

PROGRAMME

Sunday, September 10

14h00 Registration

Berlioz Auditorium: 18h00

Chairs : Raniero ROCCHI and Jean MARTINEZ

Opening Session

18h00-18h30: Leonidas Zervas Lecture:

Antonello Pessi: The Role of Peptide Research in Drug Discovery: The Case of Hepatitis C

18h30-19h30: Joseph Rudinger Lecture:

Bernard P. Roques: Insights into Peptide and Protein Functions: a Convergent Approach

20h00 Welcome Reception at the Corum Centre

Monday, September 11

Berlioz Auditorium

8h30 Introducing Session

9h00 Chairs: Raniero **ROCCHI** and Michel **MARRAUD**

L01 Robert HUBER: The Proteasome and ATP-dependent Proteolysis

L02 Luis MORODER: Multivalent Inhibition of Eukaryotic Proteasomes and Human β -tryptase

10h20 - 10h50: Coffee Break

Pasteur Auditorium: 10h50 - 12h10

Concurrent Session: Bioactive Peptides

Chairs: Paul CORDOPATIS, Annette BECK-SICKINGER

10h50: OC01 Structural inducing probes (SIP) - blows new hope into the general use of peptides as drugs.

Larsen Bjarne D, Jensen Lene H, Mork Niels E, Bjerrum Morten J, Meissner Axel, Nielsen Gerd, Frokjaer Sven.

11h10: OC02 The antitumor somatostatin analog (TT232) induced signaling cascades.

Kéri György, Stetak Attila, Vantus Tibor, Bökönyi Gyöngyi, Cseermely Péter, Vandenheede Jackie, Ullrich Axel, Sepr di Janos, Horvath Aniko, Teplan Istvan, Szegedi Zsolt, Szende Béla.

11h30: OC03 Hydroxamic acid analogs of naturally-occurring cyclic tetrapeptides, trapoxin, WF-3161, Cyl-1, HC-toxin and chlamydocin inhibit histone deacetylases.

Nishino Norikazu, Tomizaki Kin-Ya, Tsukamoto Makiko, Yoshikawa Daisuke, Shinta Ryuzo, Nishino Hidekazu, Tanaka Yuji, Kato Tamaki, Komatsu Yasuhiko, Nishiyama Makoto, Furumai Ryohei, Yoshida Minoru.

11h50: OC04 Optimization of vasoactive intestinal peptide towards better tumor imaging properties.

Bhargava Sarah, Knaute Tobias, Becker Andreas, Licha Kai, Schneider-Mergener Jens, Volkmer-Engert Rudolf.

Einstein Auditorium: 10h50 - 12h10

Concurrent Session: Structural Studies - Protein Folding

Chairs: André AUBRY, Robert HODGES

10h50: OC05 The Trp-cage: a notably stable mini-protein fold.

Andersen Niels H, Neidigh Jonathan W, Fesinmeyer R Matthew.

11h10: OC06 Structural studies of yeast mitochondrial ATP synthase subunits.

Aznar Céline, Geoffre Serge, Manigand Claude, Picard Philippe, Précigoux Gilles.

11h30: OC07 Thermodynamic control in the folding of Prouroguanylin by the N-terminal region.

Hidaka Yuji, Shimono Chisei, Shimonishi Yasutsugu.

11h50: OC08 Structure and membrane properties of trichogin GB IX from *Trichoderma Longibrachiatum*, the longest sequence among lipopeptaibols.

China Nicolas, Blond Alain, Goulard Christophe, Bodo Bernard, Rebuffat Sylvie.

12h10 - 14h00: Lunch

Pasteur Auditorium

14h00-15h20 Chairs: John DAVIES and Charles DEBER

L03 Robert BRASSEUR: Tilted Peptides: a Motif for Membrane Destabilisation

L04 Vincenzo PAVONE: Miniaturized Proteins: Application to the Design of Metallo-protein Models

15h20 - 15h50: Coffee Break

Pasteur Auditorium: 15h50 - 17h10

Concurrent Session: Bioactive Peptides

Chairs: Maurice MANNING, Matiyahu FRIDKIN

15h50: OC09 An interesting approach for cancer therapy: inhibition of the association of HDM2 with the tumor suppressor p53.

