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EFMC

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European Federation for Medicinal Chemistry
web: www.efmc.info
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The European Federation for Medicinal Chemistry (EFMC) is an independent association founded in 1970. Free from any political convictions, it represents 24 scientific organisations from 21 European countries and covers a geographical area the size of the USA with a similar scientific population. Its objective is to advance the science of medicinal chemistry by promoting cooperation and encouraging strong links between the national adhering organisations in order to promote contacts and exchanges between medicinal chemists in Europe and around the World.

EDITORIAL

Dear colleagues,

We are approaching the year 2011, and is time to make a survey of the this ending year. Brussels has hosted the 21st International Symposium on Medicinal Chemistry (ISMC), and you will find a report of the meeting in this issue. The ISMC has clearly reached a deep maturity, has indicated by the number of participants, quality of the science, and interest demonstrated by expositors. During the ISMC, new members of the Executive Committee of the EFMC have been elected, some others leave their active involvement. You will find the new composition in the News from EC/EFMC, in this issue. I just want to take this occasion to welcome the new President Elect of the EFMC, Dr. Ulrich Stilz (Sanofi Aventis, Germany) and to greet Prof. Roberto Pellicciari who leaves the Executive Committee, after several years of active and deep commitment in the Federation, culminating with his presidency. No surprise that we offer to him and his group our Lab Presentation section, as a reward to one of the most productive academic medicinal chemistry group worldwide.
The Perspective article, by David Fox, highlights collaborative research, in its various guises, as the key to continued success in the changing and evolving world of medicinal chemistry and drug discovery.

The coming year 2011 will offer several news. Many interesting symposia, schools and courses are in the pipeline, and list is reported here. The EC of EFMC, together with the committees is actively working on a reshape of the web site, with the ambition to make it an established portal for everyone interested in medicinal chemistry, from the job portal to the meeting calendar.

I quit here, not before giving to you all my best whishes for a happy and productive year 2011!

Gabriele Costantino, *Editor of MedChemWatch*

Sharing our Collective Wisdom to Design Better Medicines

BY DAVID FOX*

The model for drug discovery is changing and we, as medicinal chemists, must evolve if we are to continue to be at the forefront of breakthroughs in new medicines. This perspective highlights collaborative research, in its various guises, as the key to continued success, drawing upon recent developments in the area.

Introduction

The challenges for the pharmaceutical industry have been well-documented in terms of the continued downward pressure on pricing, the ever more exacting regulatory hurdles and the rapidly shifting landscape demanding new, unprecedented scientific approaches.[1] For EU-based researchers, the emergence of Asia as a major player creates a truly global environment where the basis for a competitive edge needs to be revisited. Such challenges create exciting new opportunities for those who embrace the need for change and indeed, one might argue that the future prosperity of EU-based medicines research is reliant on transformation in order to build the case for continued inward investment.

So what is the basis of our future competitive edge? In addressing this question it is worth considering four areas of opportunity.[2] Firstly, we have access to world class science and world class scientists. The recent International Review of Chemistry confirmed that the UK at least is as strong as ever in terms of scholarship and talent.[3] Secondly, we have access to funding to support public-private partnerships that is geared towards developing key areas of science aligned to drug discovery. Thirdly, there is a well-established network across industrial and academic researchers that forms the basis of highly effective scientific exchange. The geographical proximity of centres of scientific excellence to industrial research sites and the high density of talent in the EU are key enablers in this respect. Finally, there is a prevailing mindset amongst EU-based researchers that collaboration is genuinely a virtue rather than a threat to one's scientific achievement.

This last point is particularly important. Across the board in both academic- and industrial research, there has been a step change in the way collaboration is viewed and embraced. This is in response to the highly complex problems that face researchers and where no single discipline expert can provide the solution. The shift in academia towards research centres is testament to this, where research topics cross discipline boundaries and where discipline experts come together in a truly collaborative sense to work in areas of common interest. An equally significant change has taken place in the industrial setting, for similar reasons. Gone are the days where large pharma would assume that because they have hired the best talent if they can't find a solution from within then the solution probably doesn't exist. Instead, there is a growing realisation that the scientists within the organisation are one part of a multi-dimensional research effort where additional external scientific know-how needs to be brought to bear in order to arrive at effective solutions. This is especially important at a time when the science underpinning drug discovery is moving at such a pace that

it is unrealistic to expect that all the necessary scientific capability to address future challenges can be housed under a single roof.

If collaborative research is the way forward, the EU through the attributes outlined above, provides a particularly fertile environment for scientific partnership to flourish. It is our responsibility now to drive home our advantage in these areas, working collectively where possible rather than competitively, to deliver solutions of global impact. Through such precompetitive collaboration, the baseline capability within drug research is raised to the benefit of all and to the detriment of none, allowing each us to arrive more rapidly at new, competitive scientific discoveries. Such an approach represents a substantial shift in culture but makes sense scientifically, economically and most importantly from the patient's perspective.

The remainder of this article will highlight three areas where collaborative research involving pharma-based medicinal chemistry is assuming growing significance.

Knowledge Transfer Schemes

In October 2009, the EPSRC launched a new 3-year scheme to encourage greater scientific exchange between academia and industry.[4] The knowledge transfer schemes – Knowledge Transfer Account (KTA) and Knowledge Transfer Secondment (KTS) – would serve as vehicles for bringing the fruits of academic research into the industrial environment. Over twenty universities across the UK have received knowledge transfer grants ranging in value from £450K to £8M. This fund sits with a named university grant holder who invites bids from EPSRC-funded academics across the university to support discrete pieces of work (ranging, in our experience at Pfizer, from a few weeks feasibility study to a 1-year post-doc) that serve to demonstrate the industrial applicability of the research. From the academic's perspective, this scheme provides an opportunity to expand the scope and utility of the research and to address the 'impact' agenda that is becoming increasingly important for academic research funding. For the industrial partner, knowledge transfer schemes such as this enable an expert in an emerging scientific field to apply their know-how to a problem of immediate business relevance. Recent examples of knowledge-transfer schemes at Pfizer include the application of chemical biology methods, use of new C-H activation methodology and the investigation of emerging aryl coupling technology. A number of these schemes involve the engagement of a knowledge transfer fellow who spends a significant proportion of their time with the industrial partner. In such cases, the fellow gains invaluable experience of working in an industrial environment and is able to draw upon state-of-the-art equipment and capability. These schemes are heavily subsidised by the KTA or KTS (more so than traditional TSB-funded Knowledge Transfer Partnerships)[5] and while there may be a need for the industrial partner to provide a small cash contribution, the majority of the industry costs are covered by in-kind contributions.

Despite the clear potential of these schemes to deliver high value industry-academia collaborations, they remain relatively untapped and many chemists working in academia and industry appear to be unaware of their existence, let alone the potential value they can bring to their respective research efforts. Looking forward, it will be increasingly important for the community to engage with knowledge transfer schemes to ensure that we as a sector are able to draw as much business value from academic research discoveries.

Industry-Academia Partnership

The academic and industrial chemistry communities are coming closer together and the clear boundary that existed historically between the two is becoming increasingly blurred. In the main, this should be viewed as a positive development with the emerging partnerships between the two being mutually beneficial. Recent examples of this are the 4-year EPSRC-funded pharma synthesis PhDs[6] where academics have joined together with a consortium of industrial partners (GSK, AstraZeneca, Pfizer and most recently Novartis) and the EPSRC-funded initiative Dial-a-Molecule[7]. Centres for Doctoral Training, such as the Chemical Synthesis centre at Bristol, cross-disciplinary centres such as the Structural Genomics Consortium and an increasing emphasis on iCASE collaborations (with co-authorship by industry and academia) offer further opportunities for industrial scientists to collaborate on academic research projects. While such endeavours ensure that industrial scientists remain connected to academic research to help shape it and define the opportunity space for future research, it is imperative that industry does not end up defining the direction or scope of academic research. This is a difficult balance to achieve but one that

we should continue to work towards if we are to derive as much value as possible from university-based research whilst still ensuring there is plenty of space for the unexpected outcome from fundamental, curiosity-driven research. Much of the time, this will come down to individual relationships and one initiative that could be particularly important in this respect is the 'embedded academics' model being championed by Professor Joe Sweeney from Reading University and Royal Society Industrial Fellow at AstraZeneca[8]. As part of this scheme, Sweeney has identified a cohort of around a dozen well-respected UK academic chemists who have committed to spend a portion of their time (ranging from days and weeks to months) embedded within an industrial chemistry department. By immersing themselves in this environment, the academics will see at first-hand the technical challenges facing the industry and will develop an understanding of what is and isn't desirable/achievable within the industrial setting. This insight will provide an informed backdrop to their research activities and could for example help to shape how they exemplify their discoveries to achieve maximum impact. The potential benefit to industry is also wide-ranging; on one level, having regular access to an experienced academic who has a detailed appreciation of the chemists' projects creates a collaborative interaction that is in stark contrast to the transactional nature of ad hoc consultancy. Beyond this, the regular presence of an academic researcher could help to evolve the way problems are approached and could present new opportunities for continuing professional development (e.g. research proposal writing, publications).

The relationship between industry and academic researchers will assume ever greater importance in the future[9] and significant effort is ongoing through consortia such as SE Biopharma Skills Consortium[10] and EMTRAIN[11] (part of the Innovative Medicines Initiative) to identify the options for future models of collaborative research, education and training.

