The official EFMC e-newsletter

MedChemWatch

3 December 2007

IN THIS ISSUE

Editorial

Dear Colleague,

safety sciences and predictive toxicology are becoming increasingly an important issue in drug discovery and development. Thus, a more rational approach to safety assessments in early drug discovery is presently the focus of large centrally funded predictive toxicology initiatives both in Europe and the US. Read in this issue of MedChemWatch a condensed version of the full article published in Medicinal Chemistry in Europe, the Yearbook of EFMC. The lab-presentation features the lab of Povl Krogsgaard-Larsen at the Department of Medicinal Chemistry, The Faculty of Pharmaceutical Sciences, University of Copenhagen. Prof. Krogsgaard-Larsen is also one of the two European Editors of the Journal of Medicinal Chemistry. Each second year EFMC presents three major awards, the Nauta Award for Pharmacochemistry, the UCB – Ehrlich Award for Excellence in Medicinal Chemistry and the Prous Institute – Overton and Meyer Award for New Technologies in Drug Discovery. More information and the application deadline can be found in this issue. Last but not least we had several very successful events, the International Symposium on Advances in Synthetic and Medicinal Chemistry (ASMC) in St. Petersburg and Frontiers in CNS and Oncology Medicinal Chemistry, the first joint ACS-EFMC meeting, held in October Siena. For the latter please find a meeting report in this issue, the St. Petersburg meeting will be featured in the first issue 2008.

From the next issue on we will also include a section “letters to the editor” in order to promote exchange of ideas, thoughts, and visions for the future of Medicinal Chemistry. Once more I also encourage you to register on our web-page **www.efmc.info** to ensure that we are using the correct E-mail address.

The year 2007 almost passed and the MedChemWatch team wishes you and your family peaceful December holidays and a successful new year.

Gerhard Ecker
Editor

EFMC
European Federation for Medicinal Chemistry

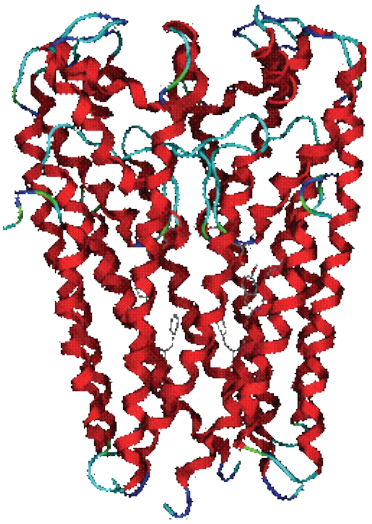
Perspective

Safety-Directed Drug Design: Failures can be successes

BY SCOTT BOYER

Few, if any, products undergo more safety testing and scrutiny than a pharmaceutical. This, of course, is for good reason as the most critical issue with regard to pharmaceuticals is the risk benefit ratio. Whilst patient benefits can be quite clear in most cases, the risk of undergoing a treatment regimen must be as carefully and broadly quantified as possible. Often this characterisation results in findings that result in discontinuation or withdrawal. Thus as drug withdrawals and experimental therapeutics that do not fulfil safety criteria during clinical trials are regarded as 'failures', they are actually successes for patient safety and for the science base of drug discovery. The lessons learned and the data gathered during this sometimes painful process is of critical importance in buttressing future efforts against similar problems.

The failure of a drug or clinical candidate is invariably associated with a massive amount of basic science that goes into problem-solving activities. This effort, if captured and integrated into the Discovery process, can contribute to the development of better and more sophisticated approaches to discovery safety assessment. Thus, the resources and momentum behind a problem solving effort, particularly around a late-stage clinical candidate present a unique opportunity to develop a more stable and valid science base upon which to build a more rational approach to safety assessment in early drug discovery. The capture, enhancement and exploitation of this science base is presently the focus of large centrally funded 'predictive toxicology' initiatives in both Europe (**http://www.ec.europa.eu/research/health/imi/index_en.html**) and the US (**http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html**).