Garcia-Echeverria Carlos, Chène Patrick, Blommers Marcel, Furet Pascal.

16h10: OC10 Chemical synthesis of maxadilan and its related peptides as agonists and antagonists of PACAP type 1 receptors.

Nokihara Kiyoshi, Yasuhara Tadashi, Nakata Yoshihiro, Wray Victor, Lerner Ethan.

16h30: OC11 Peptide mimotopes of the nicotinic receptor.

Bracci Luisa, Lozzi Luisa, Lelli Barbara, Pini Alessandro, Neri Paolo.

16h50: OC12 Application of neuropeptides in insect control.

Altstein Miriam, Ben-Aziz Orna, Scheffler Irit, Zeltser Irina, Gilon Chaim.

Einstein Auditorium: 15h50 - 17h10

Concurrent Session: Structural Studies - Protein Folding

Chairs: Teresa KUBIAK, Ernest GIRALT

15h50: OC13 CPWR spectroscopy: a new method for studying peptide-integral membrane protein interactions.

Hruby Victor J, Cowell S, Salamon Z, Tollin G.

16h10: OC14 2D-NMR and molecular modelling study of a peptide corresponding to the 603-609 disulfide loop of HIVV-1 envelope glycoprotein GP41 and of its analogues.

Phan-Chan-Du Angélique, Limal David, Semetey Vincent, Briand Jean-Paul, Muller Sylviane, Petit Marie-Christine, Cung Manh Thông.

16h30: OC15 NMR interaction studies on the isolated apical domain of GroEL with synthetic peptides.

Kobayashi Naohiro, Freund Stefan M V, Chatellier Jean, Fersht Alan R.

16h50: OC16 Sequence dependent membrane uptake of primary amphipathic shuttle peptides.

Van Mau Nicole, Vié Véronique, Divita Gilles, Le Grimellec Christian, Heitz Frédéric.

17h10: Poster Session A:
even-numbered posters 1-200
even-numbered posters 401-600

Tuesday, September 12

Pasteur Auditorium 9h00-10h20 Chairs: David ANDREU and Jean DUFORCQ
L05 Renato GENNARO: Cathelicidin-derived Antimicrobial Peptides : *in vitro* and *in vivo* Activity
L06 Samuel H. GELLMAN: Heteropolymer Folding : Proteins and beyond

10h20 - 10h50: Coffee Break

Pasteur Auditorium: 10h50 - 12h10
Concurrent Session: Immunochemistry - Immunopharmacology
Chairs: Ferenc HUDECZ, Jean-Edouard GAIRIN

10h50: OC17 Synthesis and biological evaluation of new interferon gamma receptor agonists: evidence of an intracellular action.
Bonnet Dominique, Loing Esqtelte, Melnyk Oleg, Thiam Kader,Gras-Masse Hélène, Auriault Claude.

11h10: OC18 Effect of lipoconjugation on MBP peptide epitopes for CD4+ T cell responsiveness.
Papini Anna Maria, Nardi Elena, Mazzanti Benedetta, Biagioli Tiziana, Traggiai Elisabetta, Mazzucco Silvia, Chelli Mario, Ginanneschi Mauro, Kalbacher Hubert, Massacesi Luca, Vergelli Marco.

11h30: OC19 20S standard proteasome versus 20S immunoproteasome digestion profiles of MHC class I antigen precursors.
Bulet-Schiltz O, Morel S, Lévy F, Claverol S, Van Den Eynde B, Monsarrat B, Gairin J E.