Cross-pharma Collaboration

This final section deals with what is potentially the most transformational and challenging area of collaborative research – cross-pharma precompetitive collaboration. This is a theme that has gained momentum in recent years with cross-industry consortia beginning to assume greater significance. Examples include ViiV Healthcare[12], (a company established by Pfizer and GSK for the co-development of HIV medicines), eTox[13] (an Innovative Medicines Initiative collaboration on predictive toxicology involving 11 major organisations) and Pistoia Alliance[14] (a partnership to develop data standardisation, involving up to 40 organisations).

In medicinal chemistry, however, such cross-pharma collaborations are still in their infancy, with the EPSRC-sponsored workshop on Chemical Biology being a notable exception[15]. In response, the Royal Society of Chemistry recently hosted the first in a series of precompetitive workshops intended to stimulate new collaborations across the sector[16]. The workshop, which attracted 60 participants across industry, academia, professional bodies, funding bodies and Sector Skills Councils, centred on two themes; compound attrition and continuing professional development. Following a series of short introductory presentations, scientists drawn largely from industry were given the opportunity to present posters on areas of their research that would benefit from cross-pharma collaboration (e.g. co-development of platforms or tools, data sharing). In the subsequent discussion, up to ten areas were identified where companies are already working (and potentially duplicating effort) and these will be form the basis of a series of targeted consortia. The themes include: developing a better understanding of genetic toxicology of aromatic amines; designing compounds outside of conventional rule-of-five space; new in silico tools for predicting attrition.

Around two-thirds of the participants completed an event feedback form with 100% of respondents supportive of further precompetitive workshops and over 80% of respondents stating that they were likely to engage in a cross-sector collaboration as a result of the day. Based on the success of this inaugural workshop, the Royal Society of Chemistry plans to host further precompetitive workshops for medicinal chemists through 2011. Potential themes for these workshops include: academic collaborations, knowledge transfer and funding opportunities; chemical biology and target selection; transporters and targeted delivery; hit discovery; data analysis and visualisation.

Whilst the first workshop was well-attended by scientists based in large pharmaceutical organisations (including Pfizer, AstraZeneca, GSK, Novartis, Lilly, Merck, Eisai, Takeda) biotechs, SMEs and universities were less well represented. For precompetitive collaboration of this nature is to realise its full potential impact and deliver

maximum value to medicinal chemists, it is vital that future workshops successfully draw-in scientists from all sectors of the medicinal chemistry community.

Closing Thoughts

The discovery of new and effective medicines in the future will demand new models for scientific collaboration to deliver solutions to increasingly complex scientific challenges. If we are to succeed as a sector and maintain a competitive edge, we have no choice but to collaborate in order to maximise the return on investment in research, drive continued future investment and ensure retention of the best talent. This has implications for how we train our scientists, such that they develop alongside their discipline excellence, the skills and behaviours they will need to thrive in the complex world of collaborative research.

As medicinal chemists, we have only scratched the surface in terms of what collaborative research can deliver, be it academia-industry partnership or cross-pharma collaboration. Scientists will need to be more receptive to the opportunities for collaboration and open innovation and more confident about working in pre-competitive space. This is a significant but surmountable challenge for an industry that historically has been, by default, secretive and protective and represents an exciting new frontier for medicinal chemists.

***David Fox**
Director, External Chemistry Partnerships and RSC Visiting Senior Industrial Fellow, Pfizer Worldwide Medicinal Chemistry, Sandwich

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5 www.ktponline.org.uk
6 www.pharmasynth.org.uk/PharmaSynthCMS
7 www.personal.soton.ac.uk/dialamol/index.html
8 www.rsc.org/chemistryworld/Issues/2010/August NurturingIndustrialCollaboration.asp
9 For a recent survey on industry-academic collaborations within the pharmaceutical industry, see www.abpi.org.uk/publications/pdfs/Changing%20shape%20of%20academic%20collaborations%20with%20the%20pharmaceutical%20industry.pdf
10 www.reading.ac.uk/web/files/press/B01896_biopharma_skill_report.pdf
11 www.emtrain.eu
12 www.viivhealthcare.com
13 www.etoxproject.eu
14 www.pistoiaalliance.org
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16 www.rsc.org/ConferencesAndEvents/RSCEvents PrecompetitiveWorkshops/SharingWisdom.asp

The Pellicciari Group

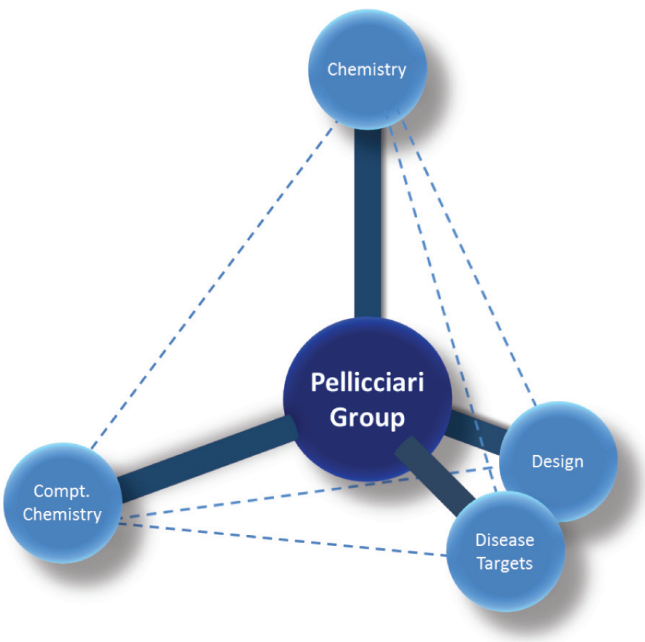
Department of Chemistry and Drug Technologies
University of Perugia, Italy

The Medicinal Chemistry research group at the Department of Chemistry and Drug Technologies of the University of Perugia (Italy), led by Roberto Pellicciari, is dedicated to the effective and efficient use of knowledge in investigating new reactions, design and synthesize bioactive molecules, and in devising new analytical procedures.

The Research Group

The group is structured in four highly complementary and integrated research areas including (i) Medicinal Chemistry, (ii) Organic Synthesis, (iii) Molecular Modelling, and (iv) Pharmaceutical Analysis. Focussing on this multi-disciplinary approach, the research activities of Pellicciari group are centred on the design and synthesis of biologically active molecules for nuclear receptors, GPCRs, and a variety of enzymes as main therapeutic targets in CNS disorders, cancer, liver and metabolic diseases. The compounds employed as chemical tools are the basis for the biological investigations carried out with several international collaborations.

Via research in both organic and medicinal chemistry, the group has synthesised more than 2000 final compounds, including natural products, semi-synthetic derivatives, and small molecules with drug-like properties across a number of target classes and diseases that are highlighted below.



Key Achievements and Main Areas of Research

Selective Modulators of Genomic and Non-Genomic Bile Acid Signalling Pathways

Bile acids have recently been rediscovered as key elements of paracrine and endocrine functions related to the homeostasis of cholesterol levels, control of lipid and carbohydrate metabolism, and regulation of the immune system. These effects are mediated by the activation of two distinct pathways: genomic signalling (transcriptional control), mediated by the activation of the farnesoid X nuclear receptor (FXR), and non-genomic cell signalling activated by TGR5, a G-protein-coupled receptor.

Extensive investigation of the chemistry of bile acids has provided insights into the conformational and structural features that control their selective activation of genomic versus non-genomic effects, and allowed the design and synthesis of novel bile acid analogues that are able to pharmacologically differentiate between these effects (Figure 1).

Moreover, the development of new synthetic methodologies for the structural modification and functionalization of bile acids are crucial not only for the synthesis of new derivatives with improved ADMET and PK/PD profiles, but also for the large scale production of these therapeutically active bile acid derivatives. We have also focused on physico-chemical profiles, for example, the critical micellar concentration (CMC) where the chromatographic index φ_o serves to indicate the propensity of bile acid derivatives to form micelles, and has been shown to be instrumental for the evaluation of the hydrophobic/hydrophilic balance of bile acids.

Culminating from this combined expertise, **Obeticholic Acid (6-ECDCA, INT-747)**, a first-in-class FXR agonist, was discovered and is now completing Phase II clinical trials, with Intercept Pharmaceuticals, for the treatment of primary biliary cirrhosis (PBC) and non-alcoholic steatohepatitis (NASH). Obeticholic acid is an analogue of the primary human bile acid chenodeoxycholic acid, the endogenous FXR agonist, and is based on the observation that FXR agonist activity is strongly increased when a small alkyl group, in particular, an ethyl group is introduced at the 6α-position of chenodeoxycholic acid. Positive Phase II results (2009) from studies in type-2 diabetes with non-alcoholic fatty acid disease (NAFLD) and in patients with refractory primary biliary cirrhosis (PBC), support obeticholic acid's potential as a novel, hepatoprotective agent in a broad range of chronic liver diseases. Currently, obeticholic acid is planned to proceed to Phase III trials for PBC, while pursuing additional studies in other indications such as, NASH and portal hypertension.

