The official EFMC e-newsletter

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The European Federation for Medicinal Chemistry (EFMC) is an independent association founded in 1970 that represents 25 scientific organisations from 23 European countries. 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 deepen contacts and exchanges between medicinal chemists in Europe and around the World. EFMC fulfils this objective by organizing symposia and short courses, by sponsoring meetings and medicinal chemistry schools, by publishing on relevant topics and by conferring awards and prizes.

EDITORIAL

Dear colleagues,

These are years of profound changes in the role that medicinal chemistry and medicinal chemists have in the drug discovery process. One of the aims of a learned society such as EFMC is to contribute to the formation of young medicinal chemists, with the hope that they will be not only able to cope with these changes, but also ready to drive and govern them. In this respect, the Education and Training Committee (ETC) of EFMC has commissioned to Sarah Houlton a survey on the state of the art of teaching and training medicinal chemistry in Europe, that we present here, with the introduction of Hein Coolen (chairman of the ETC committee), as a Perspective article.
The idea of the Perspective is to stimulate a debate, and we will be very willing to publish any further contribution that will come out from this.
This issue of MedChemWatch also contains a lab presentation, from Oliver Werz, University of Jena, and a SME presentation from Davide Madge, Xention (Cambidge, UK).
This issue of MedChemWatch will be out soon before the starting of the 22nd International Meeting of Medicinal Chemistry, Berlin, September 2-6. As the world's largest meeting in medicinal chemistry, the ISMC will be the optimal place to meet colleagues and to share high quality science.
Looking forward to meet you in Berlin !

Gabriele Costantino, *Editor of MedChemWatch*

PERSPECTIVE

Teaching and Training the Medicinal Chemistry of the Future

SARAH HOULTON

In view of the abundance of contemplations that are currently being published in the public domain, it is highly unlikely it has escaped anyone that the industrial and academic setting of medicinal chemistry is changing considerably. Changes in the field of medicinal chemistry, praised as multi- or inter- or even supradisciplinary, will affect the needs in training and education as a whole, but also in the interactions between the disciplines.

The Education and Training Committee (ETC) is one of the instruments of the EFMC to execute the policy and plans of the executive committee. One of the main objectives of this committee is to provide the community with high-quality courses. In order to define the need for specific topics, a clear insight into matter is required. Therefore, we have engaged a scientific writer, Sarah Houlton, to compile a paper on the changing landscape too, but now from another point of view. She has interviewed experts and leaders from industry and academia (or both) from different 'generations'. The result is a highly readable piece that comprises all the different aspects involved in this issue.

Read it; this is what the experts say. Note that there is apparently no consensus on the way to go. All expert opinions written down here make perfect sense but some of them seem to be opposite and a common view has not yet crystallized. With some of the statements you may agree; with others, you may not.

So, please read it and share your opinion with us. It will help us to define the needs for future training and education. We are anxious to know what you think. To this purpose, we will start a discussion on LinkedIn within the "EFMC" group. You, representative of a company, a university, or an SME, or 'just' an individual, are invited to join this group and to give your opinion about this paper and about how training and education should adapt to the future landscape of medicinal chemistry.

Hein Coolen
Chair, Education and Training Committee, EFMC

In recent years, there have been dramatic changes in the medicinal chemistry landscape. Targets are getting more complex and regulators are demanding ever-cleaner compounds, but if anything structural changes in the industry are having a bigger impact. The number of big pharma companies continues to dwindle through merger and acquisition, with the fall-out of those deals including hefty job cuts in R&D organisations. But there has been a concomitant rise in the number of spin-outs and start-ups, and big pharma is increasingly filling the holes in its pipelines by in-licensing products and even acquiring the biotechs. The science of drug discovery is also changing, and becoming ever more interdisciplinary. These are just a few of the factors that are having an impact on the education and training needs of medicinal chemistry. Historically, the normal route into a career in medicinal chemistry was a PhD in organic chemistry, and learning medchem skills in industry. But a growing number of medchem courses are now available in universities, whether postgraduate masters courses, as components of bachelors degrees, or even a degree in its own right.

What should a medicinal chemistry course contain?

There are many opinions about what such a course should contain, but one of the key components remains the ability to make molecules. 'That is something I would consider to be a core of any chemistry education,' says Ulrich Stilz, global head of innovation and external networking for Sanofi's diabetes division, and current president of EFMC. 'It is also important to learn about molecular recognition – how small molecules recognise macromolecules, what contributes to binding energy, and a solid understanding of physical chemistry.'

A sound grounding in several other key subjects is also essential. 'They need some basic knowledge of pharmacology, really strong knowledge in pharmacokinetics and ADME, maybe some basic toxicology, and some knowledge of computational techniques,' says Hanno Wild, senior vice president of global candidate generation & exploration at Bayer HealthCare in Germany.

Beat Ernst, professor of molecular pharmacy at the University of Basel, agrees. 'Here in Switzerland, we don't really educate medicinal chemists – we educate synthetic chemists,' he says. 'I think what is missing is an understanding of anatomy and physiology, and they should be aware of pharmacokinetic issues. It's too late when they start in industry. I teach students to look at the molecule and come up with an idea of its pharmacokinetic properties, whether it will be metabolically stable, its potential lipophilicity, and whether or not it will be soluble, a hERG substrate, or whatever.'

All of this boils down to giving young medicinal chemists an understanding of the mechanisms by which compounds act on physical and pathological systems at a molecular level. 'There is a circle – you design a molecule, you synthesise it, you understand the structure–activity relationship, and then you use this to design the next molecules,' says Henk Timmerman, emeritus professor of pharmaco-chemistry at the Free University of Amsterdam. 'It's a true example of a transdisciplinary field of science.'

Andre Tartar, professor in the school of pharmacy at the University of Lille, France tries to teach structure–property relationships rather than structure–activity relationships, as he says optimising leads from high-throughput screening has more to do with optimising properties than activity. 'It's difficult to optimise solubility, permeability, stability, pharmacokinetics, drug–drug interactions, ion channel problems such as hERG, and so on,' he says. 'This multifactorial optimisation is generic – when you teach someone how to handle a permeability problem, for example, you can go from one series to another.'

But it's not enough simply to teach the academic subject – there has to be an appreciation of the pharmaceutical industry. Medicinal chemistry isn't simply an academic discipline, it's an applied science with important industrial and societal aspects. 'In addition to the central aspects of organic chemistry, pharmacology and biology, I believe it is important to offer a general vision of the drug discovery process from the industrial point of view – not just designing new compounds with biological activity,' says Ferran Sanz, director of the research programme on bioinformatics at IMIM in Barcelona, Spain. It is also important they know about the discovery of new targets, about clinical trials, and are given a general view of the whole industry, he believes.

Learning by experience

Perhaps one of the most important components of a good education in medicinal chemistry, therefore, is case studies of successful drug discovery programmes. They form a key part of the medicinal chemistry course at Lille, as Tartar explains. 'Solving property problems is generic, so what you learn from a case study can be applied to your own problem,' he says. 'We start with a series of lectures on property optimisation, and then split the students into groups of three, and give each group a drug to study.' The students present their findings at a seminar to all their peers, showing how the molecule was optimised to solve various problems. Several French faculties now run a similar activity, and all the Lille presentations are available on the internet.

An appreciation of neighbour disciplines is also important. 'Students need to be exposed to a broad swathe of disciplines, and need to understand from the start that data are messy and complex, and the key is to be able to make decisions in that chaotic environment,' says Mark Murcko, former chief technology officer at Vertex Pharmaceuticals in the US, and now a consultant and strategic advisor. 'Tenacity is important, too, because science rarely works first time. But it is also important to get across the excitement of hunting for drugs. When I teach courses, I try to be a storyteller, and get people excited about what we're trying to do. It's not about hiding how difficult it is or the extreme challenges we face – but helping them understand that when it does work, it's magical.'