11h50: OC20 Sequential oligopeptide carriers (SOCs): New developments and applications.
Sakarellos-Daitsiotis Maria, Krikorian Dimitrios, Keramisanou Dimitra, Tsikaris Vassilios, Vlachoyiannopoulos Panayiotis G., Tzioufas Athanassios G., Moutsopoulos Haralampos M., Sakarellos Constantinos.

Einstein Auditorium: 10h50 - 12h10
Concurrent Session: Molecular Design - experimental and computational
Chairs: Gregory NIKIFOROVICH, Gilles PRECIGOUX

10h50: OC21 Standardization of aggregation grade and neurotoxicity of β -amyloid peptides.
Penke Botond, Soos Katalin, Szabo Zoltan, Klement Eva, Hetenyi Csaba, Molnar Zsolt, Jost Krisztina, Rojik Imre, Harkany Tibor, Zarandi Marta.

11h10: OC22 Chimeric TASP molecules as potential inhibitors in E-selectin-mediated cell adhesion.
Fernandez Jimena, Grell Daniel, Giraud Sylvain, Abbal Claire, Spertini Olivier, Tuchscherer Gabriele.

11h30: OC23 The cystine-stabilized β -sheet motif is a common and useful motif for protein engineering.
Heitz Annie, Le Nguyen Dung, Hernandez Jean-François, Gracy Jérôme, Chiche Laurent.

11h50: OC24 Conformational analysis of peptides neutralising LPS pathogenicity - NMR and molecular modelling study.
Kidric Jurkica, Primoz Pristovsek.

12h10 - 14h00: Lunch

Pasteur Auditorium 14h00-15h20 Chairs: Marc LABURTHE and Daniel VEBER
L07 Steven M. FOORD : Receptor Activity modifying Proteins
L08 Daniel FOURMY : Mapping of the CCK-A and CCK-B/gastrin Receptor

15h20 - 16h30: Coffee Break and Poster Session B:
odd-numbered posters 1-400:

Pasteur Auditorium: 16h30 - 18h10
Concurrent Session: Ligation Chemistry - Protein Modification - Analytical Methodologies
Chairs: Keith ROSE, Saburo AIMOTO

16h30: OC25 A novel generation of glycomimetics for the targeting of dendritic cells through the mannose receptor.
Grandjean Cyrille, Angyalosi Gerhild, Pancré Véronique, Gras-Masse Hélène, Auriault Claude, Melnyk Oleg.

16h50: OC26 New amino acids with side-chain oxyamino and aldehyde functions, and their use in chemoselective ligation.
Spetzler Jane C, Hoeg-Jensen Thomas.

17h10: OC27 Subnanomolar-scale methods for derivatization of peptides for sequence analysis by MALDI-TOF MS.
Jouin Patrick, Galeotti Nathalie, Pascal Robert.

17h30: OC28 Quantitative analysis of complex peptide reaction systems by mass spectrometry.
Weber Peter J A, Chavochi-Negad Asad, Ghadiri M Reza.

17h50 : OC29 Total synthesis of ion channel proteins by native chemical ligation
Kochendofer Gerd G

Einstein Auditorium: 16h30 - 18h10
Concurrent session: Chemistry of Amino acids
Chairs: Gérard CHASSAING, Dirk TOURWE

16h30: OC30 Functional α -H and α,α -disubstituted amino acids based on target oriented side-chain design.
Broxterman Quirinius B, Kaptein Bernard, Sonke Theo, Schoemaker Hans E.

16h50: OC31 Silaprolin: a surrogate of proline. Influence on peptide conformation and bioactivity.
Cavelier Florine, Vivet Bertrand, Aubry André, Didierjean Claude, Vicherat André, Marraud Michel, Martinez Jean.

17h10: OC32 Diastereoselective synthesis of β^2 -amino acids.
Ponsinet Rachel, Chassaing Gérard, Lavielle Solange.

17h30: OC33 A novel group of peptidic biological response modifiers.
Blishchenko Elena Yu, Karelin Andrei A, Ivanov Vadim T.