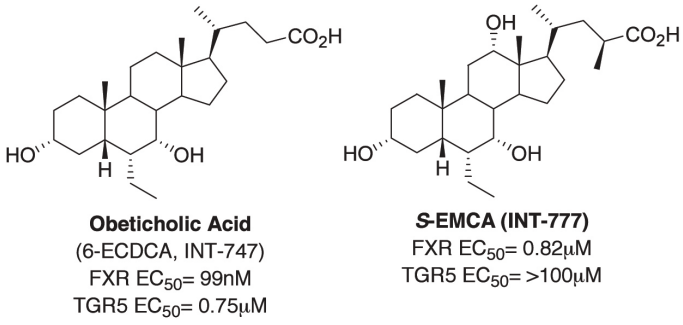


Figure 1. Switching bile acid selectivity

Building on the group's knowledge of bile acids and in particular cholic acids, a potent, selective, orally bioavailable TGR5 agonist, ***S*-EMCA (INT-777)** derived from the incorporation of a methyl and ethyl moiety respectively at the C_{23}(*S*)- and C_6α-positions was developed. In preclinical models of obesity, *S*-EMCA increases basal energy expenditure in diet-induced obese mice; prevents weight gain and adiposity; induces GLP-1 secretion and insulin sensitivity, and normalizes glycemic control. In high fat fed mice it reduces lipid levels as well as liver steatosis and fibrosis. *S*-EMCA and analogue thereof are currently being advanced for use in obesity and type-2 diabetes.

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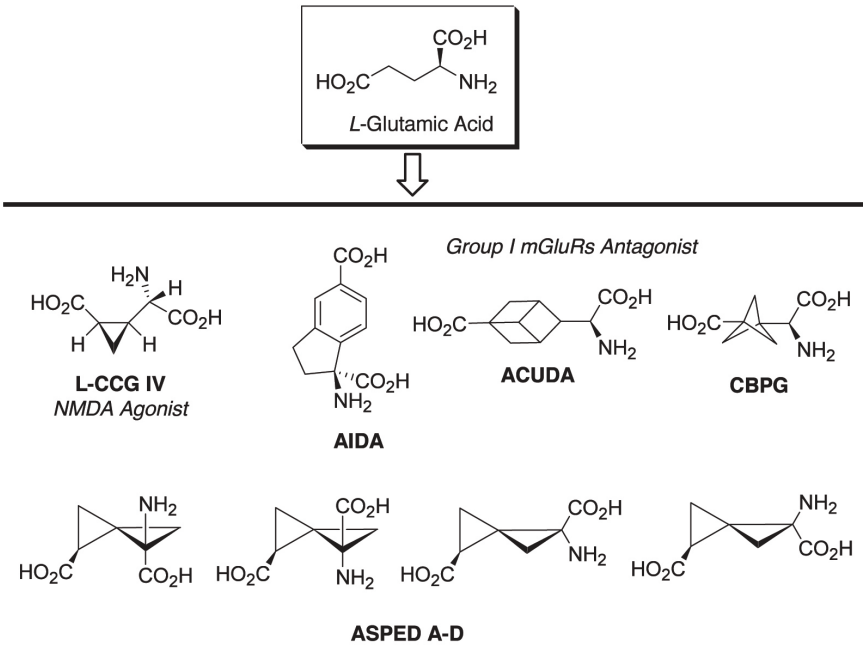

Figure 2. 'Frozen' glutamate analogues as excitatory amino acid receptor ligands

Modulators of Excitatory Glutamatergic Pathways

Neurodegenerative and neuroprotection processes are driven by highly complex and plastic signalling networks. In order to be able to generate insights into the physiological and pathological role of diverse targets within these signalling networks the development of approaches to the design and synthesis of new chemical entities capable of modulating specific enzymes and receptors is required. The synthesis of conformational constrained analogues of *L*-glutamic acid (Figure 2), for example, provided potent and selective chemical tools and has allowed the characterization of glutamatergic signalling pathways in the central nervous system and investigation of their role in neurodegenerative and neuroprotection processes.

The Pellicciari group has a long standing interest in the complex medicinal chemistry of *L*-glutamic acid (*L*-Glu), the main human excitatory neurotransmitter, addressing the design and synthesis of non-proteinogenic amino acid derived modulators of ionotropic and metabotropic glutamate receptors. For example, conformational freezing of the carbon skeleton through ring insertion and bioisosteric replacement of the distal carboxylic group, led to several classes of potent and selective glutamatergic modulators (Figure 2).

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Selective Inhibitors of Poly (ADP-ribose)polymerases

Interest in DNA damage repair mechanisms arising from hyperactivation of glutamate receptors led to an interest in poly (ADP-ribose) polymerases (PARPs).

PARP uses NAD^+ as a substrate and poly(ADP-ribos) ylates a variety of proteins, including histones, caspases, topoisomerases, and PARP itself. In the presence of moderate DNA damaging, poly(ADP-ribosyl)ation is a covalent modification which allows the enzymatic machinery to repair and maintain the genomic integrity of cells including injured neurons. In the presence of severe damage, such as those resulting from acute brain insult, the genomic integrity cannot be preserved and PARP-1 executes a death signal by consuming NAD, depleting ATP stores, and causing an energy crisis in neurons. The group has developed a novel series of thieno[2,3-c]isoquinolin-5(4*H*)-one PARP inhibitors (Figure 3) via a modelling and rational drug design approach leading to highly potent compounds such as **HYDAMTIQ** (K_i=29nM PARP-1/2) efficacious in both in vitro and in vivo models of ischemia.

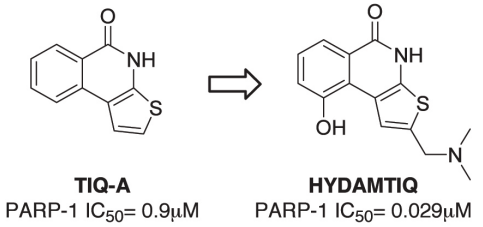

Figure 3.

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Diazo Chemistry

Diazo compounds have found numerous applications in organic chemistry because of their versatility in several synthetically useful transformations making them valuable precursors and intermediates of biologically active compounds (Figure 4).

Diazo chemistry is illustrative of the creativity and patience needed to acquire chemical control on reagents. Particular attention has been devoted in exploring the α-diazocarbonyl compounds as a source of carbenoids, and in the study of diverse reactivity of diazo substrates prepared from the reaction of cyclic and acyclic ketones, and aldehydes with ethyl diazoacetate, diazoacetone, and ethyl pyruvate by using different sets of reaction conditions. The results, have not only been instrumental for the development of new synthetic methodologies, but have also provided new insights into the mechanistic aspects of the reactions as well as an understanding of the factors and experimental conditions which govern the products formed and their relative distribution.

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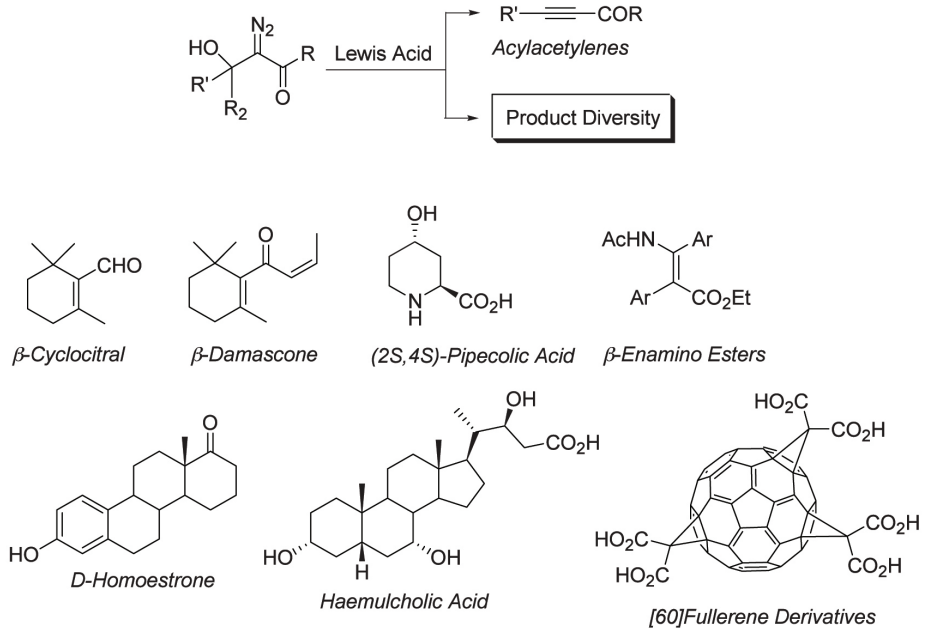

Figure 4.

The "Other Side" of Chemical Space

Recent years have seen a growing interest in exploration and navigation of the chemical space defined by the set of all possible small molecules. Accordingly, diverse strategies have been developed to explore and identify the limited portions of the chemical space where biologically active molecules lie. Our interest has been in the exploration of the "other side" of chemical space, that is, the biological counterpart of chemical space which is composed of the ensemble of protein structure binding sites. Charting the "other side" of chemical space provides a biological knowledge which when combined with chemical knowledge, aids insights into the principles that govern molecular recognition and bioisosteric relationships of functional groups. For example, applications of navigating the "other side" of chemical space have been pursued as a more effective strategy for studying the bioisosteric relationships of acidic and basic groups (Figure 5).