There is some disagreement about how broad medicinal chemistry training should be. Stilz, for example, would prefer a young medicinal chemist to have a good understanding of related areas of science, and appreciate the po-

tential and power of other fields, rather than gaining a deep knowledge early on of specific therapeutic areas.

Murcko agrees. 'Students should be helped to see how the pieces fit together, with specialisation coming later,' he says. 'People who specialise too early may be extraordinarily good at doing one thing but, in drug hunting, information from one disease area may inform your choices in another. This happens even more with the advent of systems biology, where we might learn, for example, things about an immunological pathway that might be directly relevant to, say, cancer or a gastrointestinal disorder. These lateral jumps are important. Later it is good to focus in and become an expert because of the rigour that comes with digging deeply into one specialised topic. But it's better to start broad, so people can see the forest and the trees, and then dig in.'

Bill Greenlee, formerly chemistry site head at Merck in Kenilworth, US and now a consultant, believes medicinal chemistry is definitely a cross-therapeutic area discipline. 'With people now likely to work for a handful of different biotechs during their career, they do not want to specialise too much – they need enough knowledge of different therapeutic areas to move between them,' he says. 'I do think, though, that having a deeper knowledge of one therapeutic area is of value to employers. This has, to some extent, got lost in company reorganisations and is unfortunate. But as far as training is concerned, it has to be broad.'

Dario Neri, professor in the Institute of Pharmaceutical Sciences at ETH, Zürich, for one, is less sure of the value of a broader education. 'The risk if it is too broad is they will not be competent enough to run the core business of medicinal chemistry – they might need a chemist to work out their synthesis, or maybe a biologist to do cloning expression,' he says. 'I believe breadth comes with age, although some is important, otherwise all you study is synthetic organic chemistry. Of course, the more efficient the teachers are, the more topics can be covered, but I would prefer students to have a solid education, with the breadth arriving at a later stage.'

The decline of organic chemistry

While traditional route into medicinal chemistry was from synthetic organic chemistry, this is starting to change. However, even with the advent of med chem courses, there is still a strong feeling in industry that strength in organic synthesis remains essential. 'I don't think it's possible to get the ideal medicinal chemist for industry straight out of academia,' Wild believes. 'A very strong organic chemistry background is important because of the sophisticated organic chemistry that is needed to make the necessary modifications to compounds. It's always a balance between medicinal chemistry knowledge, versus the strong organic chemistry that is a basis for the subject. Sometimes, medicinal chemistry can be taught in a way that disregards this, with the result that people might have a broad knowledge but can't synthesise the compounds they need.'

Stilz believes that learning how to make bonds and how molecules behave is a very labour intensive process, and if a scientist has never learned this, they simply cannot do medicinal chemistry. 'If we do not preserve the skill to make molecules, we will be missing an essential skill required to create novel medicines, without which we cannot have a pharmaceutical industry,' he says.

And therein lies a problem – organic synthesis is no longer perceived as 'sexy'. Academics are finding it increasingly difficult to get funding for straight organic synthesis – there is a growing trend for funding bodies to demand that scientific effort is applied to problem solving in areas such as human health. 'The big synthetic groups are moving in those directions, and rebranding themselves as chemical biology, for example,' Greenlee says. 'I think if that trend continues, organic chemistry as we know it may go by the wayside. We are going to have to train people in organic synthesis, but will it be in a large total synthesis group?'

Ernst points out that learning organic synthesis is hard work, and this is allied to a shrinking number of people studying chemistry in the first place. 'They may study, say, biological sciences or pharmaceutical science, but the chemistry is not strong enough in these to produce good medicinal chemists,' he says, adding that there will be an even bigger problem in future as young people see all the layoffs in industry, and wonder why they should study chemistry at all.

Many companies still prefer to recruit organic chemists into medicinal chemistry roles, and Wild believes the decline in organic synthesis is setting up a real problem for the future. 'You cannot train people in organic synthesis on the job later on – they have to come with this knowledge,' he says. 'It is much easier to train a skilled organic chemist in medicinal chemistry than the other way around. But if someone has a bachelor's degree in chemistry, a graduate course in medicinal chemistry and then a PhD in organic chemistry, that would be a perfect mix.'

Ernst, meanwhile, is less sure. 'Most new drug molecules are not that difficult to synthesise, so is it really necessary to have five years' education

in synthesising complex natural products? Would it be better to teach at least some fundamental principles of medicinal chemistry? I asked a group of students what the basics of medicinal chemistry are, and the whole list they gave me was synthetic chemistry. They knew nothing about the properties a molecule needs to have the chance of becoming a drug one day. I believe they should learn early that synthesis is a tool to make the right molecule, and the question the medicinal chemist has to answer is what the right molecule is.'

Timmerman thinks that while there is always going to be the need for synthetic chemistry in industry, the way new molecules are designed is increasingly reliant on other disciplines such as computational chemistry and molecular biology. 'Interdisciplinary scientists are very much needed by industry,' he believes. 'A true medicinal chemist should always be open-minded, see what is happening in other disciplines, and question how they might use it in their own research.' He cites the example of stem cells, and the possibility of influencing their growth using small molecules.

So if organic chemistry really declines, where will the medicinal chemists of the future come from? Murcko believes they should come from medicinal chemistry departments within universities. 'We need to support medicinal chemistry departments that include all these different disciplines, and give the broadest possible training, because it will give students the flexibility they need,' he says. 'This is not the way it is typically done now – while there are a few departments that offer medicinal chemistry degrees, it's fairly unusual.'

Neri believes that a lack of med chem bachelor degree courses in Europe gives the discipline a perception problem. 'People are usually turned into medicinal chemists after they have trained as chemists, and I think there is a real missed opportunity,' he says. 'I think medicinal chemistry can be more fun than conventional reaction discovery. I would hope that in future there will be formal curricula in medicinal chemistry, so students can discover drugs without having to take all the pain of conventional reaction discovery and optimisation. But there is a real problem establishing this as a standard curriculum at most universities.'

New areas of endeavour

So what new areas will medicinal chemists be expected to master in the future, whether they work in an industrial or an academic setting? There are several areas that commonly get mentioned as important in the future of biomedical science, such as chemical biology and systems biology. Are these just buzz-words, or will they have a real impact – and will a medicinal chemist need to get to grips with them?

Ferran Sanz, for one, believes that systems biology will be important. 'The paradigm of designing new drugs is changing, in great part because of the emergence of a systems biology perspective,' he says. 'It is becoming clearer that we are not just addressing single targets, but a whole system, whether in the right way to give a therapeutic effect, or the wrong way to give a side-effect. A future medicinal chemist will have to look at molecules as probes, which are able to perturb different proteins and different parts of the system.'

Timmerman is less convinced it will have an impact. 'I think it has given much insight into the machinery of physiological and pathological processes, but whether it will help us design new potential drugs, I'm not so sure,' he says. 'When you have a very complex biological system and you block one of the pathways, it will often find a way to use another pathway.'

Chemical biology is having an impact by altering the way we look at targets, and how they are discovered. Greenlee believes medicinal chemists should have a good knowledge of target identification and validation, much of which is now coming out of chemical biology. But there are other scientific disciplines he believes will also be of value. 'Nanotechnology and drug delivery technology will be important, as advances here will dictate what kinds of molecules we will look at in future, such as parenteral drugs that might only need delivering once every few months,' he says.