17h50: OC34 Are β -amino acids γ -turn mimetics.
Sewald Norbert, Müller Annett, Schumann Frank, Kolsch Mario.

Wednesday, September 13

Pasteur Auditorium 9h00-10h20 Chairs: Vadim IVANOV and Robert RAMAGE
L09 Yasutsugu SHIMONISHI: Diversity of Post-translational Modifications of Proteins Proved by MS
L10 Joachim ARRIBAS: Protein Ectodomain Shedding

10h20 - 10h50: Coffee Break

Pasteur Auditorium: 10h50 - 12h50

Concurrent Session: Peptide/Protein Synthesis
Chairs: Dietrich BRANDENBURG, Arno SPATOLA

10h50: OC35 Solid-phase synthesis of cyclic and polycyclic peptides.

Tabor Alethea B.

11h10: OC36 Copper(II)-containing racemization suppressors and their use in segment coupling reactions.

Tolle John C., Califano Jean-Christophe, Devin Chantal, Blodgett James K.

11h30: OC37 Covalent capture purification : towards the routine synthesis of proteins by solid phase peptide synthesis.

Vizzavona Jean, Villain Matteo, Rose Keith.

11h50: OC38 Striking progress in the development of peptides as drugs

Verlander Michael

12h10: OC39 Large scale chemical synthesis of T-20, a 36 amino acid HIV-1 membrane fusion inhibitor.

Bray Brian. Friedrich Paul, Kang M C, Lichty Maynard, Mader Catherine, Merutka Gene.

12h30: OC40 Sugar amino acids synthesis and applications.

Kessler Horst.

Einstein Auditorium: 10h50 - 12h50

Concurrent Session: Pharmacology of Peptides
Chairs: Catherine LABBE-JULLIE, John STEWART

10h50: OC41 Design of vasopressin and oxytocin agonists, antagonists, radioiodinatable and fluorescent ligands with good affinities for human receptors.

Manning Maurice. Cheng Lingling, Stoev Stoytcho, Durroux Thierry, Mouillac Bernard, Guillon Gilles, Morin Denis, Derick Sylvain, Barberis Claude.

11h10: OC42 Structure-based design of the first high potent inhibitors of botulinum B-toxin.

Anne C. Turcaud S, Cornille F, Fournié-Zaluski M-C, Roques B P.

11h30: OC43 Contribution of central and C-terminal regions of gastrin to receptor recognition.

Gembitsky Dmitry S. Ahmed Shawn , Ryder Caroline, Kopin Alan, Murphy Richard F, Lovas Sandor.

11h50: OC44 Bovine serum albumin differentially affects the rates of dipeptidylpeptidase-IV mediated hydrolysis of growth hormone-releasing factor and its Ala15-modified analog.

Kubiak Teresa M. Martin Roger A, Caputo James F.

12h10: OC45 New amino-acidic antagonists of the excitatory amino acid receptor.

Paruszewski Ryszard. Strupinska Marzanna, Stables James P.

12h30: OC46 Novel cathepsin K inhibitors for control of bone resorption.

Veber Daniel F.

12h50 - 14h20: Lunch

FREE AFTERNOON or POSTERS

Thursday, September 14

Pasteur Auditorium 9h00-10h20 Chairs: Yoshiaki KISO and Solange LAVIELLE
L11 Carl P. DECCICO: The Rational Design of Peptidomimetic Inhibitors of TNF- α Processing and Aggrecanase
L12 Daniel H. RICH: Design and Synthesis of New Inhibitors of Therapeutically Important Peptidases

10h20 - 10h50: Coffee Break

Pasteur Auditorium: 10h50 - 12h10
Concurrent Session: Bioactive Peptides
Chairs: Riu WANG, Jean RIVIER

10h50: OC47 In vivo active antimicrobial peptides and their bacterial protein targets.
Otvos Laszlo, Bulet Philippe, Craik David, McManus Ailsa, Rogers Mark, Bokonyi Krisztina, Condie Barry A, O Insug, Cudic Mare, Blaszczyk-Thurin Magdalena.