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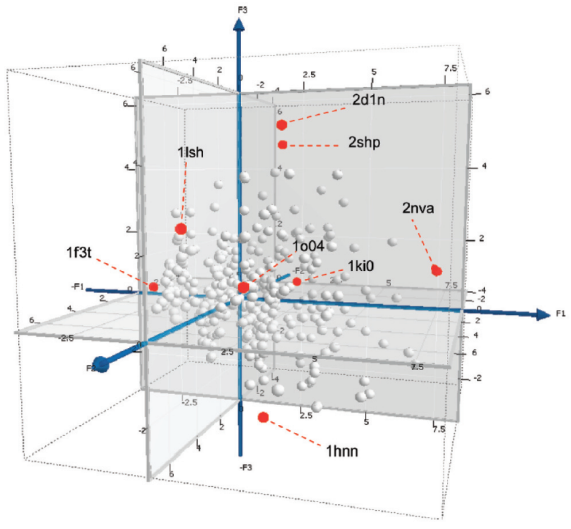

Figure 5. Amine binding sites selected at the edges of the chemical space of target site. Figure adapted from ref. 1.

Head of the Group

Professor Roberto Pellicciari initiated his scientific career working on natural products at the Istituto Superiore di Sanità and then at the Universidad de Carabobo (Venezuela) as Visiting Professor (1968-1970). From 1970 to 1973, he was Research Associate with Prof. Ernest Wenkert at the Department of Chemistry at Indiana University, Bloomington (USA) and Visiting Professor in the Department of Chemistry, University of California at San Diego (UCSD), La Jolla (1980-1981). He is currently full Professor of Medicinal Chemistry at the Department of Chemistry and Drug Technologies (University of Perugia) and adjunct Professor at the Department of Psychiatry, School of Medicine University (Maryland, USA). He is also a co-founder and Head of Medicinal Chemistry at Intercept Pharmaceuticals (New York, USA).

Professor Pellicciari enjoys an international reputation in molecular design, synthesis, mechanism of reactions, and modelling studies with more than 300 publications in international journals and 40 patents. His main research fields are; the design and synthesis of novel biologically active molecules in particular for nuclear and GPCR receptors of CNS and metabolic pathways, and the development of robust knowledge-based design and medicinal chemistry methodologies.

Professor Pellicciari has been awarded of several prizes such as the "Domenico Marotta" prize of the "Accademia Nazionale delle Scienze" (1999), the "Mentzer" prize of the French "Société de Chimie Thérapeutique" (2001), the "Giacomello Medal" of the Italian Chemical Society (SCI)" (2006) and the "Amedeo Avogadro Medal" of the "Divisione di Chimica Farmaceutica (SCI) (2009)".

Professor Pellicciari has served on many national and international committees, including; Director of the Advanced School of Medicinal Chemistry of the Italian Chemical Society and President of the Division of Medicinal Chemistry of the Italian Chemical Society (2001-2003), and President of the European Federation of Medicinal Chemistry, EFMC (2006-2008).

Organic Synthesis

In a time in which organic synthesis moves beyond its traditional objectives and major changes are introduced in the choice of synthetic targets, the area of 'Synthetic Methods Development' continue to be an issue of great impact. Having the role to define the strategies and to provide the tools within which new target molecules can be reached, organic synthesis is an obliged crossway for disciplines such as medicinal chemistry, and an effective means for the discovery of new reactions or the uncovering of new aspects of previously described ones. In Pellicciari group, Maura Marinozzi, Emidio Camaioni and Antimo Gioiello put these aims into practice. In particular, research efforts are constantly directed to the study of novel reactions and relative applications and, more in general, to the development of novel methodologies key to the synthesis of biologically active compounds.

Molecular Modelling

The Pellicciari's group was among the firsts in Italy to create an integrated environment between synthetic medicinal chemistry and molecular modelling. In 1994 the first lab of molecular modelling was installed in the group under the responsibility of Gabriele Costantino, at that time assistant professor and now professor of medicinal chemistry in Parma. The group has constantly grown up during the years and is now headed by Antonio Macchiarulo, with Andrea Carotti in the staff, and several graduate and post-graduate students completing a very productive environment which is continuously attracting students and visiting researchers also from abroad.

The aim of the lab is to provide constant computational support to the group's main activities and, at the same time, to spin off exploratory projects which could eventually be integrated in the group's platform.

Pharmaceutical Analysis

More recently, a Pharmaceutical Analysis Section has been implemented in the group under the supervision of Prof. Benedetto Natalini, with Roccaldo Sardella in the staff. Besides the analytical control in support of the organic synthesis, two main topics have been developed and are currently the subject matter of research. The former consists in the study of the mechanistic aspects and applications of new chiral selectors in the Chiral Ligand-Exchange Chromatography of amino acids. The latter is focused on the development and application of derived chromatographic indices in the physico-chemical profiling of new synthetic bile acids.

People

The Pellicciari Group comprises one full professor, Benedetto Natalini, three associate professors, Maura Marinozzi, Emidio Camaioni, and Antonio Macchiarulo, and three researchers, Antimo Gioiello, Andrea Carotti, Roccaldo Sardella. Overall, the units currently employ ca. 4 post docs, ca. 5 PhD students, and ca. 2 research assistants with, 10-15 undergraduate students researching their thesis projects each year.

Past-members of the Pellicciari group include Gabriele Costantino, who moved to the University of Parma, in 2007, as full professor in Medicinal Chemistry at the Department of Pharmaceutics. Whilst Graeme Robertson recently joined the group as Research Professor.

Contact

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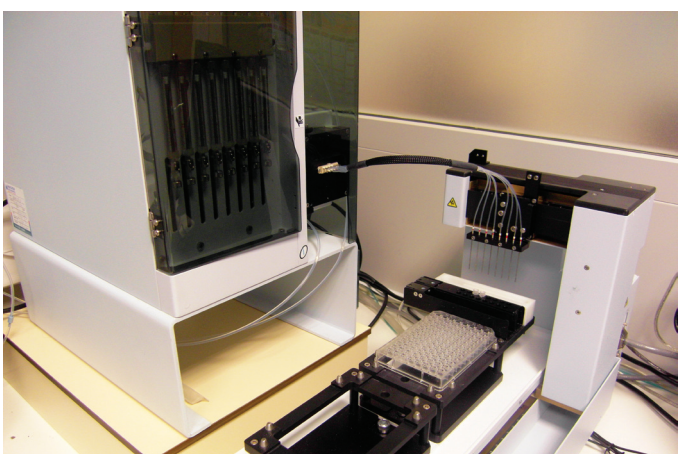
The NovAliX Group

JEAN-PAUL RENAUD

NovAliX, a innovative technology company located in the Strasbourg-Illkirch BioPark, was created in January 2009 through the merger of Novalyst Discovery, a chemistry services company, and AliX, a structural biology services company, both founded end of 2002 as spin-off companies from the Faculty of Pharmacy of the Université of Strasbourg and the Department of Structural Biology and Genomics of IGBMC, respectively. The NovAliX Group has strengthened its chemistry and biophysics capabilities ever since through the integration of complementary expertise in order to offer comprehensive services to support the pharmaceutical industry's growing outsourcing needs from discovery to manufacturing. The group's vision relies on the concept "productivity, flexibility, technology".

By combining a set of capabilities including ligand screening by SPR, non-covalent mass spectrometry (NC-MS) and NMR, protein crystallography, and medicinal chemistry, NovAliX is able to handle integrated structure-based, fragment-based, or natural-based drug discovery projects. In sum, the company implements target-driven approaches from hit identification to lead optimization.

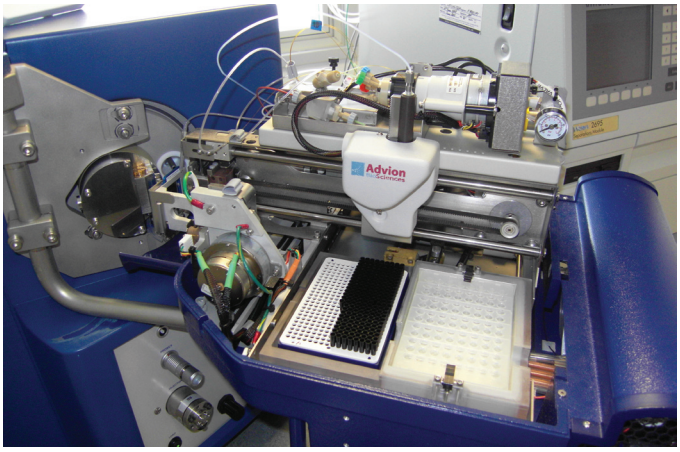
NovAliX has a strong focus on the use of biophysical techniques for drug discovery. To support its gene-to-structure platform, NovAliX has developped automated NC-MS, an approach that has emerged as a powerful tool for drug discovery[1]: (i) as a screening technique, it can efficiently remove false positives from a primary high-throughput screening or a virtual screening by assessing the physical binding of the



Nanodrop crystallization robot

primary hits to the target; (ii) alternatively, it is well-suited to screen directly fragment libraries thanks to its sensitivity; (iii) it is also a high-content technique for the detailed characterization of ligand-target interaction in terms of stoechiometry, reversibility, specificity, and affinity.

NMRTEC offers advanced NMR technologies focused on quality control to support pharmaceutical development and manufacturing teams: solution NMR for the fine characterization of biologics (Protealys) and the deformulation of drugs (DOSY[2]), solid-state NMR for the thorough analysis of APIs and polymorphism studies.