Computational chemistry

Computational chemistry is the neighbouring discipline that has, perhaps, had the biggest impact on medicinal chemistry, because of its power to predict shapes and properties, and also aid in learning from past experience. It is now an integral part of the drug discovery process, but should medicinal chemists routinely be trained in in-depth computational modelling techniques? There is a general agreement that they should not – quantitative computational techniques remain the role of the specialist. However, it is important that a medicinal chemist has an appreciation of what can be achieved using computational methods, and what is unrealistic.

'It is very rare to have someone who is very strong in both computational and medicinal chemistry,' Neri believes. 'I am not sure these two job profiles can be combined in the same person. But a medicinal chemist needs to have a basic understanding of how docking works, and be able to use a couple of

programmes so they can display and manipulate molecules on screen.'

Sanz agrees that computational and medicinal chemists are two different people. 'But they will both need to have an understanding of the possibilities of computers on one side, and the lab on the other,' he says. 'Computational chemists should also have some wet lab experience as otherwise there is a danger they will think anything is possible. They need to be aware that not all molecules can be synthesised, and not all experiments for assessing biological activity can be carried out.'

He believes lab chemists will become ever more reliant on computational techniques. 'Today we have better simulations, more sophisticated mathematical methods, and more powerful computers, so the solutions coming from simulations are more realistic, and thus more predictive,' he says. 'But we also have to be fully aware that they are also the consequence of the great accumulation of experimental data that allows the predictive models to be trained and developed. Simulations may be able to reduce future experimental work by giving good predictions, but they need good experimental data to develop them.'

This leads on to the second area where computers are having a big impact – exploiting the existing data contained in databases. While the synthetic chemist does not need to be an expert in computational medicinal chemistry, they do need to be able to interrogate databases. 'A medicinal chemist needs to be able to extract information about molecules and their biological activities from the literature, understand the background to the problem they are addressing, and take into account all the existing information and accumulated experience,' Sanz says.

'We need to teach people to think,' Ernst adds. 'You might ask a question of a database that gives you a thousand references. You have to learn to ask the right questions, particularly in an area where you are not an expert. Only with the right question can you get the right answers and find the one paper that you really have to read. If you ask the wrong one, you will get so many results you don't know where to start.'

Computers are also having an impact on teaching, with e-learning techniques becoming increasingly important in both academic and industrial settings. 'If you can sit in London and listen to a lecture at Harvard, it makes education accessible on a global scale,' Stilz says. 'I'm also sure it will drive excellence in teaching – you can choose whether to listen to lecturers at your own faculty, or someone elsewhere if they are better!'

From an industrial perspective, Greenlee says he has seen a lot of interest in e-learning. 'Merck has the Merck Polytechnic Institute, with many recorded lectures and webcasts, for example, so people can access them at evenings and weekends,' he says. 'I don't think e-learning could ever replace face-to-face teaching as you would miss the interactions, and the ability to ask questions. But for a newly hired medicinal chemist, the resources you can get online will have a big impact for the future.'

Academic institutes

While formal bachelors degrees in medicinal chemistry remain few and far between, there are increasing numbers of degree course modules and graduate courses in the subject, and the move towards applied science means more early stage drug discovery is being carried out in an academic setting, giving further opportunities – and training needs. Numerous drug discovery institutes have been set up, whether in universities or by agencies such as the US National Institutes of Health.

'While there are some opportunities for tenured teaching positions in academic institutes, there are many research fellowships, and interesting job opportunities for chemists, whether running screening labs, doing library synthesis, or other activities,' Murcko says. 'I think it's fair to say that traditional medicinal chemistry positions are going to become more rare, but there is the upside that the baby boomers are starting to reach retirement age – although this still won't lead to huge numbers of opportunities for new PhDs in big pharma.'

However, there are concerns. Stilz thinks these interdisciplinary institutes are in danger of moving too far towards applied research. 'It's important we maintain very strong basic research in academia, and in industry focus on applied research,' he says. 'I'm concerned we might lose the edge in terms of curiosity-driven research taking us off in new directions. This is my only caveat with these units – I would suggest that interdisciplinary efforts between medicine, biology and chemistry should be highly encouraged within universities as there is still a gap, especially in Europe.'

Greenlee, meanwhile, thinks that they could produce good people in future. 'With less emphasis on hardcore organic synthesis training and coming in hitting the ground running, and having collaborated on successful programmes before reaching industry, it would be good. But it's too early to tell – not least because there is so little hiring going on at the moment.'

Industrial input into academia

Many academic courses benefit greatly from industrial input, such as Beat

Ernst's at Basel. It's a small department, and Ernst is fortunate that his industrial background helps him to get former colleagues to assist with teaching. 'Students appreciate this as they want to see and hear how life in industry is, and what success means,' he says. 'We also try to organise practical courses in industry for them. Industrial companies and universities should be in close contact – we should have teachers, masterclasses and practical courses from industry.'

Equally, it can be valuable for students to have industrial placements. Wild believes these are helpful, if not mandatory. 'At Bayer, we take interns at various stages, depending on how strong their organic chemistry knowledge is,' he says. 'If it is good, they can make a real contribution to a project in a two to three month internship; shorter internships are less desirable.'

Neri is less convinced. 'Industrial experience can always come after the study programme,' he says. 'In a two-year masters, it is important to use the time efficiently, and experience in a pharma company can come later. Theory is better learnt at university, and students should learn as many different techniques as possible. Universities have the flexibility to teach many things that industry does not always have.'

Training in industry

If organic chemists start their career in industry with no med chem background, they will need to learn the skills they need in an industrial setting. 'The main education in medicinal chemistry at Bayer is on the job,' Wild says. 'We like them to get into a team quickly, where they can learn from experienced scientists. We also have a mentoring system, and we send them on courses, conferences, and have internal education programmes including lectures and seminars to strengthen their medicinal chemistry skills.'

Greenlee says that, typically for big pharma, both Merck and Schering-Plough hired organic chemists, and then trained them in medicinal chemistry. 'They tended to stay away from people with a degree in medicinal chemistry because their organic chemistry rarely stacks up with those coming out of the top academic groups trained in total synthesis or synthetic methods,' he says. 'We would then train them ourselves, both on-the-job, with our own internal medicinal chemistry course, and by sending them to short courses, like the one I help run at Drew University in the US.'

Short courses provide a valuable way of educating junior medicinal chemists, typically those who have been in industry for up to about three years. They combine lectures, workshops and case studies, giving an intensive week of learning on a wide range of topics. EFMC has links with several well-established courses, including the annual week-long European School of Medicinal Chemistry, held every July in Urbino, Italy, which is accredited by the organisation. It also sponsors five further courses: the Swiss school run by Beat Ernst in Leysin every other year, the Vienna Summer School, a summer school on pharmaceutical analysis held in Rimini, a school at the Leiden/Amsterdam Centre for Drug Research, and a residential school in Nottingham, UK. There are also short courses on specific topics, such as target selection and DMPK, run by EFMC itself.

Ernst says case studies are an important part of the Swiss school, and participants are also given basic information on target families and pharmacokinetic topics. 'They then practise these in tutorials – we often find they don't want to finish the sessions as they are enjoying them so much,' he says. 'I find it amazing – this should be their daily job, but here they are given the space, away from administrative tasks, to think about molecules.'

It's important to continue learning throughout one's time in industry, Murcko adds. 'It's mostly informal, but there are some very specific things that one can do,' he says. 'There are books that describe how drugs were discovered, there are external short courses, and there are events like the Gordon conference. This is always oversubscribed, and if I were just starting my career I would be doing everything I could to get into it. It's a great way to meet people who have invented drugs, and understand the pitfalls.'