11h10: OC48 Development of lead structures for bradykinin agonist and antagonists.
Reissmann Siegmund, Paegelow Inge, Stewart John M.

11h30: OC49 Identification of amino acid residues involved in the interaction between VIP and its human receptor VPAC1 using photoactivable VIP analogs.
Van Rampelbergh J., Couvineau A, Maoret J J, Laburthe M.

11h50: OC50 Understanding RNA-binding properties of a plant virus movement protein using synthetic peptides.
Vilar Marçal, Marcos José F, Pérez-Paya Enrique.

Einstein Auditorium: 10h50 - 12h10
Concurrent session: Molecular Design - Self Assembly
Chairs: Marie-Claude FOURNIE-ZALUSKI, Fernando ALBERICIO

10h50: OC51 Computer modeling of transmembrane proteins from scratch : test case of bacteriorhodopsin.
Nikiforovich Gregory V., Galaktionov Stan, Balodis Juris, Marshall Garland R.

11h10: OC52 The parathyroid hormone receptor : molecular insight into ligand binding.
Piserchio Andrea, Monticelli Luca, Mierke Dale F.

11h30: OC53 Modelling peptide conformations in a peptide-like solvent
Anderson R J., Clark B P, Kelly M, Mackay S P, Smith A I, Wolfson A J

11h50: OC54 Oligomerization states of transmembrane α -helices studied using peptide models.
Deber Charles, Partridge Anthony W, Melnyk Roman A.

12h10 - 14h00: Lunch

Pasteur Auditorium 14h00-15h20 Chairs: Murray GOODMAN and Vincent DIVE
L13 Renata PASQUALINI : Molecular Anatomy of Blood
L14 Nancy A. THORNBERRY : Caspases and their Roles in Apoptosis

15h20 - 15h50: Coffee Break

Pasteur Auditorium: 15h50 - 17h10
Concurrent Session: Bioactive Peptides
Chairs: Sandor BAJUSZ, John TOLLE

15h50: OC55 The antimicrobial peptides derived from chromogranins and proenkephalin-A.
Metz-Boutique Marie-Hélène, Goumon Yannick, Lugardon Karine, Strub Jean-Marc, Aunis Dominique.

16h10: OC56 New peptides from actinomyces for plant protection.
Boikova Anna, Boikova Irina, Shenin Yuriy, Novicova Irina.

16h30: OC57 Identification of biologically active peptides in Laminin alpha chains.
Nomizu Motoyoshi, Makino Masayoshi, Okazaki Ikuko, Kato Kozue, Kuratomi Yuichiro, Kleinman Hynda K, Yamada Yoshihiko, Nishi Norio.

16h50: OC58 Calcitonin derived peptide carriers are novel tools for selective drug delivery.
Beck-Sickinger Annette G., Krauss Ulrike, Meinecke Martina, Merkle Hans Peter.

17h10: OC 59 Inhibition of the Ubiquitin-proteasome pathway in Alzheimer disease
Lam Y Amy, Pickart Cecile, Alban Andrew, Landon Michael, Jamieson Craig, Robert Ramage, Mayer R John, Layfield Robert

Einstein Auditorium: 15h50 - 17h10
Concurrent Session: Peptides Conjugates - Ligation
Chairs: Hélène GRAS, Paolo MASCAGNI

15h50: OC60 Diastereoselective synthesis of α -hydroxyesters - a route to a new class of C-linked glycopeptides.
Coutrot Frédéric, Grison Claude, Coutrot Philippe.

16h10: OC61 Preparation and biological characteristics of peptide-liposome conjugates for drug targeting.
Froidavaux Sylvie, Huwyler Jörg, Cerletti Andrin, Hoch Matthias, Christe Martine, Tanner Heidi, Eberle Alex N.