Automated incubation and injection system fitted on a nano-electrospray mass spectrometer

Phytodia is specialized in the identification and the characterization of plant extracts (development of analytical methods, quantification, resolution of complex mixtures...) as well as in the demonstration of biological activities (pharmacology, *in vitro* toxicology, and early ADME) for various allegations (slimness, aging, vitality...), supporting the development of new ingredients / products for the nutraceutical, cosmetic and pharmaceutical domains[3].

eNovalys is a small spin-off of NovAliX dedicated to chemoinformatics. The company develops an intelligent search engine for the knowledge-based identification of efficient chemical synthesis pathways and reaction conditions.

Most recently, NovAliX has acquired a majority interest in Graffinity Pharmaceuticals GmbH, located in Heidelberg, a leading fragment-based drug discovery services company. Graffinity has developed a unique, patented, high-throughput SPR screening technology based on ligand immobilization on micro-arrays[4], bringing a fully complementary platform to the NovAliX Group's biophysical capabilities in ligand screening and drug design[5].

The NovAliX Group now employs more than 120 scientists continously developing and applying innovative research capabilities for its pharmaceutical clients.

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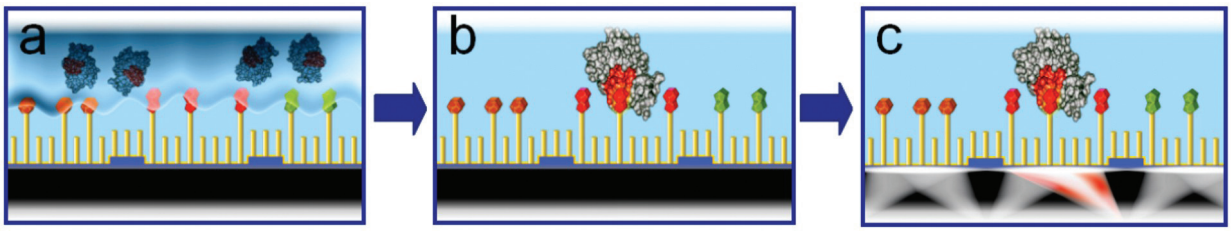
Notes and Selected Publications

1 Vivat et al., Native MS: an 'ESI' way to support structure- and fragment-based drug discovery. Future Med. Chem., **2010**, 1, 35-50
2 Balayssac et al., 2D and 3D DOSY 1H NMR, a useful tool for analysis of complex mixtures: application to herbal drugs or dietary supplements for erectile dysfunction". *J. Pharm. Biomed. Anal.*, **2009**, 50, 602-612
3 Sato et al., Anti-hyperglycemic activity of a TGR5 agonist isolated from Olea europaea. *Biochem. Biophys. Res. Commun.*, **2007**, 362, 793-798
4 Neumann et al., SPR-based fragment screening: advantages and applications. *Curr. Top. Med. Chem.*, **2007**, 7, 1630-1642
5 Renaud and Delsuc, Biophysical techniques for ligand screening and drug design. *Curr. Op. Pharmacol.*, **2009**, 9, 622-628

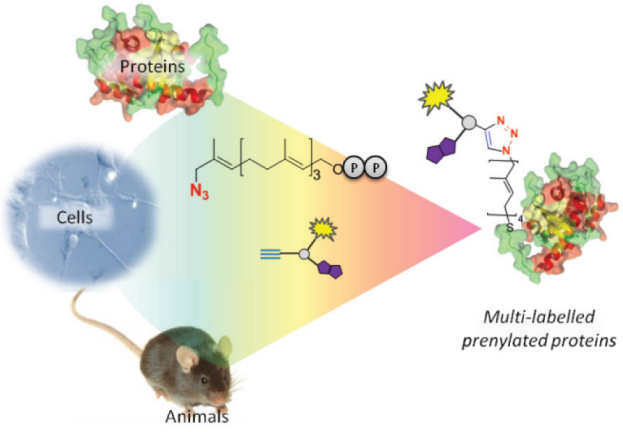


Micro-array readout by SPR imaging

Ed Tate

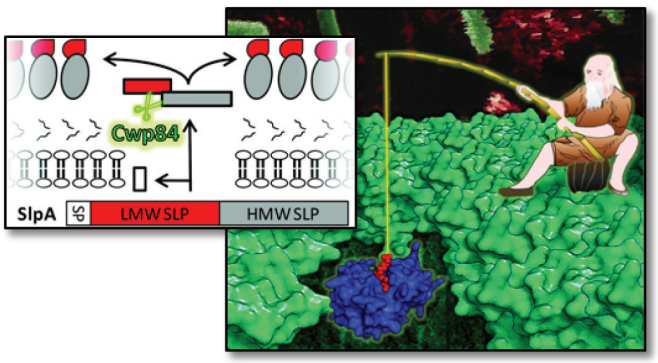
Ed Tate is currently a Senior Lecturer in Chemical Biology at Imperial College London. Following undergraduate studies at the University of Durham, he gained his PhD with Prof. Steve Ley FRS at the University of Cambridge and then worked with Prof. Sam Zard at Ecole Polytechnique (Paris) as an 1851 Research Fellow. Following postdoctoral research in molecular microbiology at the Pasteur Institute in Paris and in chemical biology at Imperial College he was awarded an independent BBSRC David Phillips Research Fellowship in 2006, and in 2010 he was appointed to his current position in the Department of Chemistry. His research group of over 20 researchers is engaged in multiple aspects of the design and application of chemical approaches to understanding living systems, with an emphasis on the roles of protein modification in disease. He has published around 40 papers and patents in the fields of organic synthesis, medicinal chemistry and chemical biology. Ed is also an integral member of theInstitute of Chemical Biology at Imperial College, where he co-convenes the first Imperial **MRes in Drug Discovery and Development**, a one year course that arms students with the knowledge and insight needed to launch a career in the rapidly evolving landscape of contemporary medicinal chemistry.

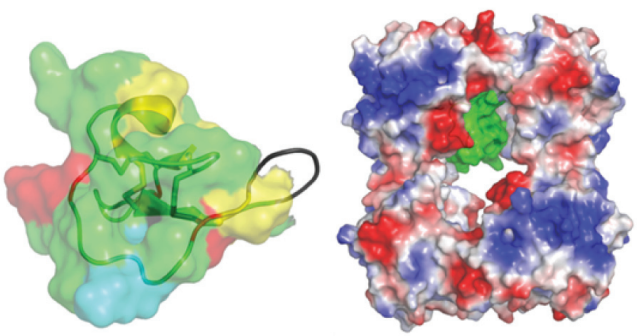
The proteome is an extremely dynamic and versatile entity, due in no small part to **post- and co-translational modification** (PTM) of proteins. Every pathway in the cell is mediated and/or regulated through PTM at some level, and these phenomena emerge from a complex network of enzyme-protein substrate interactions. My group is fascinated by the ways in which organic chemistry can be brought to bear on the formidable challenge of mapping, understanding and manipulating these PTM networks, both to reveal the basic biology of living systems and to leverage new data on druggable targets inside the cell. The main projects in our lab are dedicated to developing novel reagents for **bioorthogonal ligation**, and applying them to profile the **targets of PTM** and to profile the **activity of enzymes** that mediate PTM. For example, we have recently demonstrated new approaches for labelling **protein lipidation** in living cells, and have profiled the downstream targets of prenyl transferase inhibitors and the impact of genetic defects on **protein prenylation** *in vivo* in disease models. In collaboration with researchers at Imperial we have also described the



first example of **activity-based protein profiling** (ABPP) in the hospital superbug *Clostridium difficile*, using this powerful approach to identify and characterise the function of key proteases that remodel the surface layer of the organism.

Our second major area of activity is in developing **inhibitors** for enzymes implicated in mis-regulated PTM in disease, and as drug targets in important pathogens such as the protozoan parasites that cause malaria and leishmaniasis. In collaborative drug discovery projects we have reported the first drug-like inhibitors of the enzyme **NMT (N-myristoyl transferase)** in the malaria parasite, and the first crystal structure of this enzyme in *Leishmania donovani*. The final area we are involved in is the engineering of peptide and peptidomimetic scaffolds for the disruption of protein-protein interactions (PPIs) related to PTM. For example, we hav e re-engineered **macrocyclic cystine-knot microprotein scaffolds** for selective inhibition of a range of therapeutically important proteases, and explored the dynamics of an essential PPI in the motor that drives red blood cell invasion by the malaria parasite.





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3 J. C. Thomas, J. L. Green, R. I. Howson, P. Simpson, D. K. Moss, S. R. Martin, A. A. Holder, E. Cota and E. W. Tate, "Interaction and dynamics of the Plasmodium falciparum MTIP/MyoA complex, a key component of the invasion motor in the malaria parasite". MolBioSyst, **2010**, 6, 494.

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5 Thongyoo P., Bonomelli C., Leatherbarrow R. J., Tate E. W., "Potent inhibitors of β-tryptase and human leukocyte elastase based on the MCoTI-II scaffold". *J. Med. Chem*., **2009**, 52, 6197-6200.

6 W. P. Heal, S. R. Wickramasinghe, P. W. Bowyer, A. A. Holder, D. F. Smith, R. J. Leatherbarrow and E. W. Tate, "Site-specific N-terminal labelling of proteins in vitro and in vivo using N-myristoyl transferase and bioorthogonal ligation chemistry". *Chem. Commun*., **2008**, 4, 480-482.

