The official EFMC e-newsletter

MedChemWatch

7 July 2009

IN THIS ISSUE

Editorial

Dear Colleagues,

the launch of a new journal is always welcome as a sign of vitality for a scientific community, but the announcement by Gerhard Ecker, in the article below, of MedChemComm, a new journal of the Royal Society of Chemistry (RSC) for rapid communications in medicinal chemistry, has a special impact for EFMC (and, in some respect, also for our newsletter...).
MedChemComm, whose first issue is expected to be released by mid 2010, is the result of a partnership between RSC and EFMC, both strongly committed in ensuring the new journal with a very high scientific level and an excellent technical quality.

continued on p.2 »

Council approves the launch of MedChemComm

At the meeting in Budapest the Council approved the proposal of the Royal Society for Chemistry to jointly launch MedChemComm, which will be the official journal of EFMC.
In analogy to Chemical Communications, MedChemComm will focus on preliminary articles in communications format. Presenting new ideas and concepts in the area of Medicinal Chemistry, MedChemComm will include new studies related to biologically-active chemical or biochemical entities that can act as pharmacological agents with therapeutic potential or relevance. The journal will be suitable for readers from both academia and industry, conducting research in the field of medicinal chemistry, drug discovery, pharmacology and pharmaceutical research. This will include traditional areas of the chemical sciences together with topics at the interface with biology and physics. The journal will act globally with regional offices in Europe, Asia and Northern America. The first issue is expected by mid of next year.

Gerhard Ecker
President, EFMC

EFMC
European Federation for Medicinal Chemistry

« continued from p. 1

EFMC does not publish the journal by itself, but cooperates with RSC, a non profit organization, to sponsor and influence a cutting-edge journal in the field of medicinal chemistry with the very ambitious scope of assuring a top-quality instrument to disseminate rapid communications. MedChemComm will not overlap with established journals, but rather will complement, in worldwide oriented way, the existing offer of high quality publications with specific focus and scope.
In some ways, the launch of MedChemComm is the 'end of the beginning' of a long story between EFMC and scientific journals.
The special nature of EFMC as a federation of Societies, prevents the creation of its own journal, not only for reasons related to national languages but also for the commitment of many national societies in publishing their own, often very well reputed, journals. Don't miss, in this respect, a very interesting article by Henk Timmerman which will be published in the next issue of the newsletter.
The partnership between RSC and EFMC is an attempt, I am sure very successful, to conciliate the demand for a presence of EFMC to drive journal strategies with the need of preserving the identity and the scope of existing of national and private initiatives.

As a part of the agreement, the paper issues of MedChemComm will also contain our newsletter. We will continue to distribute the newsletter to all the registered members through the e.mail list, and the newsletter will be available through the EFMC web site (**www.efmc.info/medchemwatch**). MedChemComm will be another, important, way to disseminate information. We are sure that having the newsletter coming together with a scientific journal will increase the visibility of the contents and will also increase the eagerness of authorship. Thus, I strongly advise everyone would like to contribute to send us small articles, or comments, or suggestions, and it will be our commitment to give them the highest visibility.

This issue of MedChemWatch, the number seven in the series, contains very interesting presentations and some innovations.
Gisbert Schneider comments, in his Perspective, the state of the art of Virtual Screening in drug discovery, and I am sure his thoughtful contribution will stimulate debate.
Peter Seeberger, winner of the 2008 UCB Award for Excellence in Medicinal Chemistry, presents his new lab, at the Department of Biomolecular Systems – Max-Planck Institute for Colloids and Surfaces, Potsdam.
The idea of presenting laboratories of excellence around Europe aims at disseminating the top quality level of research, but also at providing information for potential collaborations, graduate and post-graduate positions, or for the identification of common research interest. On this basis, we thought it as appropriate to extend these presentations also to labs driven by younger researchers and to SMEs. Two SMEs, Chemotargets and Inte:ligands, and one lab, driven by Karl Gademann at the Ecole Polytechnique Federale de Lausanne (EPFL), open this series. Ideas and suggestion for future contributions are very welcome !
Last, but not the least, have a look to the EFMC events. Also for the remaining part of this year 2009 and for 2010, there is a plenty of symposia, accredited and sponsored schools, and short courses which surely fit with the interests and needs of European medicinal chemists.

Gabriele Costantino
Editor

Perspective

Virtual Screening: what are we missing?

BY GISBERT SCHNEIDER

Virtual screening for druglike molecules in general – and new agents with a defined pharmacological profile in particular – is an established concept for hit and subsequent lead candidate identification during the early phases of a drug discovery project, sometimes even in situations with much structural uncertainty and potential ambiguity of receptor-ligand interactions (Figure 1).

Coined as a term approximately a decade ago, virtual screening today stands for a rather loosely defined collection of computational methods for screening compound prioritization and design. Although many elegant and successful applications of these techniques have been published over the past years, for example those based on automated ligand-receptor docking or machine learning classifiers, it is most noteworthy that there are almost as many methods as are reported practical applications. There is no single best virtual screening technique which has emerged as *the* tool for hit identification irrespective of the drug target under consideration. While it is evident that the applicability and thus the usefulness of a certain method are target-dependent properties, a peculiar observation is that current prediction software solutions (*e.g.*, for "drug-likeness", pharmacokinetic parameters, target-ligand binding) rarely exceed 80-85% accuracy at best in retrospective tests, and 40-50% as an optimistic estimate in prospective applications. It is therefore only fair to ask for the reasons for this notorious threshold, as it is almost impossible to judge the real value of "just another virtual screening method" being published with a reported accuracy of 85.3% leading to some low affinity hits at a selected target. Simply demanding for "better training data" is insufficient, often unjustified, and cannot be presented as the only solution – despite the well-known deficiencies of primary HTS data and error-prone readouts of some cell-based assays, to name but a few.

So, what are we missing? Which information will be essential for progress in method development? It is the author's opinion that an answer to this question will have to address at least the following critical points:

Foremost, we cannot expect practical applications of any virtual screening method to produce perfect results simply because no model is perfect (and sometimes expectations are borderline silly: "If virtual screening does not produce novel hits with nanomolar affinity it is useless.").