What does an increase in the sophistication of a safety science base look like and to whom should it be directed? When faced with such an enormous problem it is always good to address the basics first. The choice of therapeutic target is one critical area and many advances have been made in recent years in the characterisation of a protein's role in various tissues. This 'target safety' aspect is not a one-time exercise to be carried out at the beginning of a project, but, as the recent experience with Vioxx has shown us, a constant vigil to relate all aspects of the complicated life of a therapeutic target to the adverse event signals coming from our preclinincal and clinical studies.

However, it is the area of chemical design that perhaps the most value can be gained from translating safety data to real, tangible decisions. This is a long, tedious process but several successful examples have been identified in which a valid set of decision-making tools can be used to warn for chemical designs that contain inherent safety liabilities. In some cases this can lead to decisions before synthesis is even undertaken. I other cases the level of confidence is such that the tool sparks the decision to do further experiments in more sophisticated model systems to investigate the probability of a real safety problem. The keys to either of these scenarios is first, a clear strategy behind the decision-making tools such that results from a simple test (QSAR, in vitro) can be followed up and confirmed in a relevant in vivo test and second, adequate throughput to

facilitate iterative design. Without this confirmation mechanism very little about the real risk of a compound or series can be concluded and without adequate throughput the chemistry will be mired in indecision.

Will it help?

With the goal of integrating as much of this rapidly expanding sophistication into chemical design, the potential for reducing safety-related failures exists, but is far from certain. One certain effect will be that promising compounds will fail less often for the reasons of today. Rather, the problems of the future will be qualitatively different, but if we have done a conscientious job in addressing the problems of today using knowledge from detailed mechanistic studies as well as screening, we will free up more time and resources within our safety groups for problem-solving around more of tomorrow's problems. That, despite the real potential for continued failure, is progress and thus a success in itself. ■

LAB PRESENTATION

Department of Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen

BY KRISTIAN STRØMGAARD, RASMUS P. CLAUSEN

The Department

The Department of Medicinal Chemistry is one of three departments at the Faculty of Pharmaceutical Sciences (PHARMA) at University of Copenhagen. The Faculty was an independent organization until 2006, known as the Danish University of Pharmaceutical Sciences and before that the Royal Danish School of Pharmacy. In 2007 the University merged with University of Copenhagen and the Royal Veterinary & Agricultural University to form the largest University in Scandinavia. One of the objectives of the merger has been to form a strong Health and Life Sciences cluster.

The mission of the Department of Medicinal Chemistry is to advance pharmaceutical sciences by performing drug-related research and research-based teaching within a range of topics including medicinal chemistry, natural products research & pharmacognosy, and biostructural research. The Department of Medicinal Chemistry encompasses a range of research projects directed towards discovery, design and development of model compounds and new potential drugs, discovery and characterization of novel macromolecular targets, and studies of their interactions at the molecular and cellular level. It is also engaged in the development of the underlying research methods and technologies.

The three major research areas of the department are:

- Natural products-based discovery and characterization of new chemical entities as potential new drugs.
- Discovery and characterization of novel macromolecular drug targets.
- Medicinal chemistry research towards development of potential drugs and structure-based design.

FACULTY OF PHARMACEUTICAL SCIENCES
UNIVERSITY OF COPENHAGEN

Information and contact
http://www.farma.ku.dk/index.php/Department-of-Medicinal-Chemis/161/0/
e-mail: pkl@carlsbergfondet.dk

The department has several medicinal chemistry research programs integrating organic synthesis, natural products research, computational chemistry, molecular modelling, molecular pharmacology, chemical biology, recombinant protein technologies and protein crystallography, with innovative work in areas where traditional scientific disciplines intersect.

Head of the group

Professor **Povl Krogsgaard-Larsen** (1941) is head of the medicinal chemistry research group at the Department of Medicinal Chemistry at PHARMA. Professor Krogsgaard-Larsen initiated his research career at The Royal Danish School of Pharmacy in 1967, and has just celebrated his 40th anniversary at the institution.

In 1970, after having finished a PhD in natural products, Professor Krogsgaard-Larsen decided to introduce medicinal chemistry to the Department and to start projects on re-design of toxic natural products with the goal of developing specific research tools and compounds of therapeutic interest. He decided to explore muscimol and ibotenic acid, which is toxic constituents of the mushroom Amanita muscaria, as lead structures in drug design projects. This lead to a number of exciting findings as described below, and Professor Krogsgaard-Larsen has published ca. 450 papers related to these areas. He is also editor of a textbook in Medicinal Chemistry – Textbook of Drug Design and Discovery – which is widely used in teaching at all levels of medicinal chemistry.