16h30: OC62 Design and synthesis of amino acid- or peptide-modified ruthenium tris(bipyridine) complexes for photoresponsive molecular devices.
Ishida Hitoshi, Heseck Dusan, Nanmyo Tsutomu, Aoki Fumiko, Inoue Yoshihisa.

16h50: OC63 Synthesis and characterization of a 64 AA carboxypeptidase by chemoselective ligation.
Brask Jesper, Nielsen Sine M, Jensen Knud J.

17h10: OC64 Interaction of RANTES with glycosaminoglycans and CCR5, receptors for HIV-1 entry
Martin Loïc, Garnier Pascale, Blanpain Cédric, Parmentier Marc, Vita Claudio

17h30: Poster Session C:
odd-numbered posters 401-600
even-numbered posters 201-400

Friday, September 15

Pasteur Auditorium 9h00-10h20 Chairs: Alex EBERLE and Bernard ROQUES
L15 Peter E. NIELSEN : Gene Regulation by Peptide Nucleic Acid (PNA)
L16 Lea EISENBACH : Of Mice and Man: Identification of TAA Peptides of Human Cancer

10h20 - 10h50: Coffee Break

Pasteur Auditorium: 10h50 - 12h10
Concurrent Session: Combinatorial Chemistry
Chairs: Gunther JUNG, André TARTAR

10h50: OC65 Inhibition of the β -amyloid peptide neurotoxicity and aggregation by imidazol-pyrido-indoles.
Blondelle Sylvie E., Crooks Ema, Reixach Natalia.

11h10: OC66 Combinatorial multiple parallel synthesis on modular grafted solid supports.
Ede Nicholas J., Bray Andrew M.

11h30: OC67 Covalent DNA-protein fusion : a novel tool for the in vitro display of peptides and proteins.
Kurz Markus, Lohse Peter A.

11h50: OC68 Combinatorial split synthesis libraries of glycopeptides for the identification of high affinity ligands for carbohydrate receptors.
Meldal Morten, Halkes Koen, St Hilaire Phaedria.

12h10: OC69 The question of mixtures in combinatorial libraries : the balance between completeness and efficiency - single compound arrays, small mixtures or large mixtures ?
Houghten Richard A.

Einstein Auditorium: 10h50 - 12h10
Concurrent Session: Peptidomimetics
Chairs: Ettore BENEDETTI, Albert LOFFET

10h50: OC70 Polyol peptidomimetics.
Geyer A., Tremmel P.

11h10: OC71 New reactions and structures for peptidomimetic drug design.
Goodman M., Baker T J, Rew Y, Creighton C J.

11h30: OC72 "Une pierre deux coups", synthesis of quinolozidinone and pyrroloazepinone amino acids from the same linear precursor.
Gosselin Francis, Lubell William D.

11h50: OC73 "Double-drugs" : a novel class of prodrug forms of HIV protease inhibitors conjugated with AZT by spontaneously cleavable linkers.
Kiso Yoshiaki, Matsumoto Hikaru, Hamawaki Tomonori, Ota Hisashi, Kimura Tooru, Hayashi Yoshio.

12h10: OC74 Structural stabilization and minimization of the potassium-channel blocker, SHK toxin.
Pennington M W., Lefievre Y, Norton R S, Lanigan M D, Rauer H, Chandy K G.

12h30 - 14h00: Lunch

Pasteur Auditorium: 14h00 - 15h40
Concurrent session: New synthetic approaches
Chairs: Fabrice CORNILLE, Morten MELDAL

14h00: OC75 A versatile 4-(4-tolyl(chloro)methyl)phenoxy linker for the solid phase synthesis of pseudopeptides.
Atkinson Gail E., Fischer Peter M, Chan Weng C.