The rise of biologics

Changes in the industry itself are also having an impact on what medicinal chemists need to learn. There has been much talk of the 'death' of small molecule drugs, with the growth in importance of biologics such as monoclonal antibodies, but despite the headlines there will still be a place for small molecules for the foreseeable future. 'Many targets, such as in the CNS or intracellular targets, will be hard to reach using macromolecules,' Greenlee says. And small molecules are being used to do new things, too, such as activating enzymes or correcting misfolded proteins.

Even in the field of biologics, chemists will continue to have a role to play, and this is something else that will demand developments in what they are taught. Antibody–drug conjugates, for example, rely on chemical skills to create the linkers that connect the antibody to the small molecule drug,

and these have to remain intact until the antibody reaches the target site, and break down once there.

Neri believes the trend towards therapeutic proteins is here to stay, and the future will be maybe half small molecules, half proteins. 'I don't think it will return to chemists dominating the drug discovery process,' he says. 'But anyone who is able to discover drugs will find a job. A good curriculum will also cover therapeutic proteins, and this will improve job opportunities for medicinal chemists.'

Structural changes in industry

Many of these novel products are being researched in small, start-up or spin-out companies, and this exemplifies another industry trend – the trend of big pharma to outsource research activities. It is increasingly using the research capacity of small start-up companies, which are experts in small parts of the field of drug discovery.

There is also a growing tendency for medicinal chemists in Europe and the US to direct the activities of scientists in China and India. 'A medicinal chemist who has the ability to see everything in context is going to be far better at managing these relationships,' Murcko says. 'It can be difficult to get maximum value out of work being done overseas. It comes down to having enough breadth of experience, and understanding the whole process, to be able to guide this outsourced work effectively.'

This drive to outsource has already led to a shift in jobs from Europe and the US to India and China, and there is a general consensus that this is a trend that is here to stay. 'In China, they have built chemistry and biology skills, and capabilities in pharmacokinetics, toxicology and pharmacology – and they can do these cheaper than we can in the west,' Stilz says. 'How can we create an environment where we have the best-trained people and the most innovative work environment, so companies want to keep jobs in the west as that's where they see the best outcomes?'

A medicinal chemist who is prepared to learn new skills will be in a better place in this changing world. 'They can move themselves up the value chain – not just making molecules, but making the kinds of molecules that require tremendous expertise, knowledge and creativity,' Murcko believes. 'Chemistries like modifying antibodies or mRNA, or making complex macrocycles, cannot be outsourced. This is a way to retain a kind of job security – working on these much higher value, much more complex and challenging activities.'

They must also not expect to find a job for life – rather than staying with the same big pharma company for 40 years, they are much more likely to work in six or seven biotechs across their career. This will further increase the need for flexibility and a broad view of the industry. They may also need to contemplate working in India, China or Singapore. 'This is already happening to some extent,' Wild says. 'But because medicinal chemistry is a knowledge-driven rather than cost-driven activity, if it is done correctly and the different disciplines are integrated, it can remain competitive in the west.'

While there are many fewer jobs for medicinal chemists in industry than there used to be, there will still be a need for medicinal chemists in the future – older chemists will retire, and they will need replacing if there is to be any pharma industry in the west at all. 'Even in large pharma, we will get back to hiring people, and the industry will continue to gravitate towards smaller companies,' Greenlee says. 'The bottom line is I don't see how the large companies so many of us have worked for are going to be able to do innovative drug discovery if everything is outsourced. They will want to employ smart people, hopefully in north America and Europe, and train them. Maybe we're training too many PhD chemists right now, but we will reach an equilibrium. My advice is that while there is a lot of competition and the job situation's not great right now, it will turn around. I certainly hope so.'

The future?

It is clear that there is little consensus among medicinal chemists, whether industrial or academic, on training needs for the future. While in the past there has been that well-worn path from a PhD in organic synthesis to learning medicinal chemistry in industry, the challenges facing synthesis in universities will clearly have an impact on the number of synthetic chemists they produce. Industry will continue to need talented, skilled medicinal chemists to design and make the drug molecules of the future, but perhaps more of that medicinal chemistry will be taught in the academic scenario in future, with the growth in popularity of undergraduate courses in more applied areas of science.

Universities, too, are increasingly looking to develop their own drug candidates, blurring the line between academia and industry further. Might the way ahead be for a medicinal chemist to hone their skills in an academic drug discovery lab before, potentially, making a move into a more traditional industrial setting?

What is needed is a clear common vision about what the future medicinal chemist will look like. Will they have a deep knowledge of a specific area, or a broad training across the board? What

will they have learned at university, and what will they need to learn once they are actually working as a medicinal chemist? There also needs to be more of a consensus about what the most important things a future medicinal chemist needs to learn at university, and courses designed specifically to meet these requirements.

Times are, undoubtedly, difficult right now, and the landscape of the pharma industry is changing. Effective education and training of medicinal chemists will be key to the future of the industry, and the scope of what they need to learn is changing and expanding, too. Courses that meet the future demands of industry – whether in a full-time academic setting or as on-the-job training – will be essential. Yet the underpinning nature of chemistry to the pharmaceutical industry means well-trained and well-rounded medicinal chemists will remain central to the drug discovery process, whatever shape it takes in future.

The Chair of Pharmaceutical/ Medicinal Chemistry

Institute of Pharmacy, University of Jena, Germany

OLIVER WERZ

The current scientific interests of the Chair of Pharmaceutical/Medicinal Chemistry at the Friedrich-Schiller-University Jena comprise the identification and cellular regulation of potential drug targets, discovery of drugs, and characterisation of drugs actions with respect to inflammation and cancer. The various research activities can be grouped into three major areas: (I) investigation of pathobiochemical mechanisms of inflammation at the molecular and cellular level, (II) research and development of bioactive compounds that interfere with concrete drug targets, and (III) identification and validation of drug targets and signalling pathways of known bioactive compounds. The research projects are characterized by multiple and intensive scientific collaborations in a multidisciplinary manner ranging from computational chemistry, design, synthesis, biochemical and pharmacological analyses to clinical studies. The compounds of interest, provided and synthesized by collaborators, include diverse natural compound from plants, fungi and myxobacteria and semi-synthetic derivatives thereof but also series of compounds from synthetic origin. Particular focus is placed on sex differences in the biological regulation of drug targets and on the influence of sex and sex hormones on the pharmacology of bioactive compounds.

The group and head of the group

In 2010, the new Chair of Pharmaceutical/Medicinal Chemistry was installed when Oliver Werz moved together with one post-doc and threes PhD students from Univ. Tuebingen to Univ. Jena. Oliver Werz studied pharmacy and received his PhD degree at Tuebingen University in 1996. As a post-doc he gained particular knowledge on eicosanoids at Frankfurt University in Dieter Steinhilber´s lab and at the Karolinska Institute (Stockholm) in the lab of the Nobel Laureate Bengt Samuelsson. After the habilitation in 2002 and a subsequent senior scientist period at Frankfurt University, be became full professor for pharmaceutical analytics at the Pharmaceutical Institute, Tuebingen University in 2005.

Today, the group, managed by Oliver Werz, encompasses five senior scientists or post-docs (with partly independent research projects), nine PhD students, eight technicians and various diploma students. The group is intensively involved in local, national and international multidisciplinary research collaborations and consortia with academic and industrial partners. The labs are fully equipped with bioanalytical devices including live-cell fluorescence microscope, fluorescence scanner/reader and related imaging systems, automated HPLC systems, UPLC-MS/MS (triple quadrupole/ion trap) etc. One characteristic of the group is the availability of a broad variety of cell-free and cell-based assays for assessment of biological activities related to inflammation and cancer. The particular expertise on the identification of molecular targets for bioactive compounds by the target fishing approach and the discovery of dual 5-LO/mPGES-1 inhibitors as novel potential anti-inflammatory drugs are additional specific features. Finally, a cutting-edge role of the group has been proposed for considering sex differences as important variable in the early process of drug research and development, aiming for a “Gender-tailored therapy“.