Professor Krogsgaard-Larsen has received a wealth of acknowledgments for his accomplishments, such as the The Lundbeck Foundation Prize (1989), The Paul Ehrlich Prize (1989), The Astra Award (1991), The W. Th. Nauta Award (1996) and The Pharmaceutical Research Achievement Award (2004). In 1998 he became the European Editor for Journal of Medicinal Chemistry. In addition to his research achievements, Professor Krogsgaard-Larsen has been a pioneer in structuring and managing a number of interdisciplinary research initiatives such as The Biotechnological Drug Research Center, PharmaBiotec, the Graduate School of Drug Research and the Drug Research Academy, all based at The Royal Danish School of Pharmacy.

Professor Povl Krogsgaard-Larsen at his 40th anniversary in September 2007 at Department of Medicinal Chemistry at the Faculty of Pharmaceutical Sciences, University of Copenhagen.

In 2001 he became rector of The Royal Danish School of Pharmacy and initiated a modernization and reorganization of the institution, and one of the outcomes was the change of name to the Danish University of Pharmaceutical Sciences. He only held this position for almost two years, as he was elected as chairman of the board of directors of the Carlsberg Foundation in 2003, a position that he currently holds along with his position as professor at the Department.

Key discoveries of the group

As mentioned before, the group of Povl Krogsgaard-Larsen originated from a drug research program in the early 70'es using the natural product muscimol from fly agaric mushroom as a lead structure for a number of novel analogues of the primary inhibitory neurotransmitter γ-aminobutyric acid (GABA). Later, ibotenic acid from this mushroom was employed as a lead structure for the primary excitatory neurotransmitter glutamate.

Two conformationally constrained muscimol analogues named THPO and THIP, which have bicyclic structures, turned out to be of key importance as fundamental pharmacological tools in studies of the GABA transmitter system. Whereas THPO was shown to be a specific inhibitor of GABA uptake, the closely related compound THIP specifically and potently activated $GABA_A$ receptors. Thus, for the first time it became possible to study the pharmacology of GABA uptake mechanisms and $GABA_A$ receptor activation specifically. Using THPO as lead, PKL subsequently predicted and proved that the related monocyclic amino acids nipecotic acid and guvacine were specific and very potent GABA uptake inhibitors, and they are now standard GABA uptake inhibitors. Nipecotic acid was further developed into Tiagabine by the drug company Novo Nordisk, Copenhagen, and is marketed as an antiepileptic agent. THIP has been shown to activate selectively and very potently extrasynaptically located $GABA_A$ receptors and interestingly, these receptors showing distinct subunit combination are not sensitive to benzodiazepines. It was calculated and subsequently proved by PKL that THIP would be capable of penetrating the blood-brain barrier in spite of its zwitterionic structure. THIP was shown to be a very potent non-opioid analgesic in man. In addition, THIP was shown to be a compound of low toxicity and in collaboration with the drug company H. Lundbeck, Copenhagen, THIP went to advanced phase III clinical studies under the company name Gaboxadol.

Ibotenic acid is an analogue of Glu, which is the major excitatory neurotransmitter in the CNS. The

compound was transformed into the structurally related AMPA, which specifically activates a subgroup of glutamate receptors. This particular subgroup of receptors has been named AMPA receptors after the compound. The impact of this compound is underlined by the 10.000 hits a PubMed search on AMPA yields. Since then a number of AMPA analogues have been made, and several have shown interesting pharmacological properties, such as ATPA (iGluR5 selective agonist) and homo-AMPA (the only selective mGluR6 ligand).

Research Focus

Today, the group consists of three groups covering the research areas: molecular pharmacology, chemical biology and medicinal chemistry.