14h20: OC76 Total synthesis by combined solid phase and solution approach of the P41 fragment.
Chiva Cristina, Albericio Fernando, Giralt Ernest, Molina Franck, Granier Claude, Inui Tatsuya, Nishio Hideki, Nishiuchi Yuji, Kimura Terutoshi, Sakakibara Shumpei.

14h40: OC77 Reductive samariation as a means for the selective C-alkylation of glycine residues : application to the synthesis of unnatural peptides.
Ricci Marina, Blaksjaer Peter, Skrydstrup Troels.

15h00: OC78 O-succinimidyl carbamate derivatives from amino acids and peptides : a general entry to urea-based peptidomimetics.
Semetey Vincent, Schaffner Arnaud-Pierre, Marraud Michel, Didierjean Claude, Aubry André, Rodriguez Marc, Briand Jean-Paul, Guichard Gilles.

15h20: OC79 Evaluation of ring closing metathesis (RCM) reactions for the preparation of peptide cyclic esters in the solid state.
Srinivasan Ananth, Wilhelm R Randy, Schmidt Michelle A.

15h40: OC80 Combinatorial libraries for sensor arrays
Jung Günther, Tünnemann Rolf, Leipert Dietmar, Mack Jürgen, Wiesmüller Karl-Heinz

Einstein Auditorium: 14h00 - 15h40
Concurrent Session: Structure-Activity Studies
Chairs: Horst KESSLER, Victor HRUBY

14h00: OC81 RXP 407, a selective inhibitor of angiotensin I-converting enzyme, blocks the in vivo degradation of the hemoregulatory peptide Acetyl-Ser-Asp-Lys-Pro with no effect on angiotensin hydrolysis.

Junot Christophe, Cotton Joël, Gonzales Marie-Françoise, Michaud Annie, Vazeux Gilles, Vassiliou Stamatia, Yiotakis Athanasios, Azizi Michel, Ezan Eric, Corvol Pierre, Dive Vincent.

14h20: OC82 Glucagon receptor interactions with two $G\alpha_s$ splice variants.
Unson Cecilia G., Wu Cui-Rong, Merrifield R B.

14h40: OC83 Expression, amyloidogenicity and cytotoxicity of human pro-islet amyloid polypeptide (ProlAPP).
Krampert Monika, Bernhagen Jürgen, Brunner Herwig, Voelter Wolfgang, Kapurniotu Aphrodite.

15h00: OC84 Inhibitors of metalloendopeptidase EC 3.4.24.15 stabilised against proteolysis by the incorporation of β -amino acids.
Steer D L, Lew R A, Gerreyn S Harte M, Bond S, Perlmutter P, Smith A I, Aguilar M.L.

15h20: OC85 Structure-function studies on human ghrelin, a new growth-hormone releasing peptide
Bednarek Maria A., Feighner Scott D, McKee Karen Kulju, Van Der Ploeg Lex, Howard Andrew D.

15h40: OC86 Synthesis of (R)-Boc-(Fmoc)-aminoglycine and its use in the design of receptor-3 selective somatostatin (SRIF) antagonists
Rivier Jean, Sypniewski Michal, Erchegeyi Judit, Hoeger Carl, Penke Botond, Simon Lajos, Kirby Dean, DeBoard Ryan, Waser Beatrice, Schaefer Jean-Claude, Reubi Jean Claude.

16h00 - 16h30: Coffee Break

Pasteur Auditorium 16h30-17h30 Chairs: Bertrand CASTRO and Shumpei SAKAKIBARA
L17 Marty O'DONNELL : Unnatural Amino Acid and Peptide Synthesis
17h10: Conclusions of the Chairman

