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Chemistry Department e-Seminar

Friday, 14.01.2022 at 15:40 using Zoom
Meeting ID: 934 0850 6496
Passcode: Chem601
https://zoom.us/j/93408506496?pwd=VlY3R1VHVHV6OVY4OEJScFJBM3dlQT09

Paul Ehrlich's Magic Bullet – A Vision Comes True: Synthesis and Evaluation of Drug Conjugates for Targeted Therapy

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Biosketch: Norbert Sewald obtained his PhD degree in Organic Chemistry (*"New Strategies for the Synthesis of Trifluoromethyl Substituted Heterocycles, Amino Acids, and Hydroxy Acids"*) in the group of Prof. Klaus Burger at the Technical University Munich. He was a postdoc in the group of Prof. Jack E. Baldwin from 1991 to 1992 at the Dyson Perrins Laboratory, Oxford University (*"Studies towards the Biomimetic Synthesis of Penicillin"*). In 1998 he finished his habilitation at the University of Leipzig (*"Peptides Containing β-Amino Acids: Asymmetric Synthesis, Solid Phase Peptide Synthesis, and Conformational Analysis by NMR Spectroscopy"*). Since 1999 he is a Professor for Organic and Bioorganic Chemistry at the University of Bielefeld. His research interests comprise Biocatalysis (*Enzymatic Halogenation*) and Chemocatalysis, Bioconjugation (*Drug Conjugates*), Peptides and Peptidomimetics, and Natural Product Chemistry He was/is coordinator of the Bilateral Bielefeld-Yaoundé Graduate School YaBiNaPA (*2016-2025*) and the Marie Skłodowska-Curie Training Networks MAGICBULLET (*2015-2018*) and Magicbullet::reloaded (*2020-2023*). He has supervised 72 MSc and 60 PhD students. Currently 16 PhD students are working with him. 3 former PhD students have been awarded Marie Curie postdoctoral fellowships. The group hosted 22 guest scientists on the postdoctoral level from 13 countries (among them 4 Marie Curie fellows and 9 Alexander von Humboldt fellows). Norbert Sewald currently is the President of the European Peptide Society.

Abstract: Cryptophycins, natural occurring cyclic depsipeptides, show high cytotoxicity against several cancer cell lines, even towards multi-drug resistant (MDR) cancer cell lines [1,2]. These characteristics made the synthetic analog cryptophycin-52 (LY355703) a promising drug for cancer treatment. However, the clinical trials had to be discontinued because of neurotoxic side effects and lacking efficacy in vivo. Selectivity issues may be tackled with in a directed therapy approach. The lack of an addressable functional group in cryptophycin-52 hampers the conjugation to a homing device. We developed efficient strategies for the total synthesis of cryptophycins and their analogues taking specific emphasis on the synthetically most challenging unit A [1,2]. Structure-activity relationship (SAR) studies have been done aiming at the introduction of a new functional group for bioconjugation while maintaining the high biological activity of the parent compound [3]. In addition, cryptophycin conjugates with peptides and antibodies have been developed for targeted delivery in tumour therapy [4].

References:
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[4] M. Anselmi, A. N. Borbély, E. Figueras, C. Michalek, I. Kemker, L. Gentilucci, N. Sewald, Linker Hydrophilicity Modulates the Anticancer Activity of RGD-Cryptophycin Conjugates. *Chem. Eur. J.* **2021**, *27*, 1015-1022.

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