News from the Societies

BY ERDEN BANOGLU

Biological & Medicinal

Chemistry Sector

THE BIOLOGICAL AND MEDICINAL CHEMISTRY SECTOR OF THE RSC

Continuous Processes & Flow Chemistry

3-4 November 2010, GSK Stevenage

The Biological and Medicinal Chemistry Sector of the RSC recently sponsored the 1st Continuous Processing and Flow Chemistry Conference in partnership with the SCI. The 2-day conference was hosted in early November at the excellent conference facilities at GlaxoSmith-Kline Stevenage, UK and was sponsored by a range of pharmaceutical and flow chemistry companies. Furthermore it attracted a strong line-up of speakers from Europe and the US including many leaders in the field from both academia and industry. The conference was a great success attracting around 200 delegates and many excellent poster presentations. Based on excellent feedback the organising committee are planning a second conference to be scheduled for 2012.

Medicinal Chemistry of Tropical Disease

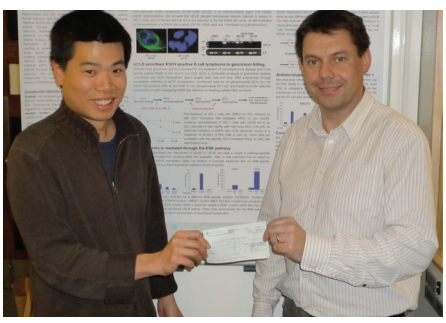
11 November 2010, The Hidden Battle, London School of Hygiene and Tropical Medicine

http://www.maggichurchouseevents.co.uk/BMCS/

This one day symposium highlighted the challenges facing medicinal chemists tackling some of the diseases which ravage the populations of the poorer parts of the world. The line-up of speakers was truly international and described 'cutting-edge research' in this field. Professor Simon Croft (London School of Hygiene and Tropical Medicine) opened the symposium with a plenary lecture highlighting the background and current status of third world diseases which was followed by recent results on the first Tetraoxane anti-malarial drug RKA 182 by Professor Paul O'Neill (Liverpool School of Tropical Medicine). Dr Alan Stone (Medical Scientific Advisory Services) outlined recent advances in the use of microbicides as oral prophylaxis to prevent HIV transmission while Professor Ian Gilbert (University of Dundee) spoke about approaches to drug discovery for the neglected tropical disease tuberculosis. Professor Anastassis Perrakis (Netherlands Cancer Institute, Amsterdam) disclosed recent results on the J-base binding protein from Leishmania while Dr Jeremy Burrows (Medicines for Malaria Venture) talked about some recent medicinal chemistry on anti-malarial drug discovery. Professor Brent Korba (Georgetown University, USA)summarised the viral and cellular targets for anti-HCV therapies while in the final talk Dr Jose-Maria Bueno (GSK Tres Cantos, Spain) summarised approaches to 4(1H)-Pyridones as anti-malarial agents.

Posters were presented over lunch by sixteen postgraduate or postdoctoral researchers working in drug discovery towards the treatment of tropical disease. These were of a very high standard and covered the whole range of scientific disciplines including molecular biology, medicinal chemistry and computational chemistry. Prizes were awarded to the poster presenters judged to have the best posters – the winners are pictured below.

Sean Hudson from the Department of Chemistry, University of Cambridge, winner of poster prize for the best poster at the symposium, pictured with his supervisor, Professor Chris Abell



Ed Tsao from the MRC Centre for Medical Molecular Virology, Division of Infection and Immunity, University College London, winner of the runner-up prize for the best poster at the symposium, pictured with his supervisor, Professor Paul Kellam

SCS

Division of
Medicinal Chemistry

DIVISION OF MEDICINAL CHEMISTRY OF THE SWISS CHEMICAL SOCIETY

March 20-23, 2011
Joint German-Swiss Meeting on Medicinal Chemistry "Frontiers in Medicinal Chemistry", Saarbrücken, Germany, for details see www.gdch.de/medchem2011.

September 09, 2011
Division of Medicinal Chemistry, oral and poster session at the Fall Meeting of the Swiss Chemical Society, EPFL Lausanne.

LÄKEMEDELSAKADEMIN
SWEDISH ACADEMY OF PHARMACEUTICAL SCIENCES

THE SWEDISH ACADEMY OF PHARMACEUTICAL SCIENCES

The 5th Anglo-Swedish Medicinal Chemistry Symposium
20-23 March 2011, Åre, Sweden
This symposium is the 5th meeting organized jointly between Medicinal Chemistry Section of the Swedish Academy of Pharmaceutical Sciences and the Biological and Medicinal Chemistry Sector of the Royal Society of Chemistry, UK. The aim of the meeting is to promote the very best of medicinal chemistry in a stimulating environment.

Frontiers in Medicinal Chemistry: Emerging Targets, Novel Candidates and Innovative Strategies
19-21 June 2011, Stockholm
The meeting is intended to bring scientists working in the medicinal chemistry field together in order to share new and exciting results and we encourage attendees to bring poster presentations. The event is co-organized by the European Federation of Medicinal Chemistry, the American Chemical Society Division of Medicinal Chemistry, and by the Swedish Academy of Pharmaceutical Sciences. We invite you to beautiful Stockholm at the bright midsummer season and hope that you will have a scientifically rewarding and enjoyable stay.

Introduction Course to Quantitative Pharmacology and PK/PD for Drug Discovery & Development Scientists
7-8 September 2011, Munich
The lack of training opportunities in quantitative pharmacology is hurting the industry. There are a lack people able to design, carry out, and analyze in vivo experiments, and then build models to extrapolate data across species and into man. All big Pharma companies are searching for people with PK/PD skills, but the demand is greater than the actual output from academia This course aims to give the course delegates confidence and encouragement to have a go at PKPD and to build relationships between bioscience, medicinal chemistry, DMPK and related scientific disciplines. The programme is comprised of lectures and afternoon group exercises. The course is suitable for preclinical and/or clinical scientists working within the fields of bioscience, safety, medicinal chemistry, biostatistics, pharmacokinetic, pharmacology etc.

Società Chimica Italiana
Divisione di Chimica Farmaceutica

DIVISION OF MEDICINAL CHEMISTRY OF THE ITALIAN CHEMICAL SOCIETY

XX National Meeting on Medicinal Chemistry
September 12-16, 2010,
Abano Terme, Padova, Italy
REPORT
The "XX National Meeting on Medicinal Chemistry", organized by the Medicinal Chemistry Division of the Italian Chemical Society under the auspices of the European Federation of Medicinal Chemistry was held in Abano Terme, a renowned spa town close to Padova on 12-16 September 2010. Continuing

a tradition initiated two years ago, the Meeting has strengthened its international character by the use of English as the official language and by the involvement of several foreign speakers both from Academy and Industry. This represented a significant step towards internationalization and allowed young scientists to get in touch with each other, to get acquainted with the recent developments in the Medicinal Chemistry area and to establish fruitful connections with high level research groups.
The following scientific topics were handled:
– CNS Medicinal Chemistry
– Epigenetics: a new pathway to Drug Discovery
– Oncology Medicinal Chemistry
– Antibacterial and Antiviral Agents
Pharmaceutical Profiling Assays in Drug Discovery and Development
– Drug Design
They are clearly relevant to pharmaceutical research and stimulated wide interest in the scientific community as they aim at rational design, synthesis, analysis and development of innovative drugs.
The Opening Lecture, delivered by K. C. Nicolaou, Scripps Research Institute, La Jolla, California was followed by 7 plenary lectures, 17 main lectures, 24 short communications and about 160 poster presentations in subsequent days.
A specific session has been devoted to the topic: "Science Meets Business" during which speakers from Industry discussed with academic researchers, including post-doctoral fellows , issues concerning R&D from a Company perspective.
Total attendance amounted to 260, with 10% foreign participants. Attendance from Industry was about 12%. These figures are satisfactory, in particular considering the present unfavorable economic trend. Finally, it is worth mentioning that attendance by young researchers and PhD students accounted for about 40% of the total, which points to an increasing interest for pharmaceutical disciplines in Italy.
During the Meeting the prestigious prize Luigi Musaio was awarded to Professor Luisa Mosti, University of Genova, past President of the Medicinal Chemistry Division for outstanding scientific achievements. Finally, two Farmindustria prizes for young promising researches were delivered to Drs. Luciana Marinelli (University of Naples) and Tiziano Tuccinardi (University of Pisa).

PFIZER

22nd Pfizer Poster Symposium

The 22nd Pfizer Poster Symposium was held on the 7th December at the Royal Society of Chemistry in London. A fantastic mix of top-quality science was on display from the 30 PhD students attending the event, ranging from complex total synthesis and novel synthetic methodologies to cutting edge chemical biology.

Don Middleton, Phil Parsons, Alastair Lennox, Mark Bunnage

The event was attended by a number of Pfizer colleagues and UK-based academics. The judging was carried out by Dr. Don Middleton (Pfizer) and Professor Phil Parsons (Sussex University). Prizes were awarded to Alex Cresswell (Oxford University, Prof. S. Davies group), Elizabeth Jones (Imperial College London, Prof. A. Barrett group) and Stephen Wallace (Oxford University, Dr. M. Smith group).

The overall winner was Alastair Lennox from the Prof. G. Lloyd-Jones group at Bristol University. The organizing committee and Dr. Mark Bunnage (Head of Medicinal Chemistry, Sandwich) would like to extend their thanks to the judges and their congratulations to the winners!