Workshops

Monday, Septembre 11, 2000

18h30 - Perkin Elmer Biosystem Workshop

Tuesday, September 12, 2000

18h30 - Argonaute Workshop

Thursday, Septembre 14, 2000

18h30 - Advanced ChemTech Workshop

Leonidas Zervas Award: Antonello PESSI

THE ROLE OF PEPTIDE RESEARCH IN DRUG DISCOVERY: THE CASE OF HEPATITIS C

A. Pessi

*Istituto di Ricerche di Biologia Molecolare P. Angeletti (IRBM), Via
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Although peptides themselves do not generally represent the end products of a drug discovery effort, peptide research often plays an important role in many aspects of this process. I will illustrate this by reviewing the experience of our own laboratory in the study of Hepatitis C virus (HCV). The target of our studies is the NS3/4A protease, which is essential for maturation of the viral polyprotein. After a thorough examination of its substrate specificity [*J. Virology* (1996) **70**:6694; *J. Biol. Chem.* (1997) **272**:9204], we fine-tuned several substrate-derived peptides for enzymology studies [*Anal. Biochem.* (1996) **237**:239; *ibid.* (1996) **240**:60; *Lett. Peptide Sci.* (1997) **4**:101], for high-throughput screening [*Anal. Biochem.* (1999) **266**:192] and as fluorescent probes for secondary binding assays [*J. Biol. Chem.* (2000) in press]. In the course of these studies we made the key observation that the protease is inhibited by its own cleavage products [*Biochemistry* (1998) **37**:8899]. Single analog and combinatorial optimization then derived potent peptide inhibitors [*Biochemistry* (1998) **37**:8906]. The crucial role of the NS4A cofactor was also addressed. NS4A is a small transmembrane protein, whose central domain is the minimal region sufficient for enzyme activation. Structural studies were performed with a peptide corresponding to the minimal activation domain [*Biochemistry* (1997) **36**:7890], with a series of product inhibitors [*J. Mol. Biol.* (1999) **289**:385] and with both [*Biochemistry* (1999) **38**:13844]. We found that NS3/4A is an induced fit enzyme, requiring both the cofactor *and* the substrate to acquire its bioactive conformation; this explained some puzzling results of "serine-trap" type inhibitors. A more complete study on NS3 activation however, requires the availability of the full-length NS4A protein. This was prepared by native chemical ligation, after sequence engineering to enhance its solubility [*J. Am. Chem. Soc.* (1999) **121**:7698]; structural studies are in progress. A novel method for the synthesis of peptide thioesters via Fmoc chemistry was also developed during this work [*J. Am. Chem. Soc.* (1999) **121**:11369; see also R. Ingenito *et al.*, EPS-26]. We are now examining the P' region of the substrate which, at variance with the P-region, is not used for ground-state binding to the enzyme, and might give rise to inhibitors showing novel interactions with the enzyme [E. Bianchi *et al.*, EPS-26].

Joseph Rudinger Memorial Lecture: Bernard-Pierre ROQUES

INSIGHTS INTO PEPTIDE AND PROTEIN FUNCTIONS : A CONVERGENT APPROACH.

B.P. Roques

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The main contribution of our laboratory has been in the development of rational approaches to the design, biological and pharmacological studies of new physiological effectors in the field of neuropeptides and their metabolizing enzymes and more recently in studies on virus life cycle and cell signaling mechanisms.

Various complementary strategies were used : i) structural studies of the endogenous effectors ; ii) effector-target recognition process ; iii) development of peptidomimetics and non peptide ligands and inhibitors ; iv) biochemical and pharmacological studies including the use of transgenic mice. Based on NMR analysis of conformational preferences of enkephalins and CCK8, highly selective agonists have been designed allowing the physiological antagonism between these two peptidergic systems and its crucial importance in drug dependence to be demonstrated. Nevertheless our most important field of research remains the study of zinc metallopeptidases involved in metabolism of neuropeptides (enkephalins) and regulatory peptides (angiotensins, atrial natriuretic peptide, endothelins ...) with the proposal of dual inhibitor concept, leading to compounds on the market or in clinical trials in the field of analgesia and cardiovascular diseases.

Our interest turn now towards the characterization of new peptidergic pathways using genomic and proteomic approaches.