To strive for perfect prediction of biochemical response profiles for a given screening compound is unrealistic and bears the risk of leading to artifactual, over-trained models. While a perfect "local" prediction model for a certain lead series and a defined target certainly is worthwhile building, it simply is unreasonable to expect perfection from any such "global" method (admittedly, the differentiation between local and global models is artificial itself and will not resolve the underlying discrepancy between the expected model quality and a poor representation of molecular objects).

Furthermore, probably all macromolecular drug targets tolerate various structurally diverse ligand chemotypes, which as yet has not been sufficiently taken into consideration during model development. Future virtual screening methods must be able to account for one-to-many and many-to-many relationships between ligands and targets, which will render them useful for off-target prediction, as well as target and ligand "de-orphanization". Appropriate data from chemo- and pharmacogenomics initiatives should play a key role here and serve as reference.

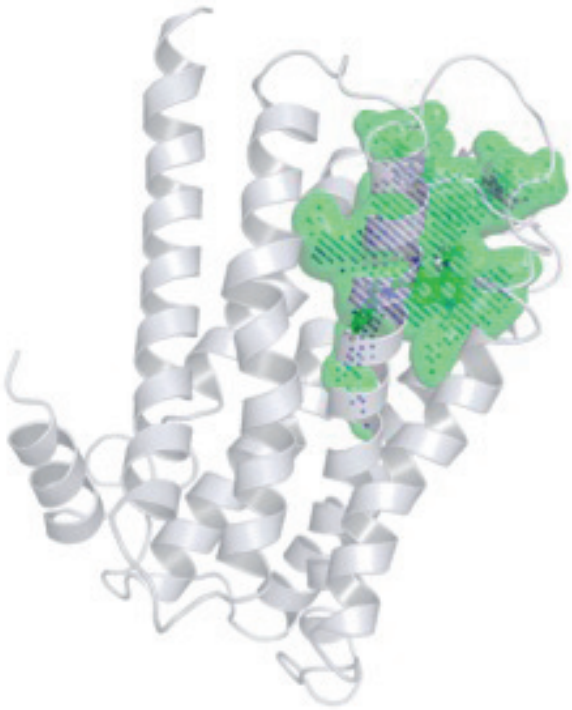
Finally, as long as entropic contributions to receptor-ligand interactions are grossly neglected, sustained success by virtual screening will be possible only for a limited set of drug-receptor complexes. While progress is being made for the modeling of water molecules involved in ligand binding, flexible fit phenomena, ligand protonation states in proteinous environments, and quantitative interaction types, reliable entropy estimations remain computationally impracticable for high-throughput virtual screening. New concepts are urgently needed to address this critical issue. This will have to include a fresh view on the existing physically and partly mechanistically

motivated molecular force fields. We have to ask ourselves whether the existing approaches are sufficient to accurately describe molecular or atomic interactions between a macromolecular receptor and a ligand and compute free energies of binding. Often this is not the case, and possibly algorithmic and technological advances will enable quantum chemical treatment of large systems and molecular complexes as a replacement of current force field approximations in the future.

Another frequently discussed but still insufficiently addressed problem in virtual screening is the stereo-selectivity of targets. To date, this pivotal property of macromolecular receptors has not been satisfactorily addressed in the absence of a reliable target structure model. Many of the established ligand-based virtual screening techniques ignore stereochemistry and might therefore present themselves unsuitable as generic approaches to hit-to-lead optimization. But even current three-dimensional ligand docking and pharmacophore-based methods largely fail to appropriately capture and describe stereo-centers and their preferred conformational ensembles. Possibly, we could learn much more from systematic receptor pocket analysis about how to construct preferred ligands than by mere automated ligand docking (even if perfect scoring functions were available). For example, ensemble shapes and property distributions of "druggable" binding pockets can serve as additional filtering criteria for fast ligand-based virtual screening. In this way, merging of receptor and ligand information might help eliminate false-positives and rescue false-negatives in a virtual screening triage.

While the main problems to overcome on our quest for better virtual screening tools certainly are of chemical nature (*e.g.* how to represent a molecule, describe pharmacophoric features, or compute energy contributions), there also remains much to be discovered in informatics. Computational chemistry and molecular modeling have a tradition in physics and theoretical chemistry, and only virtual screening applications have explored machine learning methods to a significant extent. After the initial exploration of artificial neural network models in particular, we currently witness an increasing application of so-called kernel methods for method development, *e.g.* support vector machines.

Unquestionably many more already existing algorithms and concepts may be adapted from engineering and computer sciences and taken on for virtual screening purposes – not to construct "just another virtual screening tool" but to provide an appropriate mathematical framework that is actually able to capture advanced chemical knowledge. Smart combinations of innovative machine learning approaches and advanced, innovative molecular modeling concepts might be suited to help overcome some of the limitations of current virtual screening approaches. ■



Model building and virtual screening can help generate ligand binding hypotheses and suggest practical validation experiments. The example presents a predicted ligand binding region (green) in a homology model of human histamine H_4 receptor, which was obtained by molecular dynamics simulation (Tanrikulu et al., ChemMedChem 2009, 4(5):820-827.).

ADDRESS OF THE AUTHOR:
Dr. Gisbert Schneider
Professor of Chem- & Bioinformatics
Beilstein Endowed Chair for Cheminformatics
Goethe-University
Siesmayerstr. 70
D-60323 Frankfurt am Main, Germany
e-mail: **gisbert.schneider@modlab.de**
web: **www.modlab.de**

LAB PRESENTATION

The Department of Biomolecular System, Max-Planck Institute for Colloids and Surfaces, Potsdam

BY PETER H. SEEBERGER

The Department for Biomolecular Systems, founded in 2009, conducts research at the **interface of chemistry, engineering, biology, immunology and medicine**. The core focus is the development of **synthetic methods** for the chemical synthesis of defined oligosaccharides. The compounds are the basis for **chemical tools** that aided **biochemical investigations** into the fundamental roles complex carbohydrates play in biological processes that underlie disease. The findings helped create diagnostic carbohydrate arrays to begin to understand **immunological aspects** of malaria epidemiology. **Vaccine development** of several infectious disease carbohydrate vaccine candidates is becoming increasingly more important for the laboratory. We are actively pursuing different aspects of glycobiology including the structure, function and biological role of sugars found on the surface of mammalian and bacterial cells particularly in the areas of immunology, biochemistry and human disease. Other areas of interest include ways to automate chemical synthesis and novel means to conduct chemical reactions using continuous-flow microreactors. Vaccine programs against infectious diseases including malaria, leishmaniasis, as well as a host of bacterial infections are currently progressing from synthesis to the preclinical stage.