THE EFMC PRIZE

THE EFMC PRIZE FOR A YOUNG MEDICINAL CHEMIST IN ACADEMIA

To acknowledge and recognize an outstanding young medicinal chemist (≤35 years old) working in Academia within Europe.

The **prize** is given annually and consists of a diploma, € 1.000 and an invitation to give a short presentation at an EFMC symposium. Two additional nominees will also be identified and acknowledged.

Applications should consist of:
- a one-page letter by the candidate including a short rationale for their application
- one page with his/her 5 most important publications
- a brief cv of the candidate
- abstract of potential oral presentation

THE EFMC PRIZE FOR A YOUNG MEDICINAL CHEMIST IN INDUSTRY

To acknowledge and recognize an outstanding young medicinal chemist (≤35 years old) working in Industry within Europe.

The **prize** is given annually and consists of a diploma, € 1.000 and an invitation to give a short presentation at an EFMC symposium. Two two additional nominees will also be identified and acknowledged.

Nominations should be submitted by the candidate's supervisor and should consist of:
- a letter by the supervisor
- a brief cv of the candidate
- abstract of potential oral presentation

EFMC

Deadline for Nominations is January 31, 2011

See www.efmc.info for full details

EFMC Short Course

3rd Short Course on Medicinal Chemistry

PRINCIPLES AND APPLICATIONS OF IN VITRO PHARMACOLOGY IN DRUG DISCOVERY FOR MEDICINAL CHEMISTS

April 10-13, 2011

This intensive course is intended for scientists working in the field, and the presentations will be given by senior scientists both from industry and academia. The number of participants will be limited to 35, to favour in depth discussion.

Course Outline

In the initial phases of drug discovery where compound potency and selectivity are major considerations, data derived from biologists is of prime importance to the chemist. This short course will be a mixture of talks, tutorials and case histories involving GPCRs (G protein coupled receptors), enzymes and ion channels.
The course will discuss:
The techniques and data that biologists use to assess potency and selectivity of agonists, antagonists and enzyme inhibitors. | The 'rules' under which such data is collected – and what happens if these rules are not obeyed. | Distinguishing between potency and affinity. | Equilibrium and kinetic assays. | How kinetic assays can seriously improve your project. | Translating in vitro data to the in vivo environment.

Organisers
Mike Trevethick, *Discovery Biology, Pfizer*
Henk Timmerman, *VU Amsterdam*

Deadline for registration
February 28, 2011

Venue
Castle "Oud Poelgeest", Oegstgeest (near Leiden), The Netherlands
Airport: Schiphol (Amsterdam)

Fee
€ 1275,00
Including 3 nights accommodation, breakfast, coffee breaks, lunches and dinners during the 3 days of the conference.

Contact
EFMC Administrative Secretariat
LD Organisation sprl
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Rue Michel de Ghelderode 33/2
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tel: +32 10 45 47 74 fax: +32 10 45 97 19
mail: administration@efmc.info
web: www.efmcshortcourses.org

EUROPEAN FEDERATION FOR MEDICINAL CHEMISTRY

EFMC NEWS

BY NELE COULIER AND KOEN AUGUSTYNS

At the annual EFMC Council Meeting, held on occasion of the XXIst International Symposium on Medicinal Chemistry (Brussels, September 5-9, 2010), the Council elected 6 positions for the Executive Committee, chaired by the EFMC President, Prof. Gerhard Ecker (University of Vienna, Austria). Dr. Ulrich Stilz (Sanofi Aventis, Germany) has been voted President –elect, Prof. Koen Augustyns (University of Antwerp) and Prof. Rasmus P. Clausen (University of Copenhagen, Denmark) have been re-elected Secretary and Treasurer and Dr. Javier Fernandez (Janssen R&D, Spain), Dr. Hein Coolen (Solvay Pharmaceuticals, The Netherlands) and Prof. Gabriele Costantino (University of Parma, Italy) have been voted EC members. Their term will start on Jan 1st, 2011 and last for two years. The president-elect will automatically become president on Jan 1st, 2012.

The Medicinal Chemistry Section of the Croatian Chemical Society and the Finnish Pharmaceutical Society applied for EFMC membership. At the latest Council meeting, Dr. Ivica Malnar (Galapagos, Croatia) and Dr. Erik Wallèn (University of Helsinki, Finland) gave a presentation on the means and objectives of their society. Both applications were unanimously approved by the Council.

At the Council meeting in Brussels, it has been decided that in 2014 the International Symposium on Medicinal Chemistry (EFMC-ISMC) will be held in Lisbon and organized by the Group of Medicinal Chemistry of the Portuguese Chemical Society on behalf of EFMC. The 2012 edition will take place in Berlin on September 16-20.

The new compositions of the 3 EFMC Committees, devoted to Education and Training, Industry Liaison and Information&Communication have been announced. As of Jan 1st, 2011, the Industry Liaison Committee will be chaired by Graeme Robertson (Formerly with Siena Biotech, Italy) and composed of Mark Andrews (Pfizer, UK), Christophe Genicot (UCB, Belgium), Ana Gradillas (CEU University, Spain), Rob Leurs (VU University, The Netherlands), Liz Pease (AstraZeneca, UK) and Leandros Skaltsounis (University of Athens, Greece). Members of the Education and Training Committee, chaired by Javier Fernandez (Janssen R&D, Spain), will be Armin Buschauer (University of Regensburg, Germany), Norbert Haider (University of Vienna, Austria), Peter Mohr (Hoffman La Roche, Switzerland), Silvia Ortega (Universidad Complutense de Madrid, Spain), Maurizio Recanatini (Univerity of Bologna, Italy) and Alan Stobie (Pfizer, UK). The Information and Communication Committee will be chaired by Koen Augustyns (University of Antwerp, Belgium) and consist of Terence Beghyn (Université de Lille, France), Gabriele Costantino (Editor of MedChemWatch, Italy), Laszlo Molnar (Gedeon Richter, Hungary), Christa Müller (Pharmaceutical Institute, Germany), Rino Ragno (Università di Roma, Italy), David Rees (Astex Therapeutics, UK). The EFMC Committees strengthen the links between Council and EC and help to define the mission, vision and goals of EFMC.

To acknowledge and recognize an outstanding young medicinal chemist (< 35 years old) working in academia or in industry within Europe, EFMC is conferring every year the EFMC Prize for a Young Medicinal Chemist in Academia and the EFMC Prize for a Young Medicinal Chemist in Industry. The prizes consist of a diploma, a cash prize and an invitation to give a presentation at an EFMC symposium. More information on the submission process is available on the EFMC website. Deadline for nominations is January 31, 2011.

EFMC is funding grants for EFMC organised events with the aim to support the participation of young academic scientists. Upon application, up to 50% of the registration fee for EFMC-ISMC, EFMC-ASMC, Frontiers in Medicinal Chemistry, EFMC Short Courses or the EFMC Accredited School will be covered by EFMC. Applications should reach the Administrative Secretariat (administration@efmc.info) at least six weeks prior to the event and should consist of a CV and a short motivation letter.

The EFMC website offers links to the job portals of EFMC corporate members as well as information on current vacant positions. The posting of job offers is free and is available for any medchem related jobs, in industry as well as academic positions. To have your job offer published on the website, please fill in the application form available on the site.

We also invite you to have a look at the renewed meeting calendar, aimed to become a one stop shop for all medicinal chemists. Monthly tabs and a search function give you the possibility to navigate easily through the list of worldwide organized medchem events. The calendar is updated and completed on a regularly basis.

EFMC EVENTS

BY NELE COULIER AND KOEN AUGUSTYNS

EFMC ORGANISED EVENTS

FRONTIERS IN MEDICINAL CHEMISTRY MEETING: EMERGING TARGETS, NOVEL CANDIDATES AND INNOVATIVE STRATEGIES
June 19-21, 2011
Stockholm, Sweden
http://www.malmokongressbyra.se/efmc_2011

4TH INTERNATIONAL SYMPOSIUM ON ADVANCES IN SYNTHETIC AND MEDICINAL CHEMISTRY
August 21-25, 2011
St-Petersburg, Russia
http://www.ldorganisation.com/produits.php?langue=english&cle_menus=1238915414

EFMC SPONSORED EVENTS

2ND NATIONAL MEETING ON MEDICINAL CHEMISTRY
November 28-30, 2010
Coimbra, Portugal
http://www.spq.pt/eventos/enqt2010/

5TH ANGLO-SWEDISH MEDICINAL CHEMISTRY SYMPOSIUM
March 20-23, 2011
Are, Sweden
http://www.lakemedelsakademin.se/templates/kurs/kurstillfalle.aspx?id=4256

EFMC SPONSORED SESSION AT ACS SPRING MEETING 2011
March 27-31, 2011
Anaheim, California, USA
http://portal.acs.org/portal/acs/corg/content?_nfpb=true&_pageLabel=PP_SUPERARTICLE&node_id=431&use_sec=false&sec_url_var=region1&__uuid=2fa0105c-54a3-45ab-8a0a-ffecb4d61952

EFMC SPONSORED SESSION AT THE AFMC MEETING 2011
November 29-December 2, 2011
Tokyo, Japan

http://www.aimecs11.org/

EFMC SPONSORED SESSION AT PHARMSCIFAIR 2011
June 13-17, 2011
Prague, Czech Republic

http://www.pharmscifair.org/

4TH BBBB INTERNATIONAL CONFERENCE ON PHARMACEUTICAL SCIENCES
September 29-October 1, 2011
Bled, Slovenia
http://www.sfd.si/?mod=aktualno&action=viewOne&ID=223 (but website not yet updated)