Research area I

Pathobiochemical mechanisms of eicosanoids biosynthesis and sex differences

The biosynthesis of eicosanoids, in particular of leukotrienes via the 5-lipoxygenase (5-LO) pathway, is tightly regulated and a concerted action of many cellular factors, such as protein-protein interactions, phosphorylation, redox-tone, and cations or small messengers, determine the capacity to produce these mediators. Stably transfected HEK cells expressing mutated 5-LO and FLAP proteins are studied for protein (co-)localisation by fluorescence microscopy techniques and for 5-LO product release by UPLC-MS/MS and offer an excellent tool for analysis of modulation of the 5-LO pathway by endogenous and exogenous factors or pharmacological agents. The upstream signalling and the concrete molecular interactions are studied to understand the regulation of the synthesis of eicosanoid as well as to deduce novel concepts and aspects for improved pharmacological interference, in vitro and in vivo.

The incidence and severity of leukotriene-related disorders (e.g., asthma, allergic rhinitis) differs significantly between the genders but the biochemical mechanisms beyond this sex bias are unknown. Accordingly, we found that male sex due to higher testosterone suppresses leukotriene biosynthesis in vitro and in vivo by altering the subcellular localisation of 5-LO. We investigate the testosterone/ 5-LO signalling and we could show that extracellular signal-regulated kinases (ERK)-1/2 and phospholipase D are controlled in a sex-dependent manner. It is intriguing that the sex-dependent differential regulation of 5-LO causes differences in the molecular pharmacology and thus efficacy of some anti-leukotriene drugs.

Selected recent papers

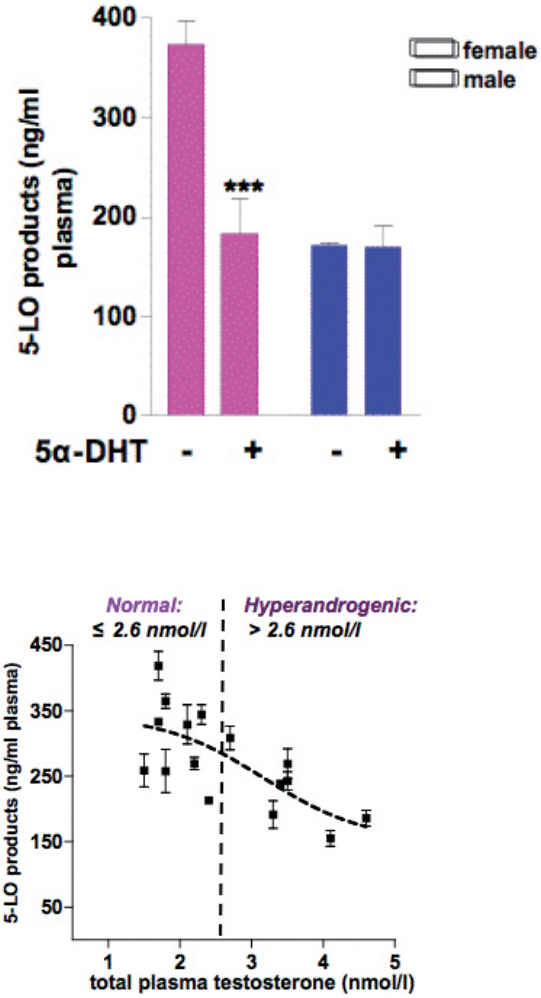
1 Pergola, C., Rogge, A., Dodt, D., Northoff, H., Weinigel, C., Barz, D., Rådmark, O., Sautebin, L., Werz, O. (2011) Testosterone suppresses phospholipase D causing sex differences in leukotriene biosynthesis in human monocytes. *FASEB Journal,* 25, 3377-87

2 Greiner, C., Hörnig, C., Rossi, A., Pergola, C., Zettl, H., Schubert-Zsilavecz, M., Steinhilber, D., Sautebin, L., and O Werz. (2011) 2-(4-(Biphenyl-4-ylamino)-6-chloropyrimidin-2-ylthio)octanoic acid (HZ52) – a novel type 5-lipoxygenase inhibitor with favorable molecular pharmacology and efficacy in vivo Br. *J. Pharmacol.,* 164, 781-93

3 Feißt, C., Pergola, C., Koeberle, A., Dodt, G., Rakonjac, M., Hoffmann, M., Hoernig, C., Fischer, L., Steinhilber, D., Rådmark, O., Franke, L., Schneider, G., and Werz, O. (2009) Hyperforin inhibits 5-lipoxygenase by interference with the C2-like domain. *Cell Moll Life Sci,* 66, 2759-2771

4 Pergola, C., Dodt, G., Rossi, A., Neunhoeffer, E., Lawrenz, B., Hinnak, H., Samuelsson, B., Rådmark, O., Sautebin, L., and Werz, O. (2008) ERK-Mediated Regulation of Leukotriene Biosynthesis by Androgens: A Molecular Basis for Gender Differences in Inflammation and Asthma. *Proc Nat. Acad Sci* USA, 105,19881-19886

5 Albert, D., Pergola, C., Koeberle, A., Dodt, G., Steinhilber, D., and Werz, O. (2008) The role of diacylglyceride generation by phospholipase D and phosphatidic acid phosphatase in the activation of 5-lipoxygenase in polymorphonuclear leukocytes, *J Leuk Biol,* 83:1019-1027



Testosterone suppresses 5-LO product synthesis and causes lower 5-LO product formation in males versus females. Left Panel: Formation of 5-LO products in stimulated blood from male (blue) and female (pink) donors and its suppression by 5α-dihydrotestosterone (5α-DHT) in female blood. Right Panel: 5-LO product formation is higher in females with low testosterone in plasma but is suppressed in hyperandrogenic females with high testosterone plasma levels.

Research area II

Inhibitors of microsomal prostaglandin E_2 synthase-1 and 5-lipoxygenase and related anti-inflammatory active agents

The research aims at identifying novel anti-inflammatory agents, as alternatives to non-steroidal anti-inflammatory drugs (NSAIDs) that block cyclooxygenases, able to inhibit the 5-lipoxygenase (5-LO) pathway or microsomal prostaglandin E_2 synthase (mPGES)-1 but also compounds that dually block 5-LO and mPGES-1. The idea behind such pharmacological profiling is to obtain (i) selective and efficient enzymes inhibitors lacking the disadvantages of former drug candidates, (ii) effective anti-inflammatory agents with synergistic action against both prostaglandin E2 and leukotrienes, (iii) drugs with less side effects as compared to traditional NSAIDs. The discovery of potential compounds is guided by pharmacophore models and (natural) compound library screens as well as by identification of molecular mechanisms of known anti-inflammatory agents (synthetic or natural ones). The computer-aided design, the isolation and synthesis of compounds is performed together with specialized collaborators world-wide. Plenty of cell-free and cell-based assays are available but still are optimized for smart-screening. Investigations of the molecular pharmacological profile of inhibitors are conducted that consider in-vivo relevant influences of their action. Examples of successful developments are series of benzo[g]indole-3-carboxylates, triazoles, benzimidazoles, γ-hydroxybutenolides, and α-substituted pirinixic acid derivatives, and the natural compounds myrtucommulone, hyperforin, arzanol, boswellic acids and semisynthetic derivatives thereof, respectively.