As a new department of the Max-Planck Institute for Colloids and Surfaces in Potsdam, the setup structure is build around a new director – Prof. Peter H. Seeberger who previously was a full professor at the laboratory for organic chemistry at the ETH Zurich. Seven group leaders that direct groups ranging from material science to glycoimmunology will oversee research that is arranged around the core technology – automated oligosaccharide synthesis to access the molecules of interest. A new building is currently constructed in Potsdam to provide space for about 100 graduate students, postdocs and technicians. A wealth of equipment is available to support chemists, biologists and engineers. The aim is to provide an ideal environment to bring scientists of these different areas together.

Three major classes of polymers are responsible for the storage of information and signal transduction processes in biological systems. Nucleic acids make up the genetic material that transfers information from generation to generation. Proteins constitute the catalytic machinery carrying out most of the reactions in the cell. Carbohydrates, the third class of biopolymers, are branched, most complex and diverse. Access to pure carbohydrates was exceptionally difficult and therefore, all aspects of glycomics are less well understood than genomics and proteomics.

A general, straightforward method for the procurement of oligosaccharides was needed to jump-start glycobiology the way molecular biology was impacted by the automated methods for DNA and peptide synthesis.

Max Planck Institute of Colloids and Interfaces

Information and contact
Read more about people, projects and publications on our webpage:
www.mpikg.mpg.de/english/025-BiomolecularSystem/index.html
e-mail: **peter.seeberger@mpikg.mpg.de**

Peter Seeberger's Lab

Automated Synthesis of Carbohydrates

The Department of Biomolecular Systems developed prior to the arrival in Potsdam at MIT (1998-2003) and at ETH Zürich (2003-2009), by solving a host of chemical problems, the first automated oligosaccharide synthesizer as a platform to pursue glycomics as the next frontier in biology and medicine. This instrument provides now access to many complex carbohydrates in *days* rather than *years*. Prototype instruments have been built to achieve these syntheses in a fully automated manner. This platform is currently being expanded to all classes of carbohydrates including glycolipids, glycoproteins, and heparin. All aspects of automated synthesis are being improved as novel methods resulted in excellent efficiency, selectivity and versatility of the synthetic process. The Department is closing in on the ultimate goal of creating a commercially available instrument that uses a defined set of monosaccharide building blocks to assemble most oligosaccharides reliably.

Thus, non-specialists will be able to access defined sugars for biological or medical applications.

Synthetic Tools for Glycobiology

Rapid access to usable quantities of defined oligosaccharides has enabled the creation of synthetic tools that have been commonplace in genomics and proteomics research. These tools include carbohydrate microarrays, carbohydrate affinity columns to isolate carbohydrate-binding proteins and labeled carbohydrates for *in vitro* and *in vivo* imaging. The tools permitted us to explore fundamental aspects of glycobiology. The Seeberger group pioneered the use of carbohydrate microarrays to: 1) *define HIV oligosaccharide antigens* for the development of potential AIDS vaccines; 2) determine the *ligands for carbohydrate-binding proteins*; 3) understand the *specificity and resistance problems of aminoglycoside antibiotics*; 4) *screen blood for disease patterns*; and 5) detect pathogenic bacteria in blood and other body fluids. Particularly the ability to detect bacteria very sensitively in biological samples holds applications in food safety and the detection of blood poisoning. These more applied avenues are currently being expanded.

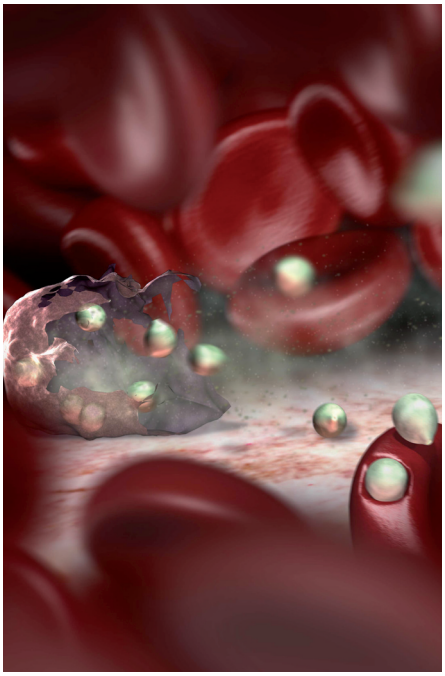
Synthetic Carbohydrate Vaccines

Based on the synthetic chemistry and tools platform, the Department has developed several applications. The presence of specific oligosaccharides on the surface of particular cell types including parasites, bacteria and cancer is the basis for the creation of synthetic carbohydrate vaccines against a host of diseases. An anti-toxin *malaria* vaccine candidate we identified is currently in late preclinical development at a spin-off company and is expected to enter clinical trials in 2011. Carbohydrate arrays have provided the basis to demonstrate in epidemiological studies malaria resistance in endemic areas in Africa. It has been clearly shown that anti-toxin antibodies protect people in endemic areas after age two. This finding strongly suggests that our vaccine candidate will provide protection for infants and naïve individuals much like that enjoyed by resistant individuals in endemic areas. Other vaccine candidates against infectious diseases are currently at different stages of development: *anthrax* (animal tests), *leishmaniasis* (animal tests), tuberculosis (synthesis completed), avian flu (synthesis completed), and a host of bacterial diseases that are at different stages of development. Synthetic glycolipids have been found to be powerful immunostimulants for use as vaccine adjuvants.

Biochemistry of Infectious Diseases

The identification of the **malaria toxin** as a glycosylphosphatidyl inositol (GPI) anchor provided the basis for more detailed biological studies into the role of these complex molecules. In this context the department has been able to identify new signaling and entry mechanisms that are of crucial importance in malaria pathogenesis. These studies have provided the basis for different modes of intervention to fight this devastating protozoan parasitic disease.