19TH EUROQSAR - KNOWLEDGE ENABLED LIGAND DESIGN
August 26-31, 2012
Vienna, Austria
http://www.ldorganisation.com/produits.php?langue=english&cle_menus=1238915416

COURSES AND SCHOOLS

3RD EFMC SHORT COURSE ON MEDICINAL CHEMISTRY
Principles and Applications of in Vitro Pharmacology in Drug Discovery for Medicinal Chemists
April 10-13, 2011
Oegstgeest (near Leiden), The Netherlands
http://www.ldorganisation.com/produits.php?langue=english&cle_menus=1238915410

31TH EDITION OF THE EUROPEAN SCHOOL OF MEDICINAL CHEMISTRY (ESMEC)
July 3-8, 2011
Urbino, Italy
http://www.esmec.eu
(but website not yet updated)

SUMMER SCHOOL ON PHARMACEUTICAL ANALYSIS (SSPA)
September 19-21, 2011
Pavia, Italy
http://www.scpaweb.org/home.htm
(but website not yet updated)

20TH LACDR SCHOOL ON MEDICINAL CHEMISTRY
October 2011
Oegstgeest (near Leiden), The Netherlands
http://medchem.lacdr.gorlaeus.net/node/3039
(but website not yet updated)

SUMMER SCHOOL ON DRUG DESIGN
Vienna, Austria
Sept 11-16, 2011, Vienna
www.oephg.au

RESIDENTIAL SCHOOL: MEDICINAL CHEMISTRY
Nottingham, UK
No information received

XXIst EFMC-ISMC 2010 in Brussels

BY ERDEN BANOGLU

REPORT

With more than 1,150 participants from 47 nations, the XXIst EFMC-International Symposium on Medicinal Chemistry (ISMC 2010), held at the Brussels meeting centre SQUARE from September 5-9, 2010, has been a very successful symposium with a diverse and high quality program.

ISMC 2010 was jointly organized by the Medicinal and Bioorganic Chemistry Division of the Royal Flemish Chemical Society (KVCV) and by the Medicinal Chemistry Division of the Société Royale de Chimie (SRC), on behalf of the European Federation for Medicinal Chemistry (EFMC).

The opening ceremony, led by Dr Edmond Differding (formerly with UCB) and Prof. Koen Augustyns (University of Antwerp), symposium chairmen, and Prof Gerhard Ecker (University of Vienna), EFMC President, was the start of a five day symposium with many scientific highlights. With an introduction to IMI, the Innovative Medicines Initiative Joint Undertaking (IMI JU), by Prof. Michel Goldman (Executive Director of IMI, Belgium), the tone was set for what became a successful symposium with about 100 speakers, more than 500 poster presentations, 50 exhibitors and 30 sponsors.

The three prestigious biennial EFMC Awards were also conferred during the opening ceremony by EFMC President Prof. G. Ecker:

– The winner of this year's "Nauta Award for Pharmacochemistry" was Prof. Camille G. Wermuth (Université Louis Pasteur Strasbourg and Prestwick Chemicals) for his significant contribution to the science of medicinal chemistry, both by scientific achievements and by educational activities. Prof. Wermuth contributed to the development of three marketed drugs and the results of his work are documented in more than 250 publications and 60 patents.

– The "UCB-Ehrlich Award for Excellence in Medicinal Chemistry" was granted to Dr. Anthony Wood from Pfizer Global Research for his instrumental role in the discovery of Maraviroc, the first small molecule antagonist of the CCR5 receptor marketed for the therapy of HIV infections. Maraviroc represents the first successful advancement of a chemokine receptor modulator to the market and for the first time provided an antiviral therapy that targets a host protein rather than a viral protein.

– The "Prous Institute - Overton and Meyer Award for New Technologies in Drug Discovery" was given to Prof Klaus Müller (ETH Zürich) for his pioneering work in the field of computer assisted molecular modeling and for his seminal contributions to the understanding of multipolar interactions and fluorine effects in protein-ligand interactions. Prof. Müller has been instrumental in implementing and further developing computational techniques for use in the drug discovery and development process both through his leading role in pharmaceutical industry and his teaching activities in academia.

Additionally, ISMC 2010 welcomed Dr Arun K. Ghosh, the recipient of the "IUPAC-Richter Prize in Medicinal Chemistry". He received this award in recognition of his outstanding use of structure-based design of HIV-1 protease inhibitors using his novel concept of "backbone binding" to withstand drug resistance. This work produced the novel drug Darunavir which was approved by the FDA in 2006 as the first treatment for multidrug resistant HIV. He has also pioneered structure-based design of β-secretase inhibitors for treatment of Alzheimer's disease. One such compound has now entered into advanced clinical trials.

Furthermore, on occasion of ISMC 2010 the newly created "EFMC Prize for a Young Medicinal Chemist in Industry" and the "EFMC Prize for a Young Medicinal Chemist in Academia" were conferred for the first time. Dr. Antonio Nardi (Grünenthal) and Dr. Andreas Bender (Leiden/Amsterdam Center for Drug Research), have been honoured for their outstanding achievements related to drug discovery research.

Three plenary lectures were among the highlights of the program:
– Prof. Sir Tom Blundell from University of Cambridge presented a lecture entitled "Genomes, Structural Biology and Drug Discovery: New Challenges from Difficult Targets and Neglected Diseases" to emphasize how the increasing knowledge emerging from genomics of man and pathogens and from biochemical and structural proteomics programs may accelerate the drug discovery, and where we stand in the practical implementation of these novel information in medicinal chemistry approaches.
– The second plenary lecture was entitled "A Chemical Approach to Controlling Cell Fate", presented by Prof. Sheng Ding from Scripps Research Institute. During the lecture, Prof. Ding highlighted the findings from his discovery efforts to advance the ability to control stem cell fate, survival, differentiation and reprogramming of pluripotent stem cells.
– The closing lecture was given by Prof. Greg Verdine from Harvard University, on 'Drugging the Undruggable'. Given the fact that an estimated 80-90% of all potential targets are undruggable by classical approaches, his group has developed a new chemistry-based platform, relying on "synthetic biologics" such as hydrocarbon-stapled alpha-helical peptides that are capable of targeting large flat surfaces, while at the same time remaining fully synthetic and therefore modifiable at will.
Over four days, the participants attended a busy program with 29 sessions, and 3 poster sessions, which covered drug discovery advances in all major therapeutic areas, as well as the most recent advances in lead identification and optimization strategies, in drug design and development, and in prediction of activity as well as of adverse effects. An emphasis was on first time disclosures, emerging drugs and emerging technologies, including nanotechnologies and the chemical modulation of stem cells. ISMC 2010 also illustrated the impact of the omics and biomarker areas on the interfaces between chemistry, informatics, biology and experimental medicine.
Many presentations illustrated the developing changes in the drug discovery process since it has become a highly multi- and interdisciplinary endeavor within only a few decades, leading to

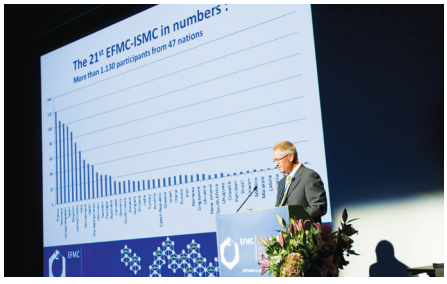

Figure 1

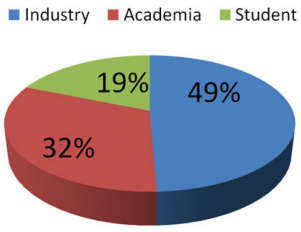

Figure 2

Figure 3

continuous development of new technologies and novel concepts in many areas of chemistry, biology, biophysics, molecular pharmacology as well as bioinformatics.

Some of the presentations especially from industrial speakers clearly illustrated the fact that chemical databases provided - and will keep providing - increasingly important support for drug discovery research. In addition, some presentations also demonstrated that an increasing application of spectroscopic tools through molecular imaging also offers a powerful approach for dissecting biological pathways and identifying novel therapeutic targets. However, at end of the meeting, there could be a message that finding synthetic small (or even larger) molecules that affect cellular function, and identifying their molecular targets, will remain the key challenge in drug discovery.
ISMC 2010 has attracted participants from all over the world. The top twenty list of numbers of delegates per country is shown in Fig. 1. A distribution of the delegates according to their affiliation (Fig. 2), shows that there was almost a 1:1 ratio of medicinal chemists and researchers from industry (49%) and academia (32% faculty, 19% students). The congress venue "SQUARE", Brussels' fully renovated conference centre, offered state of the art facilities for speakers, exhibitors and participants (Fig. 3).
The next edition of this biennial symposium will take place in 2012 in Berlin, Germany and will be jointly organized by the Division of Medicinal Chemistry of the German Chemical Society (GDCh) and the Section of Pharmaceutical/Medicinal Chemistry of the German Pharmaceutical Society (DPhG). ISMC 2012 will continue the tradition of the ISMC Symposia to create an international platform where scientists from all over the world meet and exchange their view and ideas. The first details can be found on the regularly updated symposium website www.ismc2012.org or via the EFMC website www.efmc.info.