Selected recent papers

1 Waltenberger, B., Wiechmann, K., Bauer, J., Markt, P., Noha, S.M., Wolber, G., Rollinger, J.M., Werz, O., Schuster, D., and Stuppner, H. (2011) Pharmacophore Modeling and Virtual Screening for Novel Acidic Inhibitors of Microsomal Prostaglandin E2 Synthase-1 (mPGES-1). *J Med Chem,* 54, 3163-74

2 Banoglu, E., Çalışkan, B., Luderer, S., Eren, G., Özkan, Y., Altenhofen, W., Weinigel, C., Barz, D., Gerstmeier, J., Pergola, C., and Werz, O. (2012) Identification of novel benzimidazole derivatives as inhibitors of leukotriene biosynthesis by virtual screening targeting 5-lipoxygenase-activating protein (FLAP). *Bioorg Med Chem,* 20, 3728-41

3 Pergola, C., Jazzar, B., Rossi, A., Northoff, H., Hamburger, M., Sautebin, L., and Werz, O. (2011) On the inhibition of 5-lipoxygenase product formation by tryptanthrin: mechanistic studies and efficiency in vivo. *Br. J. Pharmacol,* 165, 765-76

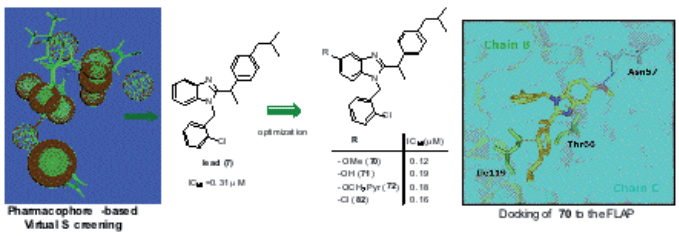
4 Hieke, M., Greiner, C., Dittrich, M., Reisen, F., Schneider, G., Schubert-Zsilavecz, M., and Werz, O. (2011) Discovery and biological evaluation of a novel class of dual microsomal prostaglandin E2 synthase-1/5-lipoxygenase inhibitors based on 2-[(4,6-diphenethoxypyrimidin-2-yl) thio]hexanoic acid. *J Med. Chem.,* 54, 4490-507

5 Pergola, C., Jazzar, B., Rossi, A., Buehring, U., Luderer, S., Dehm, F., Northoff, H., Sautebin, L., Werz, O. (2011) Cinnamyl-3,4-dihydroxy-α-cyanocinnamate (CDC) is a potent inhibitor of 5-lipoxygenase. *J Pharmacol Exp Ther,* 338, 205-13

6 Greiner, C., Hörnig, C., Rossi, A., Pergola, C., Zettl, H., Schubert-Zsilavecz, M., Steinhilber, D., Sautebin, L., and O Werz. (2011) 2-(4-(Biphenyl-4-ylamino)-6-chloropyrimidin-2-ylthio)octanoic acid (HZ52) – a novel type 5-lipoxygenase inhibitor with favorable molecular pharmacology and efficacy in vivo *Br. J. Pharmacol.,* 164, 781-93

7 Koeberle, A., Rossi, A., Zettl, H., Pergola, C., Dehm, F., Bauer, J., Greiner, C., Reckel, S., Hoernig, C., Northoff, H., Bernhard, F., Dötsch, V., Schubert-Zsilavecz, M., Sautebin, L., and Werz, O.(2009) The molecular pharmacology and in vivo activity of YS121 {2-(4-chloro-6-(2,3-dimethylphenylamino)pyrimidin-2-ylthio)octanoic acid}, a dual inhibitor of microsomal prostaglandin E2 synthase-1 and 5-lipoxygenase, *J Pharmacol Exp Ther,* 332, 840-848

8 Werz, O., Greiner, C., Koeberle, A., Hoernig, C., George, S., Popescu, L., Syha, I., Schubert-Zsilavecz, M., Steinhilber, D. (2008) Novel and potent inhibitors of 5-lipoxygenase product synthesis based on the structure of pirinixic acid. *J Med Chem,* 51, 5449-5453



Virtual screening using a combined ligand- and structure-based pharmacophore model for 5-lipoxygenase-activating protein (FLAP) inhibitors led to the identification of 1-(2-chlorobenzyl)-2-(1-(4-isobutylphenyl)ethyl)-1H-benzimidazole (7) as developable candidate. Compound 7 potently suppresses leukotriene formation in intact neutrophils (IC50 = 0.31 μM) due to interaction with FLAP. A series of 46 benzimidazole-based derivatives of 7 were synthesized leading to more potent analogues (70-72, 82) with IC50 = 0.12 - 0.19 μM in intact neutrophils.

Research area III

Identification and validation of drug targets and signalling pathways of bioactive agents

Natural products of interest include plant-derived triterpenic acids (e.g., boswellic acids, tirucallic acids, lupanic acids), acylphloroglucinols (e.g., hyperforin, myrtucommulon), curcumin, EGCG and similar polyphenols (e.g., resveratrol) but also structurally more complex myxobacterial compounds (archazolid, pretubulysin and chondramide). We aim to identify the molecular targets and the related molecular/biochemical mechanisms as well as the pharmacological relevance of the drug/target interaction. The established methods for compound immobilisation and target-fishing are used for identification of (novel) targets of known bio-

active agents (resveratrol, myrtucommulone, testosterone) or drugs (dexamethasone, atorvastatin) and the methodology is further optimized. Moreover, the suitability of these compounds as tools for investigating signalling pathways in cell-based models is of interest. In collaboration with others total syntheses of selected natural products (e.g., myrtucommulon, arzanol) are attempted in order to design semi-synthetic compound libraries for SAR studies and search for hits as well as to allow covalent linking to insoluble resins to be applied for target-fishing. The molecular/pharmacological evaluation strongly considers *in vivo*-relevant regulatory mechanisms in optimized test systems and is supposed to identify possible points of attack/target sites for the molecular interference (e.g., C2-domains). Such knowledge offers on one hand the development of advanced therapeutics and on the other hand enables to reveals novel protein functionalities in pathobiochemical processes (active agents as tools).

Selected recent papers

1 Verhoff, M., Seitz, S., Northoff, H., Jauch, J., Schaible, A.M., Werz, O. (2012) A novel C(28)-hydroxylated lupeolic acid suppresses the biosynthesis of eicosanoids through inhibition of cytosolic phospholipase A2. *Biochemical Pharmacol.,* in press

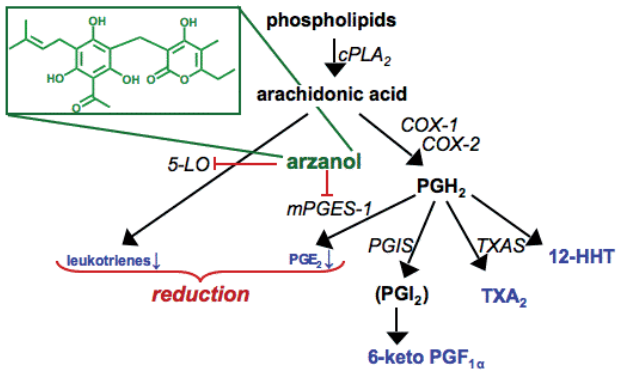
2 Henkel, A., Kather, N., Mönch, B., Northoff, H., Jauch, J., Werz, O. (2012) Boswellic acids from frankincense inhibit lipopolysaccharide functionality through direct molecular interference. *Biochem Pharmacol.,* 83, 115-21.