Synthetically derived GPIs aid the quest to understand the role of glycolipid signaling in the inflammatory cascade, insulin independent signaling in diabetes and nerve growth. The past year has seen breakthroughs in the assembly of complete GPI-anchored prion proteins, an area that is now rapidly expanding. Biological investigations aiming at understanding prion infectivity in vivo are currently being initi-



Malaria burst

ated. With the development of powerful synthetic tools in the department to generate carbohydrates the situation is increasingly changing leading to a better design of carbohydrate-based drugs and vaccines. A research group focuses on the development of peptide mimotopes of carbohydrates for vaccine development and to inhibit lectin-glycan interactions. Structural characterisation of peptide mimotopes of carbohydrates has provided important insights into the molecular mechanism of mimicry. Based on this information we will design phage-display libraries to improve the binding affinity of peptide mimotopes.

Continous Flow Microreactors as Tools for Organic Chemists

Traditionally, organic chemists have performed chemical transformations in batch mode. Our department has pioneered the use of continuous flow microreactors for use by synthetic organic chemists. The department has utilized commercially available as well as internally developed microreactor systems to develop an automated reaction screening platform for organic chemists. Using these microreactor systems a host of chemical transformations has been rendered more efficient. In particular, dangerous, highly exothermic reactions as well as radical chemistry and photochemistry have benefited from the new way to run synthetic organic chemistry. Currently, these systems are being expanded to a host of applications in the area of total synthesis, methods development but most importantly, also to the preparation of organic and inorganic nanoparticles and colloids. ■

SME PRESENTATION

Chemotargets

BY JORDI MESTRES

Chemotargets S.L. (**http://chemotargets.com/**) was created in March 2006 as a spin-off initiative from the Chemogenomics Laboratory (**http://cgl.imim.es/**) under the auspices of the Municipal Institute of Medical Research (IMIM-Hospital del Mar: (**http://www.imim.es/**). The company is located within the impressive new premises of the Barcelona Biomedical Research Park (**http://www.prbb.org/**), in an area that is called to become the "San Diego of the Mediterranean" for its recent growth in the biotechnology sector.

Chemotargets' core *in silico* pharmacology platform currently allows for profiling small molecules on almost 1,500 protein targets from the main protein families of therapeutic relevance, including, 837 enzymes, 233 GPCRs, 198 ion channels and transporters, and 32 nuclear receptors. This platform has been internally thoroughly validated and is being exploited through contract service agreements with chemical, biotech, and pharma companies to i) identify new chemical entities with customised target affinity profiles (hit identification), ii) identify potential off-targets at which compounds designed for a particular target may have residual affinity (target fishing), and iii) design chemical libraries directed to particular sets of disease-related targets or entire protein families. The company has also developed proprietary software for the construction of medchem isosteric libraries around known bioactive ligands which, when combined with target profiling, provides a

Chemotargets

For further information on Chemotargets, please visit its website at:
http:/www.chemotargets.com/
or send an email to:
infochemochemotargets.com

unique means for synthesis planning as well as anticipating all protein targets worth considering in hit and lead optimisation programmes.

In these last three years, Chemotargets has serviced drug discovery projects for 8 pharma companies, 2 chemical companies, and 4 academic institutions and has contributed to the identification of novel hits for known targets, as well as novel targets for known ligands, for many of them. As a result of Chemotargets' activities, two patents have already been filed and several other projects are currently being pursued internally in those companies to follow up on the hit/target identifications. ■

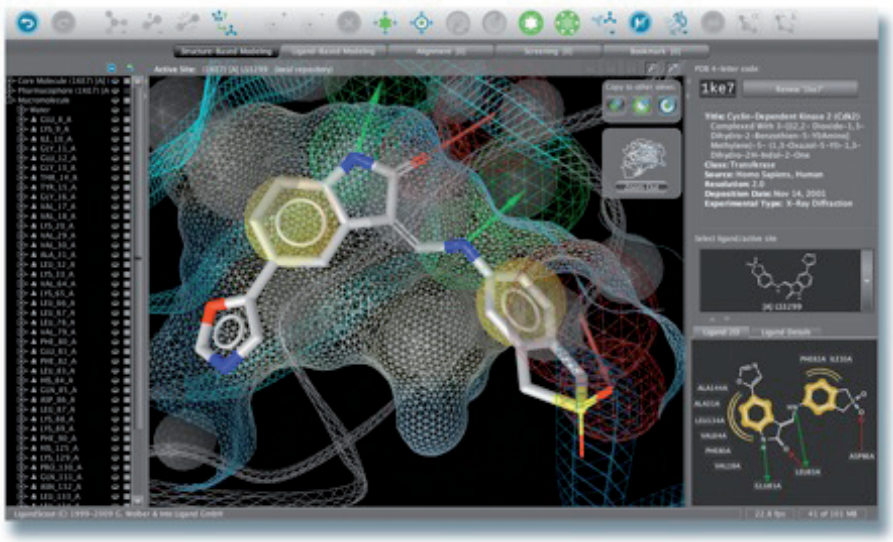
Inte:ligand

BY GERHARD WOLBER

inte:ligand
Your partner for in-silico drug discovery.

Inte:Ligand is a scientific software and contract research company that was founded 2003 by Prof. Thierry Langer, Dr. Gerhard Wolber and Prof. Hermann Stuppner. Since its foundation, the company has been steadily growing, and now employs 10 scientists, has established several major contract research collaborations and is currently marketing two software products. Inte:Ligand combines expertise in applied molecular modeling supporting medicinal chemistry in form of contract research with software development. In this way, the needs and problems of medicinal chemistry are directly transported to the software developers and can be addressed directly.

Inte:Ligand's key research topic has always been 3D pharmacophore modeling and virtual screening. Their lead product LigandScout, which allows for structure-focused 3D pharmacophore generation has just recently been complemented by ligand-based pharmacophore elucidation [1]. One of the key components of Inte:Ligand's software is a novel, three-dimensional pharmacophore overlay algo-



Screenshot of Inte:Ligand's pharmacophore modeling platform LigandScout showing the interactions of a CDK2 protein-ligand complex.