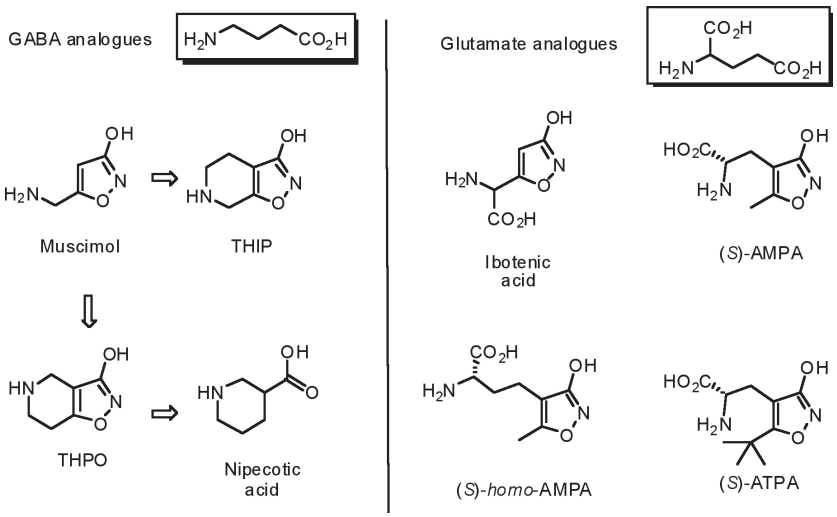
In general, the research focuses on neurotransmitters and their receptors and transporters. A combination of chemical, computational and pharmacological approaches is used in an integrated and interdisciplinary fashion to study neurotransmitters and their targets at the molecular level. Although GABAergic and glutamatergic neurotransmission are of primary interest other areas have caught attention within recent years also comprising studies of acetylcholine and glycine receptors, γ-hydroxybutyric acid (GHB) and its putative receptor, as well as various orphan receptors.

The research activities are still ongoing on design and synthesis of novel ligands for neurotransmitter receptors and transporters but the increasing structural knowledge on the proteins has shifted focus to a structure-based approach which involves strong collaboration with the biostructural group at the department covering molecular modeling and protein x-ray crystallographic studies. Thus, modeling is an important tool in the design of ligands but also in the design of point mutation studies. For example, highly integrated mutational studies on glutamate receptors and serotonin transporters have been completed, where both compounds and target proteins are complementary altered/mutated to give information on the recognition of ligands and activation mechanisms.

People

Professor Povl Krogsgaard-Larsen is heading the medicinal chemistry research group, in close collaboration with five associate professors, Lennart Bunch, Rasmus P. Clausen, Tommy N. Johansen and Bente Frølund, who are all working on various aspects of structure-based drug design. In addition, the Head of Department, associate professor Ulf Madsen is also a member of the team. Moreover, the group is very closely associated to the Molecular Pharmacology group and the Chemical Biology group headed by Professors Hans Bräuner-Osborne and Kristian Strømgaard, respectively.

The three groups currently employ two senior researchers, five post docs, ca. 15 PhD students, ca. 3 research assistants and ca. 5 laboratory technicians. Moreover, between 15-20 MSc students carry out their projects in these groups each year.



A selection of key pharmacological compounds affecting GABAergic and glutamatergic neurotransmission in a specific manner developed by Professor Povl Krogsgaard-Larsen.

Selected publications

- Krogsgaard-Larsen P, Johnston GA, Lodge D, Curtis DR, *A new class of GABA agonist*, Nature, 1977, 268, 53-55.
- Krogsgaard-Larsen P, Honoré T, Hansen JJ, Curtis DR, Lodge D, *New class of glutamate agonist structurally related to ibotenic acid*, Nature, 1980, 284, 64-66.
- Bräuner-Osborne H, Egebjerg J, Nielsen EØ, Madsen U, Krogsgaard-Larsen P, *Ligands for glutamate receptors: design and therapeutic prospects*, J. Med. Chem. 2000, 43, 2609-2645. ■

The XXVII Edition of the European School of Medicinal Chemistry has successfully been held in Urbino (Italy)

