At the Zürich University of Applied Sciences, **Professor Dr Rainer Riedl** is pursuing translational drug discovery and development projects for the treatment of unmet medical needs

Fighting the resistance

AT the Center of Organic and Medicinal Chemistry at the Zürich University of Applied Sciences' (ZHAW) site in Wädenswil, we pursue an integrated approach in modern small molecule drug discovery. Our research and product pipeline includes *de novo* structure-based design, biophysical interaction analyses, computer-aided drug discovery techniques, and natural product-derived drug discovery projects facilitated by our in-house cheminformatics platform. Multi-step organic syntheses and analytics, including pharmacokinetics, constitute the basis of our activities. Biological *in vitro* and *in vivo* assays are performed either within the centre or in collaboration with external partners. Besides the research and development operations, teaching programmes in medicinal chemistry represent a vital component of the centre's activities.

Currently, we focus our research and development efforts on antibiotic resistance (AR), diabetes, cancer and infectious diseases. For instance, the Swiss Commission for Technology and Innovation (CTI) supports a research consortium of drug development to combat AR with a total budget of CHF2.1m (~€1.7m). The consortium consists of research groups at the universities of Basel, Bern and Geneva, the University of Applied Sciences and Arts Northwestern Switzerland, as well as the Basel-based biotechnology company, BioVersys. It is under the direction of the Center of Organic and Medicinal Chemistry at the ZHAW.

Antibiotic resistance

Switzerland's academic research network, which spans the country, combines expertise in biology, chemistry and medicine to develop, alongside BioVersys, new drugs to combat AR. The occurrence of pathogenic bacteria that can no longer be treated by antibiotics is a global threat to world health, as was articulated by the World Health Organization as part of the initiative to combat antimicrobial resistance. There is an urgent need to develop new therapies to combat resistant bacteria. The co-operation of high-profile research partners from the academic sector and its innovative industrial implementation partner (BioVersys), together with substantial funding from the CTI, should allow the development of a clinical candidate to overcome AR.

The supported research project is pursuing a new strategy in the fight against resistant bacteria. This involves using novel small molecule drugs that knock off the resistance mechanism of bacteria at their genetic level; conventional, ineffective antibiotics thus become effective again. This has two beneficial effects: it disables the possibility of further development of AR, and it reopens the door for conventional antibiotics. Bacterial resistance, although a complex and flexible mechanism, follows a general principle that is genetically encoded. Resistance genes are clustered and regulated by global transcriptional regulators that either recognise the antibiotic and its derivatives or act as stress sensors. Based on structural information of the transcription factors, the project partners develop compounds that specifically inhibit global transcriptional regulators of bacterial resistance genes. The objective is a combined preparation that is composed of the novel active ingredient and conventional antibiotics.

Professor Dr Rainer Riedl

Our strong expertise in medicinal chemistry, rational drug design, synthetic organic chemistry, natural product chemistry and cheminformatics fosters a stimulating environment for translational drug discovery projects. Of particular value is our core competence in the *de novo* design of novel small molecule drugs with tailored biological activity, giving us strong IP-positions. For example, we succeeded in the very efficient *de novo* development of potent and selective protease inhibitors by natural product-inspired fragments without any cost intensive screening campaigns.

Those protease inhibitors are excellent lead molecules for the treatment of serious diseases such as cancer and inflammatory diseases, and they have great potential to be developed into clinical drug candidates. This would be of great benefit to patients, both as a medicine in therapy and as a tool, combining to generate knowledge of the mode of action of the underlying pathogenic processes.

HORIZON 2020

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