Information and contact:
Dr. Gerhard Wolber
Mariahilferstrasse 74B/11
1070 Vienna, Austria
web: **www.inteligand.com**
e-mail: **office@inteligand.com**

Selected publications:

[1] G. Wolber and T. Langer. **LigandScout: 3-D Pharmacophores Derived from Protein-Bound Ligands and Their Use as Virtual Screening Filters.** *J. Chem. Inf. Model;* 2005; 45(1); 160-169.

[2] **Efficient overlay of small organic molecules using 3D pharmacophores** *J. Comput. Aided Mol. Des.;* 2007; 20(12); 773-788.

[3] G. Wolber, T. Seidel, F. Bendix, and T. Langer. **Molecule-Pharmacophore superpositioning and pattern matching in computational drug design.** Drug Discov Today. (1-2):23-29 (2008).

[4] T. M. Steindl, D. Schuster, G. Wolber, C. Laggner, T. Langer. **High Throughput Structure-based Pharmacophore Modeling as A Basis for Successful Parallel Virtual Screening** *J. Comput. Aided Mol. Des.*, 20, 703-715 (2006)

rithm that takes into account pharmacophoric molecule points and uses pattern recognition for high computational efficiency [2,3]. This pattern recognition bears several advantages over classical multi-point filtering procedures when applied to virtual screening.
Another upcoming research area is de-novo design using information from fragment-based screening. The combination of fragments with weak affinity to potent ligands can be performed combining Inte:Ligand's library enumeration technology while geometrically optimizing pharmacophore fitting.

The third research topic of Inte:Ligand is addressing polypharmacology challenges by activity profiling [4].
A collection of approx. 2500 validated 3D pharmacophores have been developed to help in risk assessment in early development stages of drug candidates and are available for parallel virtual screening. They cover 300 unique clinically relevant pharmacological targets originating from major therapeutical classes, such as antiinfectives, cardiovascular, endocrine, gastrointestinal, immunologic, metabolic, neurologic, oncolytic, renal-urologic, and respiratory agents as well as antitargets such as hERG, and members of the cytochrome P450 family.

Inte:Ligand is combining applied research with innovative software development focusing on three-dimensional pharmacophores.
Specializing on this area, it has become a key player in the cheminformatics and virtual screening community. ■

YOUNG RESEARCHER

KARL GADEMANN

Information and contact
Ecole Polytechnique Federale de Lausanne (EPFL), Chemical Synthesis Laboratory, SB-ISIC-LSYNC, BCH 4304 (bat. Chimie UNIL), CH-1015 Lausanne, Switzerland
web: http://lsync.epfl.ch
phone: +41 21 693 93 15
e-mail: karl.gademann@epfl.ch

Karl Gademann (1972) was educated at ETH Zürich and Harvard University (PhD with Prof. Dr. Dieter Seebach, postdoctoral studies with Prof. Dr. Eric N. Jacobsen, Habilitation associated with Prof. Dr. Erick M. Carreira). He is currently an assistant Professor (tenure-track) at the Swiss Federal Institute of Technology (EPF Lausanne) and will move to the University of Basel in January 2010. He has published over fifty publications, holds two patents and received several awards including the Latsis Prize, Lilly Lecture Award, the Schläfli award of the Swiss Academy of Sciences, and, most recently, the Liebig Lectureship of the German Chemical Society. He was awarded the European Young Investigator grant related to natural product synthesis research. His research interests range from the isolation and synthesis of natural products to their chemical biology and potential therapeutic applications.

Natural products contain the evolutionarily enshrined wisdom of ages, and only synthetic organic chemistry can unlock their full potential. We are isolating and preparing natural products and derivatives in order to understand and to control biological processes on a molecular level. For example, we are using a chemoecological approach to the discovery of **novel antiplasmodial agents** from cyanobacteria, taking advantage of allelopathic compounds produced by phototrophs that target the apicoplast in *Plasmodium falciparum*. We have identified nostocarboline and aerucyclamide that display potent and selective activity against the malaria parasite. On a second line of research, we are generating **antimicrobial surfaces** by natural product hybrids. These surfaces could be beneficial in addressing the problem of nosocomial infections related to stents, catheters and implants. A third area under investigation is related to **neuritogenic natural products** that stimulate neurite outgrowth, which is of significance related to neurodegenerative diseases. Lastly, we are working on small molecules that **control protein transport** in cells. Anguinomycin C is a natural product that affects nuclear localization of proteins in exposed cell lines.

Selected publications

• S. Bonazzi, S. Güttinger, I. Zemp, U. Kutay, K. Gademann
Angew. Chem. Int. Ed., **2007**, *46*, 8707-8710.
• J.-Y. Wach, S. Bonazzi, K. Gademann,
Angew. Chem. Int. Ed. **2008**, *47*, 7123-7126
• C. Portmann, J. F. Blom, M. Kaiser, R. Brun, F. Jüttner, K. Gademann
J. Nat. Prod. **2008**, *71*, 1891-1896. ■

BY ERDEN BANOGLU

SOCIETÀ CHIMICA ITALIANA

DIVISION OF MEDICINAL CHEMISTRY OF THE ITALIAN CHEMICAL SOCIETY (SCI)

AWARDS

The "Amedeo Avogadro" Medal for Excellence in Chemistry for Professor Roberto Pellicciari
University of Perugia, Italy
Professor Roberto Pellicciari, Past President of EFMC, has been awarded with the "Amedeo Avogadro" Medal during the XXIII National Congress of the Italian Chemical Society, held in Sorrento from 5 to 10 July, 2009. The Italian Chemical Society, that at the Sorrento Congress celebrated the 100 years (1909-2009) of its activity, typically confers the "Amedeo Avogadro" Medal to an eminent scientist who gave outstanding contributes for amplifying the chemical knowledge, and distinguished himself by excellent chemical researches at a international level.
Professor Pellicciari was honored with the "Avogadro" Medal for the relevant results obtained in the development of innovatory synthetic and computational methods, aimed to prepare new stereochemically complex entities, greatly useful for pharmacology characterization of receptors and enzymes highly involved in CNS pathologies. This central role in the Medicinal Chemistry research field, at both national and international level, was always joined to a deep engagement and a great enthusiasm, profusely shown by Professor Pellicciari with his significant research team.