BY GABRIELE COSTANTINO

The XXVII edition of the European School of Medicinal Chemistry (ESMEC) has been held in the capturing Renaissance scenario of Urbino from July 1 to 6, 2007. Of a total of 235 participants who have attended the this years's edition, more than 65% was constituted by PhD, master of post-doctorate students, 20% by researchers from the academia and 15% by researchers from industry. Although the participation to the School is a requirement for many Italian doctorate programs in medicinal chemistry, and thus the majority of the registrants came from Italy, the 11% of non Italian participants is an indication of the growing interest that the School is gaining around Europe. Interest that this year was particularly pushed by the appealing scientific program and by the quality of the invited speakers. In line with the well established format based on a four daily sessions, this year the School has covered the following topics: Biologicals and Small Molecules for Molecular Targets in Oncology; New Paradigms in Drug Absorption; Advanced Methodologies in Organic Synthesis; Biomarkers in Drug Discovery. The first session on Molecular Targets in Oncology has seen Ciro Mercurio (Genextra, Milan; I) and Jascha-Nikolai Rybak (ETH, Zurich, CH) introducing biologicals approaches to treat and to veicolate drugs for treatment of oncological diseases. In the second half of the session, Carlos Garcia-Echeverria (Novartis, Basel CH) and Martin Drysdale (Vernalis, Cambridge; UK) have focused on medicinal chemistry approaches to small molecules modulating new targets in cancer research. The second session was devoted to New Paradigms in Drug Absorption. After an introduction given by Han Van de Waterbeemd (AstraZeneca, Macclesfield; UK), Pierre-Alain Carrupt (University of Geneve, CH) has focused on physico-chemical models for drug absorption, while Jean-Michel Scherrmann (University of Paris, F) has introduced the very important topic of BBB permeability. In the afternoon, two case studies were offered by researchers from industry: Patrizia Crivori (Nerviano Medical Sciences, Milan, I) has focused on the role of active transporters, while Stefania Beato (GSK, Verona, I) has presented an overview on the impact of predicting and oprimizing absorption in drug discovery.

The third session on Advanced Methodologies in Organic Synthesis has seen the presentation of very interesting approaches and methodologies in organic synthesis directed to potential drug molecules. Cesare Gennari (University of Milan, I) has presented an example on the total synthesis of Eleutherobin: Peter H. Seeberg (ETH, Zurich, CH) has introduced the topic of Synthesis of Biomolecules in Microreactors. Luca Banfi (University of Genova, I) has presented the impact of multicomponent reactions while Allison Hulme (University of Edinburgh, UK) has focused on recent advances in the aldol reaction and to its applications to natural product synthesis. Finally, Giuseppe Guercio (GSK, Verona,I) has presented an example of environmentally friendly synthesis in chemical development. The last day has covered a very hot topic, namely the impact that biomarkers may have in drug discovery. Orest Hurko (Wyeth Research-USA- and University of Dundee, UK) has offered a very stimulating overview of the state of the art of the field. Paolo Rovero (University of Florence, I) has presented an example of synthetic modified peptides for the identification of auto-antibodies, biomarkers of autoimmune diseases. Mahmoud Hamdan (GSK, Verona; I) introduced the impact that mass spectrometry may have in biomarkers discovery, while Goran Westerberg (SienaBiotech, Siena, I) has presented an example of the use of biomarkers to accelerate drug discovery. The didactic program of the School was completed by the keynote lecture of Napoleone Ferrara (Genentech, San Francisco, USA) on

VEGF-A as a target to treat cancer and other disorders. Two workshops on molecular targets in oncology and on advanced synthetic methodologies have completed the didactic program, promoting a closer interaction between students and lecturers and among students with different background and know-how.
As confirmed by the analysis of the evaluation questionnaires completed by participants, the School has certainly achieved its scientific and didactic aims, thus confirming the success of a format that nicely mixes up advanced seminars and didactic introductions and workshops. The informal environment and the appealing social program have also contributed to promote a productive interchange between participants. In conclusion, the ESMEC-Urbino school certainly contributes, together with the Swiss School, the Leiden/Amsterdam School and the Vienna School, to keep at a very high level the didactic offer of the EFMC. With the hope to continue along this way, the Scientific Committee is looking forward to see you in Urbino for the XXVIII edition, in July 2008. ■

COMMITTEES

Within this chapter we will give regular updates on the activities of our Committees.

