene, receptors (A Arimura); Molecular evolution of PACAP precursor and PACAP receptors (BKC Chow, RTK Pang and SSM Ng); Development of selective ligands for PAC1, VPAC1 and VPAC2 receptors (P Robberecht, P Vertongen, I Langer and J Perret); Molecular pharmacology and structure-function analysis of PACAP/VIP receptors (M Laburthe, A Couvineau and P Nicole); PACAP receptor signaling (S Shioda, CJI Zhou, H Ohtaki and T Yada); Function of

PACAP in the central nervous system (B Gonzalez, D.Vaudry, M. Basille, C. Roussele, A. Falluel-Morel and H. Vaudry); Function of PACAP in the hypothalamo-pituitary complex (MM Malagon, JP. Castaño, S. Garcia-Navarro, A.J. Martínez-Fuentes and F Gracia-Navarro); PACAP in the endocrine pancreas (B. Ahrén); Function of PACAP in the adrenal cortex (GG. Nussdorfer); PACAP: an «emergency response» co-transmitter in the adrenal medulla (C. Hamelink, E. Weihe and L.E. Eiden); PACAP in the urogenital tract (J. Fahrenkrug, J. Hannibal and S. Gräs); Function of PACAP in the cardiovascular system (A. Miyata); Function of PACAP in the respiratory system (J.C. Prieto); Function of PACAP in the immune system (M. Delgado, J. Leceta and R.P. Gomariz); PACAP receptor knockout and transgenics. What have we learnt? (P. Brabet, F. Jamen, N. Rodriguez-Henche, G. Bertrand and J. Bockaert); Consequences of PACAP gene knockout (N.M. Sherwood, S.L. Gray and K.J. Cummings); The biological significance of PACAP and PACAP receptors in human tumors: from cell lines to cancers (V. Lelièvre, N. Pineau and J.A. Waschek).

Contributed by Jean Martinez

BOOK Reviews

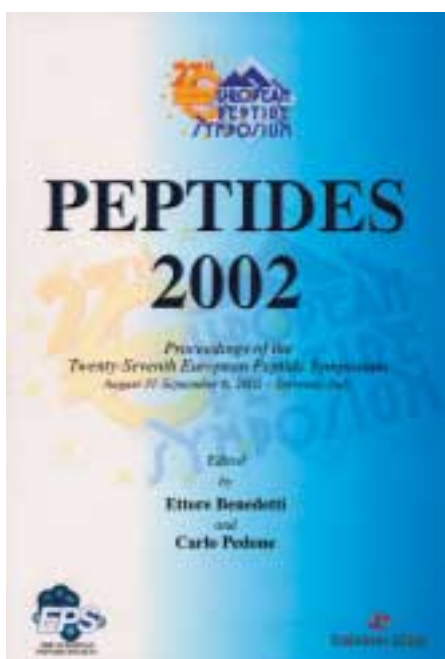
Peptides 2002. Proceedings of the Twenty-Seventh European Peptide Symposium

E. Benedetti and C. Pedone (Eds.)

Edizioni Ziino. Castellammare di Stabia

(Na), Italy, LVI+1057pp. 2002.

ISBN 88-900948-1-8.



The 27th European peptide Symposium was held in Sorrento on August 31st–September 2002 under the chairmanship of Prof. Ettore Benedetti from the University of Naples. The Proceedings Peptides 2002, edited by the chairman and by Prof. Carlo Pedone, and published by Edizioni Ziino, Naples, Italy, appeared with valuable speed and efficiency two months ago. The extremely successful Symposium deserved *Proceedings* of outstanding quality. The Proceedings book Peptides 2002 meets this requirement. The editorial work is very accurate and the book exhibits a very nice typographic aspect. There are 636 research articles, including those relative to oral presentations and to a

high number of Posters presented by scientists coming from 43 countries. The text is provided with a very accurate index system based upon titles, topics and authors, which makes very easy to find the desired articles. The book is provided with a CD version, which makes even more easy the consultation of the papers. The scientific contributions cover a broad spectrum of topics related to Peptide Science. This book is a must for every peptide chemist and for the Libraries of scientific institutions.

*Contributed by Evaristo Peggion
and Raniero Rocchi*

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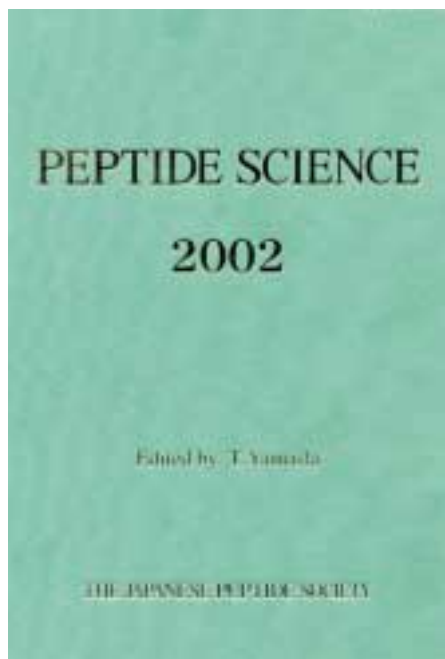
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**Peptide Science 2002
Proceedings of the 39th JPS**

T. Yamada (Ed.)

The Japanese Peptide Society,
444 pp. HC, 2003.
ISBN 4-931541-03-8

This volume is consisted of one Akabori Memorial Award Lecture, two distinguished Young Scientist Award Lectures, two invited lectures and 127 well-presented and well-documented with related literature contributions from more than 400 Japanese researchers reflecting their most recent research achievements in the broad field of

peptide science. The areas covered range widely and include amino acid, peptide and peptidomimetics synthesis methodologies in liquid and on solid phase with contributions in combinatorial peptide synthesis, peptide detection and analysis methodologies, peptide structural studies and ligand-receptor interaction studies and delivery-related studies of peptide-based drugs whereas the majority of contributions is focused to the synthesis and biological studies of a large variety of peptides with potential medicinal interest. It will be certainly of special interest to amino acid and peptide chemists, to whom it is warmly recommended.