Prof. Pellicciari receives the Avogadro's Medal from Luigi Campanella, President of the Italian Chemical Society, and Ettore Novellino (left) and Vincenzo Barone (right), chairmen of the XXIII National Congress of the Italian Chemical Society

The "Pietro Pratesi" Medal for Professor Ettore Novellino
University of Neaples, Italy
The Medicinal Chemistry Division of the Italian Chemical Society awarded Professor Ettore Novellino with the "Pietro Pratesi" Medal, a prize assigned to an eminent scientist for his prominent Medicinal Chemistry researches at international level.Professor Novellino has been awarded for his relevant contributions on computer-aided design and synthesis of novel therapeutics, ranging from anticancer to neuroprotective, antidiabetes, and antiobesity agents, by creating a wide network of collaboration with national/international high-level research groups.

EVENTS

The XIXth National Meeting on Medicinal Chemistry (NMMCVerona 2008)
The event, organized by the Medicinal Chemistry Division of the Italian Chemical Society, under the auspices of the European Federation of Medicinal Chemistry (EFMC), took place at the GlaxoSmithKline R&D Auditorium, September 14-18, 2008. In 2008, the Medicinal Chemistry Division of the Italian Chemical Society took the bold decision to hold the XIXth National Meeting on Medicinal Chemistry in English. The result was a truly international conference, with delegates and speakers from around the world.
This National Congress has arisen from a close relationship between the academic world and GlaxoSmithKline Verona (Italy) which offered their wonderful hospitality and cooperation.
There were 360 participants; 12 different countries outside Italy were represented, with a significant number of attendees coming. Furthermore, the participation of industry was consistent,

with coming from several national and multinational companies.
The Awards ceremony was held in honour of Prof. Giorgio Tarzia (University of Urbino), recipient of the Giacomello Medal, and the opening lecture was given by Nobel Laureate Richard R. Ernst (ETH Zürich), who gave an enthusiastic and very attractive speech on who benefits from drug discovery -industry, society, or both?. At a challenging time for the field of chemistry, particularly for medicinal chemistry, the NMMCVerona2008 reached the aim to improve the global profile of medicinal sciences by promoting relationships and interdisciplinary approaches among national and international academic and industrial pharmaceutical organizations and by launching any possible initiatives, for young medicinal chemists in particular, to give them opportunities in the early stages of their careers.

KVCV, BELGIUM

On April 29, 2009 the University of Antwerp, Belgium conferred upon Prof. Henk Timmerman (Vrije Universiteit Amsterdam, The Netherlands), the degree of Doctor Honoris Causa in Pharmaceutical Sciences for his eminent and internationally acclaimed contributions to research into histamine receptors and his prominent and stimulating role in the development of the field of medicinal chemistry in Europe. On this occasion the laudation was presented by Prof. Koen Augustyns.
Henk Timmerman has served several terms as the EFMC's chairman and secretary, and continues to be one of the federation's driving forces to this day.

Prof. Henk Timmerman

DIVISION FOR MEDICINAL CHEMISTRY (DMC), SWISS CHEMICAL SOCIETY (SCS)

The Division participated in the Joint German-Swiss Meeting on Medicinal Chemistry, "Frontiers in Medicinal Chemistry", in Heidelberg (Germany), in March 2009. This congress focused on recent developments and trends in the fields of: Target-Families: Kinases and Nuclear Hormone Receptors - Inflammatory Diseases / Atherosclerosis – Neuropsychiatry – New Technologies / Drug Proteomics – and other Highlights in Medicinal Chemistry. The concept of a well-balanced mixture of case studies and more educative lectures proved to be very attractive.

Future activities of division planned in 2009 and 2010:

• **September 04, 2009**
Division of Medicinal Chemistry oral and poster session at the Fall Meeting of the Swiss Chemical Society, EPFL Lausanne.
• **May 27, 2010**
Mini-Symposium on 'Channels and Transporter'; Department of Chemistry,University of Basel, comprising overview lectures by Beat Ernst, Raimund Dutzler and Dietrich Keppler and two specific case studies (no registration, free entrance).
• **September 16, 2010**
Division of Medicinal Chemistry oral and poster session at the Fall Meeting of the Swiss Chemical Society, ETH Zürich.
• **September 21-24, 2010**
ILMAC Scientific Forum on Polymers, with a specific section dedicated to Biopolymers and Polymer Based Drug Delivery, MCH Basel.
• **October 10-15, 2010**
9th Swiss Course on Medicinal Chemistry, organized by Professor Beat Ernst in Leysin, a pittoresque Swiss mountain village. These courses are held biennially. They offer young scientists with a few years of experience in the pharmaceutical industry and interested Ph.D. students a broad overview of key disciplines important for modern preclinical drug research. Active participation in tutorials and a broad variety of lectures and case histories are important elements of the course (see also **http://www.swiss-chem-soc.ch/events/index.cfm**).

TURKISH ASSOCIATION OF MEDICINAL AND PHARMACEUTICAL CHEMISTRY

The *1st Turkish-Russian Joint Meeting on Organic and Medicinal Chemistry* will be organized on October 14-17, 2009 in Antalya, Turkey with the collaboration between the Turkish Association of Medicinal and Pharmaceutical Chemistry and the D.I. Mendeleev Russian Chemical Society, Medicinal Chemistry Section. Further information can be found at **http://www.jmomc2009antalya.org/**
■

EFMC EVENTS

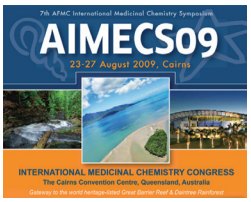
BY GABRIELE COSTANTINO AND AGOSTINO BRUNO

The 3rd Edition of International Meeting on Advances in Synthetic and Medicinal Chemistry (ASMC09) will be held in Kiev (Ukraine) August 23-27, 2009

EFMC and Chembridge Corporation agreed to continue the series of meeting on Advances in Synthetic and Medicinal Chemistry which was successfully initiated by the meeting of Moscow 2004 and St. Petersburg 2007. The 3rd edition of the International Symposium on Advances in Synthetic and Medicinal Chemistry (ASMC09) will be held in Kiev (Ukraine), August 23-27, 2009, chaired by Prof. Erick Carreira, ETH Zurich, Switzerland and Dr Scott Biller, Novartis Institutes for BioMedical Research, Cambridge, USA. Topics of the 3rd edition includes New Synthetic Methodologies, Total Synthesis of Natural Products and Heterocyclic Chemistry; Diversity- and Target-Oriented Synthesis and Chemical Biology; Medicinal Chemistry and Drug Discovery & Development. Commercial exhibition will also be organized along with a half-day Business Mini-Symposium "Small Molecule Libraries from Russia and Ukraine and Screening-Based Drug Discovery".