European Commission R&D Initiatives Committee (ECIC)

BY FERRAN SANZ

The Innovative Initiative continues its long bureaucratic trip towards the creation of the Joint Technology Initiative (the autonomous IMI managing institution). It is currently under the consideration of the European Parliament and was approved by the Innovation European Council of Ministers in November. A key issue that is at the centre of the current negotiations (between the member states, the Commission and EFPIA) is about the procedures of the project calls. The headquarters of IMI will be located in Brussels. It is expected that the first IMI calls will be published by the beginning of next year. It seems that Safety and Efficacy will be the IMI pillars considered in the first call. The other two (Knowledge Management and Education & Training) will be considered in future calls.

Beyond IMI and within the FP7 Cooperation Programme, the HEALTH calls include topics related drug discovery. Regarding the FP7 Capacities Programme, there is an initiative for creating a European-wide infrastructure supporting the chemical biology and drug discovery research. It would include tools for the visibility of and access to chemical diversity generated by academic groups, as well as platforms for the biological screening of the academic libraries. To some extend, it would a European extension of the German initiative ChemBioNet (**www.chembionet.de**).

ECIC would welcome your knowledge, experience and ideas.
If you wish to contribute towards our objectives, please contact
fsanz@imim.es

Information & Communication Committe (ICC)

BY GERHARD F. ECKER

The Editorial Board of the newsletter MedChemWatch had a meeting in Barcelona to discuss further improvements of the newsletter and a reorganisation of the Web-page. For next year the newsletter will be published in four issues (March, June, September, December) and also include selected book reports. With respect to the Web-page, the menus will be rearranged in order to achieve a better presentation of the main activities of EFMC. This also will include the presentation of the abstract books of EFMC sponsored events. Furthermore, as already decided by the Council, we will start to implement a job-portal. In a first implementation phase, this service will be offered to our corporate members. Later on it will also be possible that individuals upload their CV and key data. Last but not least we installed a tracking system which allows a thorough analysis of the traffic related to our web-page. This revealed that we have already around 200 page views per day. ■

ICC would welcome your knowledge, experience and ideas.
If you wish to contribute towards our objectives, please contact
gerhard.f.ecker@univie.ac.at

GRANT ALERT

Marie Curie Research funding and Conference, 14 Jan 2008 in Brussels

BY JORDI MESTRES

A call for proposals for a European Commission funding scheme providing **full funding for research projects** involving partnerships between public and private research organisations has been published recently: the **Marie Curie Industry-Academia Partnerships and Pathways (IAPP) scheme**.

This scheme funds partnerships between public and private research organisations based on a common research project. They Taim to foster co-operation between the public and private sectors, to stimulate long-term collaboration between the sectors and to address the perceived or real barriers which inhibit movement of researchers between the public and private research domains.

Each IAPP project involves at least one research active private sector company and at least one research active public sector organisation. The private partners may range in size from the smallest micro-companies with a research capability to very large multinational enterprises. Public sector organisations can include universities, NGOs, government research institutes. Funding is typically for 4 years and is up to 100% of the costs of the project; no matching financing is required.

Support is provided for:
• Exchange of know-how and experience through inter-sectoral secondments of research
• Staff of the participants;
• Research and Networking activities;
And optionally:
• Recruitment of experienced researchers from outside the partnership, for involvement in
• Organisation of workshops and conferences, involving the participants' own research staff and external researchers
• For SMEs: research equipment (up to 10% of the EC contribution for each SME participant) on a duly justified basis

A new call for proposals has been published with a deadline of March 25th 2008. The total budget for this call is €45m. Further information including a guide for applicants is available at: **http://cordis.europa.eu/fp7/people/industry-academia_en.html**

To help interested participants achieve the most from an Industry-Academia collaborations and to prepare a proposal for the scheme a conference will be held in Brussels on January 14th 2008. Anyone wishing to participate in the conference may find the agenda and registration form at **http://ec.europa.eu/research/mariecurieactions**.