Contributed by Dionyssios Papaioannou

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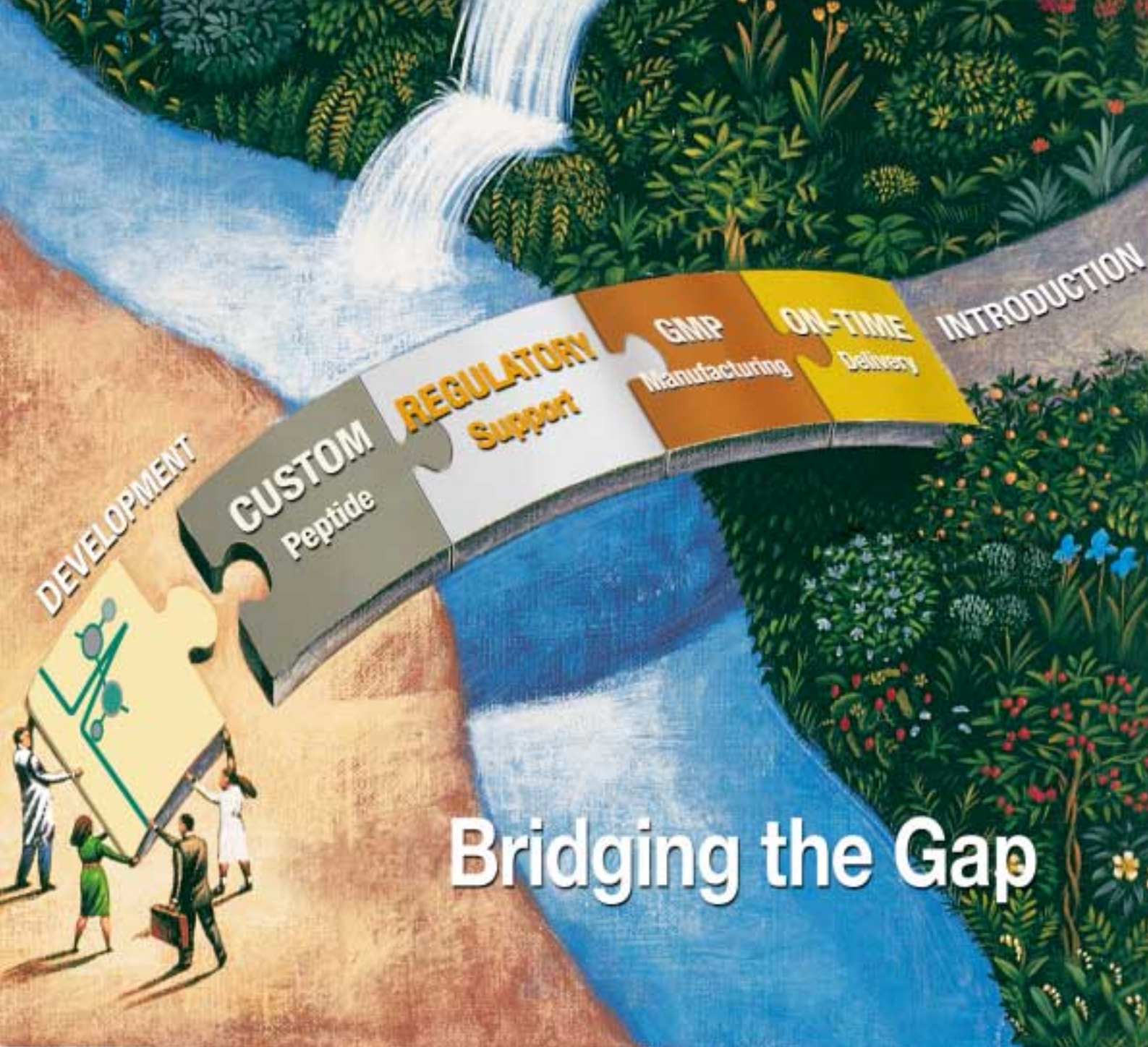
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13th AMERICAN PEPTIDE SYMPOSIUM

Boston, Massachusetts, 19–23 July 2003

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17th POLISH PEPTIDE SYMPOSIUM

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31 August – 4 September 2003

For further information please contact:

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University of York, England, UK

30 August – 3 September 2005

For further information please contact:

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MISCELLANEOUS NOTES and News in Brief



Professor William F. DeGrado will receive the 2003 Merrifield Award from the American Peptide Society at the 18th American Peptide Symposium!

- The Merrifield Award Ceremony and Lecture will be held on Thursday July 22, 2003 at the 18th American Peptide Symposium at the Boston Marriott Copley Place.
- Professor DeGrado's Merrifield Award Lecture is entitled "*de novo design of proteins and protein mimetics*"

Professor DeGrado is George W. Raiziss Professor of Biochemistry and Biophysics at the University of Pennsylvania School of Medicine. Dr. DeGrado has a distinguished record of scientific contributions to peptide and protein research as well as drug discovery. His primary research interest is in the *de novo* design, in which one designs proteins beginning from first principles. This approach critically tests our understanding of protein folding and function, while also laying the groundwork for the design of proteins and biomimetic polymers with properties unprecedented in nature. A comprehensive summary of his work is available at his website: (<http://www.med.upenn.edu/~biocbiop/faculty/pages/degrado.html>).

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