More information, the detailed program and the list of invited speakers are available at **www.asmc09.org**

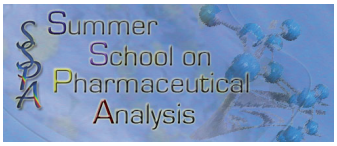
Under the sponsorship of EFMC, the AIMECS 09 will take place in Cairns, Queensland, Australia August 23-27, 2009



Main topics include:
- Epigenetics , which is the official EFMC Session
- Peptides/peptidomimetics
- Tropical/emergent diseases
- Metabolic and GI
- Protein folding disease
- RNAi
- New Frontiers & Methods
- Protein:protein interactions
- Coagulation cascade
- GPCRs and ion channels

For a more detailed description on this event, please feel free to visit:
www.aimecs09.org
Contact person:
Raci Professional Conference Organizer
Probarti Milton, Royal Australian Chemical Institute
e-mail: **probarti.milton@raci.org.au**

Summer School on Pharmaceutical Analysis (SSPA) will take place in Milan, Italy September 7-9, 2009



The SSPA is planned under the auspices of the Division of Medicinal Chemistry of the Italian Chemical Society and the EFMC (European Federation for Medicinal Chemistry) and it is mainly addressed to researchers and PhD students of the Faculties of Pharmacy and Sciences and to young scientists from pharmaceutical industries.
The 14th SSPA is part of a three-year program on the most advanced analytical methodologies involved into the launch of new drugs. In particular, following the 2008 edition focused on "Advanced Analytical Methodologies in Drug Discovery", this second year of SSPA covers '**Advanced Analytical Methodologies in Drug Development**'.
Specifically, SSPA 2009 main topics will be:
1) ADME/PK as part of a rational approach to drug discovery
2) Biomarkers in drug discovery and development.

For further information and for the detailed program please visit:
http://www.scpaweb.org
or contact the Director of the school, Vincenza Andrisano at:
vincenza.andrisano@unibo.it

The29th Edition of ESMEC, an EFMC Accredited School, will take place in Urbino (Italy)
September, 13-18, 2009

The Division of Medicinal Chemistry of the Italian Chemical Society is organizing, in Urbino (Italy), the XXIXth edition of the European School of Medicinal Chemistry (ESMEC), an EFMC-Accredited School.
This year the School will take place exceptionally in September, 13-18, 2009, and will cover the following topics:
- Neuromuscular Diseases: Focus on Multiple Sclerosis, Amyotrophic Lateral Sclerosis, and Muscular Dystrophy
- Carbohydrate Chemistry;
- Toxicity and Drug Discovery;
- Hot Topics.

The School, characterized by a truly interdisciplinary approach which nicely mixes up advanced seminars with more didactic and interactive workshops, is directed to European PhD students, and to junior researchers from both academia and industry. Registration fees, including full lodging for five days are as low as 450 Euro. Free fellowships are also available.

For further information and for the detailed program go at: **www.esmec.eu**
or contact the Director of the school, Gloria Cristalli, *at:*
gloria.cristalli@unicam.it

The 5th Edition of the EFMC-Sponsored Summer School on Drug Design will take place in Vienna (Austria),
September 13-18, 2009

Topics will include:
- Ligand-based Design
- Structure-based Design
- Binding free energy calculations
- Data bases, data mining
- Multitarget profiling/systems biology and PI

For further information, contact
Prof. Dr. Gerhard Ecker
University of Vienna
Althanstrasse 14, A-1090 Wien, Austria
ph: +43-1-4277-55110
fax: +43-1-4277-9551
e-mail: **gerhard.f.ecker@univie.ac.at**
or visit: **www.summerschool.europin.at**

First Balaton Course in Medicinal Chemistry, will take place in Balatonszemes, Hungary
September 27-30, 2009

The course is basically organized for junior scientists in English and open for participation of scientists from foreign countries too. Main focus will be lead finding and lead optimization, chemical development.

Early registration fee until July 15.

For more information on this event, please feel free to visit:
www.1bcmc.mke.org.hu/home.html
Contact: Aesculap Foundation
Semmelweis University
1092 Budapest, Hogyes u. 7
e-mail: **ckriszti@szerves.sote.hu**

The second event of the Frontiers in Medicinal Chemistry series will take place in Barcelona
October 4-6, 2009

EFMC and the Spanish Society of Medicinal Chemistry (SEQT) organises in Barcelona, October 4-6, 2009, the Frontiers in Medicinal Chemistry – Emerging Targets, Novel Candidates and Innovative Strategies.

The detailed scientific program and further information are available on line at
www.fmc2009.org

This event is the second on the series initiated in Siena (Italy), in 2007. This three-day international meeting will bring together medicinal chemists and related scientists in order to share exciting new results and first-time disclosures in various areas of drug discovery and development, including cancer, infectious diseases, CNS, inflammation, pain and metabolic disease. Twenty-three internationally recognized plenary speakers will present lectures with a focus on emerging targets, novel drug candidates and new strategies and technologies.

The 18th Edition of the EFMC-Sponsored LACDR School on Medicinal Chemistry will take place in Oegstgeest, The Netherlands
October 27-30, 2009

The course provides a thorough introduction in pharmacodynamics, pharmacokinetics and toxicology (ADME-Tox). The impact of molecular biology, genomics and molecular modeling on drug research are also discussed.
Newly introduced to the course are cheminformatics and fragment-based design approaches.