3 Golkowski, M., Pergola, C., Werz, O., and Ziegler, T. (2012) Strategy for catch and release of azide-tagged biomolecules utilizing a photolabile strained alkyne construct. *Org Biomol Chem.,* 10, 4496-9
Bauer, J., Koeberle, A., Dehm, F., Pollastro, F., Appendino, G., Northoff, H., Rossi, A., Sautebin, L., and Werz, A. (2011) Arzanol, a prenylated heterodimeric phloroglucinyl pyrone, inhibits eicosanoid biosynthesis and exhibits anti-inflammatory efficacy in vivo. *Biochem Pharmacol,* 81, 259-68

4 Koeberle, S., Romir, J., Fischer, S., Koeberle, A., Schattel, V., Albrecht, W., Grütter, C., Werz, O., Rauh, D., Stehle, T., Laufer, S. (2011) Skepinone-L: a p38 mitogen activated protein kinase (MAPK) inhibitor with unsurpassed selectivity and outstanding in vivo efficiency. Nat. Chem. Biol., 8, 141-3

5 Siemoneit, U., Koeberle, A., Rossi, A., Dehm, F., Reckel, S., Maier, T.J., Jauch, L., Northoff, H., Bernhard, F., Doetsch, V., Sautebin, L., and Werz, A. (2011) Boswellic acids inhibit microsomal prostaglandin E2 synthase-1: A molecular basis for the anti-inflammatory actions of the bioactive ingredients from frankincense *Br. J. Pharmacol,* 162, 147-62

6 Tausch, L., Henkel, A., Siemoneit, U., Poeckel, D., Kather, N., Franke, L., Schneider, G., Angioni, C., Geisslinger, G., Skarke, C., Holtmeier, W., Beckhaus, T., Karas, M., Jauch, J., and Werz, O. (2009) Identification of human cathepsin G as a functional target of boswellic acids from the anti-inflammatory remedy frankincense. *J Immunol,* 183, 3433-3442.



Arzanol, a prenylated acylphloroglucinol from Helichrysum italicum, as representative of several dual 5-LO/mPGES-1 inhibitors identified by Werz group. The compound blocks the synthesis of proinflammatory leukotrienes and PGE2 within the arachidonic acid cascade but leaves the formation of other important eicosanoids unaffected. cPLA2, cytosolic phospholipase A2; COX, cyclooxygenase; PG, prostaglandin; 5-LO, 5-lipoxygenase; mPGES-1, microsomal prostaglandin E2 synthase-1; TXA, thromboxane A; TXAS, thromboxane A synthase; PGIS, prostaccylin synthase.

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Xention

DAVID MADGE

Xention Ltd. is a drug discovery company that specializes in the discovery of orally available, small molecule, ion channel modulators. The company, which has over 50 employees, is located in Cambridge (UK). Over the last decade, Xention has accumulated extensive expertise and capabilities in the ion channel drug discovery area, which has led to its status as a global leader in its core disciplines; electrophysiology and ion channel medicinal chemistry. The key elements of Xention's capabilities comprise:

– Comprehensive manual and automated electrophysiology screening capabilities, which cover a wide range of throughput capacities.
– A highly experienced medicinal chemistry team with ion channel-focussed experience and comprehensive discovery chemistry capabilities.
– Extensive ion channel tissue culture experience and expertise, enabling the development of stable cell lines expressing single channels of interest in recombinant systems, and provision of suitable cells for automated electrophysiology screening.
– Expertise in developing detailed translational assays through the use of electrophysiological recordings from relevant tissue types. For example, Xention routinely obtain human atrial tissue, which has allowed the development of an *ex vivo* proof-of-concept assay that enables the characterization of compounds on action potentials measured from disease relevant tissue.
– An extensive compound screening collection, which includes a collection of around 70,000 compounds focused towards ion channels.
– Detailed *in silico* ion channel databases and efficacy prediction capabilities based on large datasets from proprietary sources and literature data.

The decision to concentrate its discovery capabilities exclusively on target class, rather than on a particular disease focus, has allowed Xention to work on projects across a wide range of therapeutic areas, whilst continually building expertise and facilities that can be rapidly implemented for any ion channel target. This discovery platform has been leveraged to support both internal projects in the cardiovascular area, as well as enabling the provision of an integrated drug discovery service for companies that share an interest in ion channels as drug targets.

In the cardiovascular area, Xention has focused its resources on two targets, IKur and IKACh, which are widely recognised by cardiologists as the preferred targets for the prevention of atrial fibrillation. Xention's lead drug candidate XEN-D0103, an IKur antagonist, has recently completed a Phase 1 clinical study, and is expected to progress into a Phase 2 clinical study later in 2012. XEN-D0103, which is highly selective to IKur over other atrial and non-atrial ion channels, was observed to be well tolerated with no significant adverse effects being reported. In addition, Xention has successfully identi-

fied highly potent and selective antagonists of IKACh, which have been observed to selectively prolong the human atrial action potential in *ex vivo* studies. A clinical development candidate is expected to be selected shortly.

Furthermore, Xention has signed two major research collaborations, with Ono Pharmaceutical Co. Ltd. and with the Grünenthal Group, which are focused on the identification of pre-clinical candidates for exciting ion channel targets in other therapeutic areas. This discovery service is an aspect of the business that Xention plan to expand by establishing further collaborative research alliances, which may build on existing internal programmes already in place at Xention or may involve new targets selected by our collaborators.

In addition to the major research alliances with Ono Pharmaceutical and Grünenthal, Xention has also forged collaborations with other pharma and academic research partners by participating in FP7 sponsored projects.

– EDICT – a consortium focused on generating structural information on ion channels and transporters, as well as providing computational tools focused on ion channel targets.
– Eurostars – Xention partnered with Axxam SpA to identify novel, orally bioavailable, small molecule inhibitors of the ICRAC current as new autoimmune therapies for the treatment of diseases, such as rheumatoid arthritis and multiple sclerosis.
– MAREX – a consortium investigating the potential of new marine-sourced bioactive molecules as ion channel modulators.
– EUTRAF – a consortium that undertook a five-year research project with the objective of improving the diagnosis, prevention and treatment of AF through the application of a highly integrative research approach.

The expanding number of collaborative projects at Xention has been paralleled by the identification and validation of further ion channel targets, as well as an increasing global awareness of the tractability and attractiveness of ion channels as a drug target class. This is reflected by the fact that the average number of ion channel publications retrieved by Pubmed, over five year periods, has increased progressively over the last 20 years. Xention plans to capitalize on the growing interest in ion channels by continuing to expand its discovery expertise and capabilities, with the intention of developing more research collaborations. Dr David Madge

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EFMC NEWS

BY NELE COULIER AND KOEN AUGUSTYNS

EFMC | ISMC 2012

The 22nd edition of the EFMC International Symposium on Medicinal Chemistry (EFMC-ISMC) is coming closer and more than 1200 participants already registered for the event, which will take place in Berlin, Germany on September 2-6, 2012! ISMC 2012 is jointly organised by the German Chemical Society (GDCh) Division of Medicinal Chemistry and the German Pharmaceutical Society (DPhG) Section of Pharmaceutical/Medicinal Chemistry, on behalf of the European Federation for Medicinal Chemistry (EFMC).

Over 1.200 scientists coming from 59 nations will gather at the Estrel Convention Centre for this 5-day symposium. About 100 expert speakers and 500 poster presenters will lead you through the latest advances in drug discovery approaches to treat severe diseases in many different therapeutic areas such as inflammation, cancer, infections, diabetes or cardiovascular and CNS disorders. The scientific programme will also cover the most recent advances in lead identification and optimisation strategies, drug design and profiling approaches as well as metabolism and safety testing and prediction. It will highlight the impact of chemical biology at the interface between chemistry and biology, the need for treatments of neglected diseases, and the expansion of the medicinal chemistry tools from small molecules to antibody-drug conjugates. A particular emphasis will be put on first time disclosures. ISMC 2012 will also include lectures by the winners of the EFMC Awards and the IUPAC Prize.