Participation is free but numbers are limited to 250, therefore early registration is advised. ■

CONFERENCE REPORT

The Launch of a New Joint ACS-Medi Division and EFMC Meeting

Siena, Italy, October 7-9, 2007

BY GERHARD F. ECKER AND ROBERTO PELLICCIARI

SOCIETÀ CHIMICA ITALIANA

ACS EFMC

Frontiers in CNS and Oncology Medicinal Chemistry

ACS-Medi Division and EFMC have agreed to launch 'Frontiers in Medicinal Chemistry' as a new series of high quality scientific meeting to be held every two years in collaboration, each time, with the EFMC-associated national society of an European country. A major aim of this initiative, which builds on the already strong ties between the two organizations, is to bring together leading US and European medicinal chemists from academia and industry in a meeting intended to build collaborative bridges between the participants The first of these meetings, organized in collaboration with the Division of Medicinal Chemistry of the Società Chimica Italiana and chaired by Giovanni Gaviraghi (Siena, Biotech), was held in the beautiful and historic city of Siena, Italy, from October 7 to 9, 2007. Mainly focused on the medicinal chemistry of diseases of the central nervous system and cancer, the meeting has seen the participation of 200 medicinal chemists of 20 countries from both academia and industry (61 companies). On the opening day, two plenary lectures given by Julian Adams (Infinity Pharmaceuticals, Cambridge, MA) and Carlo Melchiorre (University of Bologna) were followed by a very interesting session on the hit to lead process. Further sessions focused on cancer and cns research. The lectures, given by leading scientists of USA, Italy and UK were complemented by two poster sessions, which showed excellent attendance. Among the 93 posters presented, four were selected for oral presentation and three of them were awarded with prizes offered by the Journal of Medicinal Chemistry, by the EFMC and by Siena Biotech.

The second meeting is planned for the second half of 2009 in Barcelona, Spain, and the first organizative details will appear shortly on the ACS-Medi Division and EFMC websites.

Santa Maria della Scala in Siena, a prestigious Middle Age building for an outstanding medicinal chemistry meeting

Roberto Pellicciari, President of EFMC, presents the EFMC Poster Prize to Riccardo Zanaletti, of Siena Biotech

Luisa Mosti, President of the DCF-SCI, Italy presents the Poster Award to Klaus Wanner, University o Munich

Dave Rotella, Chair of the ACS-Medi Division presents the JMC Poster Prize to Thomas Bridges, Vanderbilt University

CONFERENCE REPORT

Drugs for Ischemia: Treatment of Cerebral Ischemia – Recent Therapeutic Strategies

EFMC sponsored session at the Fall ACS Meeting
Boston, Italy, August 19, 2007

BY GERHARD F. ECKER AND ROBERTO PELLICCIARI

EFMC

American Chemical Society 234th National Meeting & Exposition

This years's EFMC-sponosred session at the Fall ACS Meeting was organised and chaired by Roberto Pellicciari and focused on neurodegenerative diseases. The programme covered a broad mix ranging from cerebral ischemia via neuroprotection up to necroptosis. Although nearly two decades have been devoted to anti-ischemic research, only one drug is currently approved for use in acute ischemic stroke.

Wayne Childers (Wyeth Research) gave an excellent overview on recent approaches and mechanistic targets currently under investigation for treatment of stroke. His talk was followed by a presentation given by Tiziana Borsello (Istituto Mario Negri, Milano), who outlined her work on the JNK signalling pathway. She convincingly could demonstrate that inhibition of the c-jun N-terminal kinase (JNK) by the highly specific JNK inhibitor peptide (D-JNKI1) offeres a promising new therapeutic approach for human neuroprotection. David Becker (Florida International University, Miami, FL) presented the use of azulenyl nitrone spin traps, a completely different approach for neuroprotection. In animal models, the free radical scavenging stilbazulenyl nitrone STAZN conferred neuroprotecion at extremely low doses. The design, structure-activity relationship studies and biological evaluation of novel Sonic Hedgehog (SHh) activators was presented by Simon Haydar (Wyeth Research). Sonic Hedgehog (SHh) activators have been shown to promote neuroprotection and regeneration in models of stroke. Last but not least Gregory Cuny from the Harvard Medical School outlined the concept of necroptosis inhibitors for therapy of cerebral ischemia. Necroptosis, a type of cell death different from apoptosis, is the prevalent form of acute cell death in many pathologies, including cerebral ischemia. Despite a current working model of the necroptosis cell death pathway Dr. Cuny also presented several new lead series active as inhibitors of necroptosis.