For further information, contact:
Mrs. E.F. Dekker, LACDR-Secretariat
P.O. Box 9502, 2300 RA Leiden,
The Netherland
ph: +31 71 527 4406 *fax:* +31 71 527 4277
e-mail: **bdekker@lacdr.leidenuniv.nl**
or visit: **www.lacdr.nl/events/18th-school-on-medicinal-chemistry**

Annual One-Day Meeting on Medicinal Chemistry of SRC & KVCV, will take place in Brussels, Belgium
November 6, 2009

This conference of six plenary lectures, three oral communications and a poster session will explore how larger size molecular architectures have expanded the range of pharmaceutically active compounds well beyond so-called 'small molecules'. It will address the technological challenges of these compounds and highlight recent achievements, including how synthetic and medicinal chemistry approaches can contribute to explore and optimize this new chemical space.

For more information on this event, please feel free to visit:
www.medchem.be
Contact: LD Organisation sprl
Scientific Conference Producers
Rue Michel de Ghelderode 33/2
B-1348 Louvain-la-Neuve
ph: +32 10 45 47 77 *fax:* +32 10 45 97 19
e-mail: **secretariat@ldorganisation.com**

The First RSC/SGC Symposium on Chemical Biology for Drug Discovery will take place in Oxford (UK)
December 8-9, 2009

This two-day symposium brings together chemists and biologists to explore how the interdisciplinary field of chemical Biology is enhancing our understanding of the molecular mechanisms of disease.

Scientific topics will include:
- Discovery of chemical probes
- Proteinprotein interactions
- Chemical modification of biological molecules
- Cathway deconvolution
- Chemical genetics
- Association of molecular targets with disease

These will be accompanied by perspectives on the growing trend of academic-industrial collaborations impacting chemical biology for drug discovery.
Keynote lecturers will include Prof. Andrew Hamilton, *Vice-Chancellor elect of Oxford University*; Dr Tony Wood, *Pfizer UK*; Profs Ben Cravatt and Sheng Ding, *Scripps*; Prof. Andrew Hopkins, *Dundee*; and Dr Corey Nislow, *Toronto*.

For further information see:
www.confsec.co.uk
Contact person: Elaine Wellingham,
Conference Secretariat
e-mail: **confsec@blueyonder.co.uk**

Registration will cost in the region of £200 for RSC members, £250 for non-members and £100 for students.

28th Camerino-Cyprus-Noordwijkerhout Symposium
Camerino, Italy, May 16-20, 2010
http://www.unicam.it/farmacia/symposium/index.html

XX National Meeting on Medicinal Chemistry
Padova, Italy, September 2010

18th European Symposium on Quantitative Structure-Activity Relationship
Rhodes, Greece, September, 19-24, 2010
www.eurpqsar2010.gr

XXIst International Symposium on Medicinal Chemistry
September 5-9, 2010 Brussels, Belgium

EFMC COMMITTEES

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

NEWS FROM EFMC COMMITTEES

Industrial Liaison Committee

BY MARK BUNNAGE

The Industrial Liaison Committee is focussed on developing strong links between the EFMC and the industrial medicinal chemistry community. The team comprises the following members:
Mark Bunnage - Chair *(EFMC EC Member, Pfizer, UK)*
Javier Fernandez *(EFMC EC Member, J&J, Spain)*
Graeme Robertson *(Siena Biotech, Italy)*
Brigitte Lesur *(Servier, France)*
Dave Alker *(Independent Consultant, UK)*

The committee has recently taken a fresh look at the conditions for corporate membership of the EFMC and has significantly re-vamped the range of benefits available to companies that become corporate members. Any companies interested in becoming corporate members are requested to contact **administration@efmc.info** for further details.
In addition, the committee are now looking at ways to support the broader medicinal chemistry community in Europe through a number of new initiatives. For example, plans are in development to hold a major careers event as part of the ISMC meeting in Brussels next year.

In addition, the committee are also now planning to launch a new EFMC prize for the **"Young Industrial Medicinal Chemist in Europe".** This prestigious prize will be awarded annually and presented to the recipient at one of the major EFMC meetings. Full details of the prize, and the applications procedure, will be included in the next issue of MedChemWatch. ■

The **First EFMC Short Course on Medicinal Chemistry – Improving Compound Quality** was held in Oegstgeest, The Netherlands from March 22-25, 2009 and was organised by Henk Timmerman and Han Van den Waterbeemd. The course was of high quality and the feedback from the 36 participants was very positive. The executive committee and council decided to organize a second short course in 2010. The organization will be done by the Education & Training Committee.

The council in Budapest decided to establish two new EFMC prizes. One for a **Young European Medicinal Chemist in Industry and a similar one for a Young European Medicinal Chemist in Academia.** Official announcements for these prizes will be send out later.

The president Gerhard Ecker proposed to establish an **EFMC Advisory Board** to advise EFMC on strategic decisions. This board will be chaired by Roberto Pellicciari and will furthermore consist of Peter Ettmayer, Giovanni Gaviraghi, Povl Krogsgaard-Larsen, Christian Noe, Ferran Sanz and Henk Timmerman.

On proposal of the Industry Liaison Committee the council decided on new procedures and benefits for **Corporate Members**. More information will follow on the website.

At the council meeting in Budapest, the highly successful outcome of **ISMC 2008 in Vienna** was presented by Peter Ettmayer, Chair of the Organizing Committee.

The official EFMC e-newsletter
MedChemWatch

MedChemWatch no.7 July 2009
Editor
Gabriele Costantino
University of Parma, IT

Editorial Committee
Erden Banoglu
Gazi University, TR
Jordi Mestres
MIM-UPF, ES
Wolfgang Sippl
University of Halle-Wittenberg, DE
Kristian Stromgaard
University of Copenhagen, DK
Mark Lansdell
Pfizer, UK

Design
Pupilla grafik
www.pupilla.eu

Web Design
Antalys Sprl
www.antalys.be

EFMC

European Federation for Medicinal Chemistry
www.efmc.info
info@efmc.info

Executive Committee
Gerhard F. Ecker *President*
Roberto Pellicciari *Past President*
Koen Augustyns *Secretary*
Rasmus P. Clausen *Treasurer*
Javier Fernandez *Member*
Mark Bunnage *Member*
Péter Mátuys *Member*