Abstract submission is now closed, but **it is still possible to register via the online registration tool on the website www.ismc2012.org** The final scientific programme as well as the list of speakers is available on the dedicated webpages.

At ISMC Berlin, Sunset Sessions will be organised by the Industry Liaison Committee (ILC) and the Education and Training Committee (ETC) of EFMC. **The ILC Session, "How the Industrial/Academic Interface is Changing Medicinal Chemistry",** will focus on the rapidly evolving medicinal chemistry interface between industry and academia and on how this is likely to impact on the discipline itself.

The session organised by the ETC is entitled "Productivity vs. Development of Independent and Creative Thinking During the PhD Period". Finding the best ratio between research and training for a PhD student is not a simple task. Training activities need to be balanced to avoid losing focus on the own research project and to have the experiments done. Creativity needs to be put in practice by participating in formulating the research strategy and experimental design, and independence should be stimulated by providing a framework of autonomy and freedom to operate. However, on the down side, this can increase the risk of failure and competes with the pressure to produce results and publications. In the ETC Sunset Session all these aspects will be analysed and discussed by a panel of speakers at different stages of their academic careers.

Both sunset sessions will be followed by a discussion and a drink. More information is available on www.ismc2012.org

EFMC 2012 AWARDS

To acknowledge outstanding achievements in the field of Medicinal Chemistry , EFMC is conferring every two years three EFMC Awards: "the Nauta Award for Pharmacochemistry", "the UCB-Ehrlich Award for Excellence in Medicinal Chemistry" and "the Prous Institute-Overton and Meyer Award for New Technologies in Drug Discovery". Dr Uli Stilz, EFMC President and Chair of the Jury, proudly announces the names of the 2012 laureates.

Prof. Alexander Levitzki
Hebrew University of Jerusalem, Israel

Winner of the 2012 Nauta Award for Pharmacochemistry

Dr. Krzysztof Józwiak
Medical University of Lublin, Poland
Winner of the 2012 UCB-Erhlich Award for Excellence in Medicinal Chemistry

Dr. Harren Jhoti
Astex Pharmaceuticals, UK
Winner of the 2012 Prous Institute-Overton and Meyer Award for New Technologies in Drug Discovery

The three Awards will be conferred on the occasion of the XXIInd International Symposium on Medicinal Chemistry (Berlin, Germany – September 2-6, 2012), where the award winners will present a plenary lecture.

THE EFMC PRIZES

The Selection Committees of the "EFMC Prize for a Young Medicinal Chemist in Industry" and the "EFMC Prize for a Young Medicinal Chemist in Academia" are very pleased to announce the names of the winners and the most meritorious runners-up.

EFMC Prize for a Young Medicinal Chemist in Industry
Sharan Bagal, *Pfizer, UK*
Laure Bouchez, *Novartis, Switzerland*
Fabrizio Giordanetto, *CVGI Innovative Medicines, Sweden*

EFMC Prize for a Young Medicinal Chemist in Academia
Stuart Conway, *University of Oxford, UK*
Chris De Graaf, *VU University Amsterdam*
Andrew Wilson, *University of Leeds, UK*

The prizes are established to acknowledge and recognize an outstanding young medicinal chemist (≤35 years old) working in industry or in academia within Europe. The winners will be awarded at the XXIInd International Symposium on Medicinal Chemistry (EFMC-ISMC), where they will give a short presentation.

At the EFMC Council Meeting, which will take place on occasion of EFMC-ISMC 2012, the council will elect 4 positions for the Executive Committee. The positions to be elected are secretary, treasurer, and two additional members. The terms for all the elected EC-members will start on Jan 1st, 2013 and last for two years.

The EFMC Council will also decide on the organizers of the 2016 edition of the International Symposium on Medicinal Chemistry. EFMC is the initiator and sponsor of this series of symposia, each of which is organized in a European city in collaboration with one or more EFMC National Adhering Organization(s). ISMC 2014 will be held in Lisbon, Portugal.

EFMC EVENTS

BY NELE COULIER AND KOEN AUGUSTYNS

EFMC ORGANISED EVENTS

XXIInd International Symposium on Medicinal Chemistry (EFMC-ISMC 2012)
September 2-6, 2012
Berlin, Germany
www.ismc2012.org

6th EFMC Short Course on Medicinal Chemistry Improving Compound Quality: Physical Chemistry and DMPK Properties in Drug Discovery. Principles, Assays and Predictions
October 21-24, 2012
Oegstgeest, The Netherlands
www.efmcshortcourses.org

In modern drug discovery, it is important that the Medicinal Chemist understands how to balance potency and ADME properties in order to provide high quality compounds for progression to clinical studies. This short course will be a mixture of talks and worked exercises designed to further the understanding of DMPK.
The course will include: Outlines of the key DMPK in vitro assays: physicochemistry for ADME; Oral drug absorption; Fundamentals of drug distribution; drug metabolizing enzymes; drug transport proteins; basic PK principles and human PK prediction; PKPD relationships.

5th International Symposium on Advances in Synthetic and Medicinal Chemistry (ASMC 2013)
May 5-8, 2013
Moscow, Russia
www.asmc2013.org

Frontiers in Medicinal Chemistry: Emerging Targets, Novel Candidates and Innovative Strategies
June 23-26, 2013
San Francisco, US
www.fmc2013.org

EFMC SPONSORED EVENTS

19th EuroQSAR Knowledge Enabled Ligand Design
August 26-30, 2012, Vienna, Austria
www.euroqsar2012.org

EFMC Sponsored Session at the 4th EuCheMS Chemistry Congress
August 26-30, 2012
Prague, Czech Republic
www.euchems-prague2012.cz/

Annual One-Day Meeting on Medicinal Chemistry of SRC and KVCV
November 30, 2012
Liège, Belgium
www.medchem.be

EFMC SPONSORED SCHOOLS

10th Swiss Course on Medicinal Chemistry
October 14-19, 2012
Leysin, Switzerland
www.swiss-chem-soc.ch/smc/leysin/leysin.html

EFMC Short Course

6th Short Course on Medicinal Chemistry

IMPROVING COMPOUND QUALITY: PHYSICAL CHEMISTRY AND DMPK PROPERTIES IN DRUG DISCOVERY. PRINCIPLES, ASSAYS AND PREDICTIONS

October 21-24, 2012

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

Course Outline

In modern drug discovery, it is important that the Medicinal Chemist understands how to balance potency and ADME properties in order to provide high quality compounds for progression to clinical studies.
This short course will be a mixture of talks and worked exercises designed to further the understanding of DMPK.

The course will include: Outlines of the key DMPK in vitro assays: physicochemistry for ADME; Oral drug absorption; Fundamentals of drug distribution; drug metabolizing enzymes; drug transport proteins; basic PK principles and human PK prediction; PKPD relationships.

Course Organisers
Kevin Beaumont, *Pfizer, USA*
Local Organiser
Henk Timmerman, *VU University Amsterdam, NL*

Deadline for preregistration
September 15, 2012

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

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EUROPEAN FEDERATION FOR MEDICINAL CHEMISTRY
MCW151

First Announcement

ASMC MOSCOW 13

International Symposium on

Advances in Synthetic and Medicinal Chemistry

May 5-8, 2013
Moscow, Russia

SYMPOSIUM CHAIRMEN
Prof. Peter SEEBERGER (Max Planck Institute, Germany)
Dr Alan PALKOWITZ (Eli Lilly & Co., USA)

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