The session was very well attended and once more the strong scientific ties between the ACS Medicinal Chemical Division of ACS and EFMC. The next EFMC sponsored session will be organised at the Spring 2009 National Meeting and Exhibition in Salt Lake City, UT. ■

Three years old the Boston Convention & Exhibition Center, with its dramatic roof, is accessible from all major highways and secondary streets

EFMC 2008 AWARDS

Call for Nominations open

DEADLINE: JANUARY 31, 2008

The EFMC confers every two years, on the occasion of the EFMC-ISMC Symposium, three awards including the Nauta Award for Pharmacochemistry, established by the Dutch Foundation "Stichting Prof. Dr.W.Th. Nauta Fonds", the UCB-Ehrlich Award for Excellence in Medicinal Chemistry, established by UCB and the Prous Institute-Overton and Meyer Award for New Technologies in Drug Discovery, established by Prous Institute for Biomedical Research.
All 3 awards consist of a diploma, € 7.500 and an invitation for a lecture by the Award recipient at the upcoming EFMC-ISMC International Symposium on Medicinal Chemistry.

The Awards will be conferred on the occasion of the XXth EFMC, 'International Symposium on Medicinal Chemistry' (ISMC), to be held in Vienna, Austria, 31st August to 4th September, 2008

Nauta Award for Pharmacochemistry

For the advancement of medicinal chemistry and the development of international organisational structures in Medicinal Chemistry. The award will be given for outstanding achievements in the field of Medicinal Chemistry.

UCB - Ehrlich Award for Excellence in Medicinal Chemistry

To acknowledge and recognise outstanding research in the field of Medicinal Chemistry in its broadest sense by a young scientist. This award has been established with the support of UCB Pharma.

Prous Institute – Overton and Meyer Award for New Technologies in Drug Discovery

To encourage innovation and investigation in technological development related to drug discovery, this Award established with the support of Prous Institute will be given for the discovery, evaluation or use of new technologies.

Nominations for these Awards should consist of a nomination letter, a brief CV, including a list of selected publications, and two supporting letters.
The nominations should be submitted to the Chairman of the Juries:
Professor **Roberto Pellicciari**,
President of EFMC, Dipartimento di Chimica e Tecnologia del Farmaco, Via del Liceo 1, 06123 Perugia, Italy
Fax: +39-075-585-5124,
E-mail: EFMCAwards@efmc.info

Please visit www.efmc.info for more information and Award regulations.

EFMC NEWS

Right after the first **ACS-EFMC meeting in Siena**, which was very successful both on scientific and on financial means, *ACS-MEDI Division* and *EFMC* started to prepare the next meeting of this new series **"Frontiers in Medicinal Chemistry"**.
The second meeting is planned for **autumn 2009 in Barcelona, Spain.**

The **yearbook "Medicinal Chemistry in Europe"** has been delivered to all National Adhering Organisations and should soon arrive in your office. It will also be available for download from our web-page.

The **Web-site** soon will provide the possibility to place **job-offers**. This service is offered free of charge to our Corporate Members. For further information please contact Dave Alker at *davidalker@btinternet.com*. ■

CALENDAR OF EVENTS

28th European School of Medicinal Chemistry (ESMEC)
July 6-11, 2008
Campus Sogesta, Urbino, Italy
Web: *http://www.esmec.eu/*

Metabolic Disorders – from Bench to Bedside
August 28-31, 2008
Sopron, Hungary
Web: *http://www.metdis2008.mke.org.hu*

XXth International Symposium on Medicinal Chemistry
August 31 – September 4, 2008
Vienna, Austria
Web: *http://www.ismc2008.org*

XIXth National Meeting on Medicinal Chemistry
September 14 – 18, 2008
GlaxoSmithKline Auditorium,
Verona, Italy
Web: *http://www.nmmcverona2008.unimore.it*

8th Swiss Course on Medicinal Chemistry
October 12-17, 2008
Leysin, Switzerland
E-mail: *beat.ernst@unibas.ch*

17th LACDR School on Medicinal Chemistry
October 28-31, 2008
Noordwijkerhout, the Netherlands
E-mail: *e.devries@leidenuniv.nl*

XXIst International Symposium on Medicinal Chemistry
August, 2010
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