Wed 22. May 2019
Time: 16:30 h

Dept. of Chemistry and Biochemistry (DCB)
Freiestrasse 3, 3012
Bern, Room EG 16

Everybody is welcome

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Steven Cobb is Associate Professor and Deputy Coordinator of the GCRF/ MRC Global Network for Neglected Tropical Diseases at the Univ. of Durham (UK).

This lecture is hosted by Prof. Jean-Louis Reymond (DCB) in collaboration with Berner Chemische Gesellschaft.

NCCR TransCure Lecture in Drug Design
by Steven Cobb

The Development of Peptide- and Peptoid-based treatments for Neglected Tropical Diseases

Neglected tropical diseases (NTDs) are a significant global health burden, affecting approximately one-sixth of the world's population. The illnesses classified as NTDs by the World Health Organization (WHO) include conditions that have historically been overlooked by international public health efforts, leading to insufficient prevention and treatment options. These diseases are typically endemic in resource-poor, developing countries where populations have limited access to healthcare, and a lack of resources to tackle the disease. NTDs such as leishmaniasis (both visceral and cutaneous), and Chagas disease are infections caused by insect vector-borne protozoan parasites. Combined, these vector-borne diseases affect some of the world's poorest communities, particularly in tropical and sub-tropical regions. Research efforts from our own group have identified antimicrobial peptides (AMPs) derived from amphibians as potential anti-protozoal compounds. However, AMPs are limited by their susceptibility to proteolytic degradation, which is detrimental to their bioavailability in pharmaceutical applications. Hence, there are very few AMPs in current or planned clinical trials. To overcome this challenge of proteolytic degradation, there has been considerable interest in the development of compounds inspired by AMPs that retain their biological activity but that also exhibit improved chemical and biological stability. So called peptidomimetics are now a highly active field of research and one of the key aims is to develop new therapeutics against a wide variety of bacterial, fungal or protozoan diseases. Peptoids class of peptidomimetics are comprised of *N*-substituted glycines where side-chains are located on the nitrogen atom of the amide backbone rather than the α-carbon in peptides. This causes a substantial increase in chemical and biological stability for peptoid sequences in comparison to short, linear peptides. We have design and prepared a range of peptoids containing a wide variety of chemical functionalities and evaluated their activity against a range of protozoan targets. From our studies in this area we have identified several peptoids that have potent anti-parasitic activity and good selectivity indices (SI). For example, the cationic linear peptoid [*N*amy*N*spe*N*spe)(*N*hArg*N*spe*N*spe)]2 had an IC50 of 0.089 µg/mL against *Plasmodium falciparum* and a SI > 100. Our related work towards the development of novel peptoid-based antimicrobials (e.g. targeting mixed species biofilms) will als be discussed.

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