BRIDGING THE DISCIPLINES

Professor Dr Rainer Riedl, head of the Center for Organic and Medicinal Chemistry at the Zurich University of Applied Sciences, on why organic chemistry is the catalyst for drug discovery

IN medicinal chemistry and chemical biology, there is a constant need to modulate biological processes by chemical means in order to decipher the function of biomolecules, to enable novel and better therapies, to reduce healthcare costs or to make existing treatments more effective. At the Center for Organic and Medicinal Chemistry at the Zurich University of Applied Sciences (ZHAW) in Switzerland, we approach this problem by groundbreaking research into the organic synthesis and medicinal chemistry of novel bioactive molecules at the interface between chemistry and biology. The centre is following a collaborative approach with partners across industry and academia to create novel treatment options for a variety of medical indications.

Experienced leadership

For more than a decade I have successfully run academic and industrial drug discovery projects. Research is focused on the rational design and synthesis of novel bioactive molecules for the treatment of unmet medical needs.

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Based on my experience of drug development projects from my career in BigPharma, I know how drug discovery works and how it will not. Drug discovery projects within academic research consortia with small biotech companies have specific characteristics in terms of number of people and budget involved. I am pleased to see how much can be achieved if the right partners come together in such a consortium. I am running such consortia with the minimal critical size to have all required competencies on board. This keeps the team flexible and assures fast responses, which is a key component in reducing the costs of drug discovery.

International team

The centre represents an international team of 20 enthusiastic scientists in different stages of their careers and with different expertise required for successful drug discovery projects.

Professor Dr Rainer Riedl

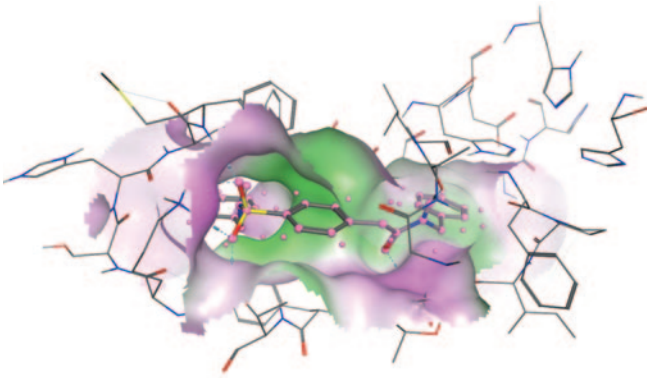
We have a splendid mix of young and more experienced members, which creates a stimulating working environment. Our focus is obviously on medicinal chemistry, but as this is an interdisciplinary science, we cover organic synthesis, computer-aided drug design and cheminformatics, as well as natural products and analytics. This mix of overlapping and complementary know-how allows us to tackle a variety of difficult problems in medicinal chemistry and related disciplines.

Chemistry-driven value chain in drug discovery

The centre's medicinal chemistry activities span from hit identification, through hit to lead development and lead optimisation to delivering active pharmaceutical ingredients for *in vitro* and *in vivo* studies. The work includes the structural analysis of the target proteins and their complexes, resulting in the delivery of novel and patentable drug molecules for clinical trials by using a combination of classical structure activity relationship (SAR) profiling and state-of-the-art computer-aided drug design as well as natural products-derived and fragment-based synthetic approaches. With respect to the synthetic challenges of drug discovery, the centre aims at efficient multi-step organic syntheses of novel scaffolds and focused libraries of organic drug molecules for validated therapeutic targets. Employing modern and powerful synthetic techniques such as microwave assisted, automated and parallel syntheses ensures a constant flow of organic molecules from the chemist's lab to their collaborators for driving the projects forward quickly.

Optimising drug molecules

Drug discovery projects at the centre involve the optimisation of potency and selectivity profiles as well as absorption, distribution, metabolism and excretion (ADME) properties of drug molecules. For clinical candidates, additional efforts are needed to achieve beneficial pharmacological profiles and *in vivo* efficacy in order to develop novel drug molecules for the patients.



Rational drug design

During the hit to lead to candidate optimisation process, the molecules are chemically fine-tuned in order to fulfil all the above mentioned requirements. Therefore it needs creative, skilled and experienced organic and medicinal chemists. Every target and indication has different requirements for a drug molecule which makes this process a novel scientific adventure every time.

Fighting cancer and antimicrobial resistance

I have always been keen on synthesising molecules with biological function. As a medicinal chemist, I can do exactly what thrills me most; making molecules by organic synthesis for the treatment of diseases. Besides the synthetic part of medicinal chemistry, I enjoy the design aspect of drug discovery, as the three-dimensional structure of the biological target guides our creativity to design complementary small organic molecules.

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The principles of medicinal chemistry can be applied to a multitude of therapeutic targets and indications. Current projects in the group involve the treatment of cancer, antibiotic resistance, and inflammatory diseases. Organic chemistry plays a vital role in all of these drug discovery projects because organic chemists have structural understanding and are capable of modifying a given chemical structure by organic synthesis. This is a key component in drug discovery, as we have to respond to the biological effect of our molecules and make them better by modifying their chemical structure.

Focus on rational structure-based design

A core competence of the research is the rational structure-based design and synthesis of novel bioactive molecules. This allows for the targeted discovery of new compounds with defined biological properties. Compared to conventional methods such as high-throughput screening, this process delivers much more efficiently potent compounds. This international group received several scientific awards for the discovery of protease inhibitors with excellent activity against targets involved in rheumatoid arthritis and cancer as well as for novel molecules for the treatment of antibiotic resistance by using structure-based design techniques. Those novel molecules have great potential to be developed into clinical drug candidates. This would be of great benefit to the patients, both as a medicine in therapy and as tool compounds to generate knowledge of the mode of action of the underlying pathogenic processes.

Fruitful collaborations

An important part of the centre's work is its research and development collaborations both with industry and other academic institutions. These collaborations stand to benefit both sides, as each has access to resources and expertise which they would not otherwise have. For example, a spin-off company from a university usually has very strong expertise on a certain technique but for drug discovery it needs more than that. The collaboration between a partner with robust and innovative biological skills and my group covering the medicinal chemistry part is, in my eyes, a showcase for a very successful drug discovery and development consortium.

Bridging the disciplines

In addition, we are networking as organic chemists with other academic groups to provide proficiency in synthetic, analytical and computational chemistry to foster research activities. This is especially fruitful in collaborations with groups with a strong biological background such as cell biology or microbiology. The process of drug discovery and development is very complex and requires the interplay between specialised scientists such as chemists, biologists, pharmacologists and physicians in order to be successful. The centre aims to bridge the gaps between these disciplines to enable the development of new and improved treatments for a range of conditions.

These complementary arrangements of expertise serve as the basis for scientifically exciting projects and represent a win-win situation for all partners.

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