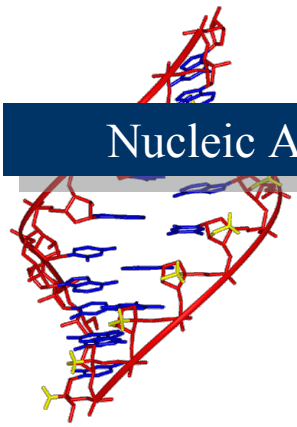
SDU
DEPARTMENT OF PHYSICS, CHEMISTRY AND PHARMACY



Nucleic Acid Center **Seminar** no. 77

Friday 13 January 2017
at 10:30 in the FKF Meeting-room

Prof. Dr. Christian Ducho

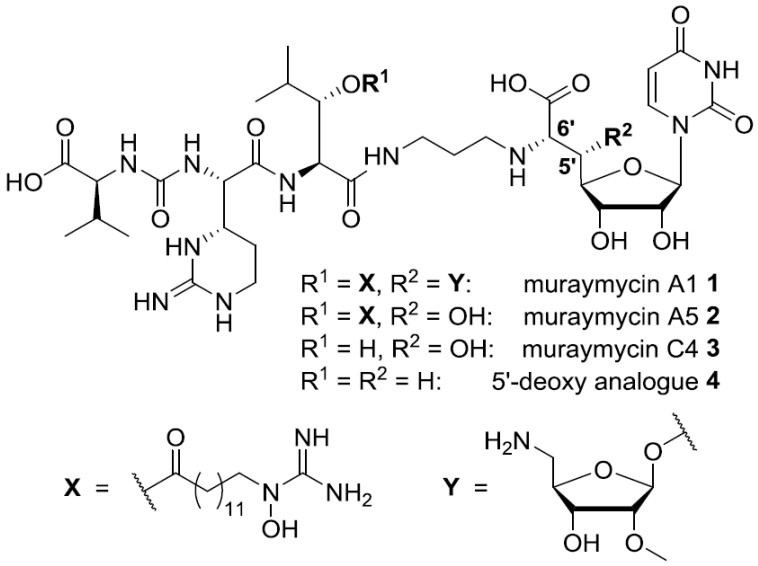
Saarland University
Department of Pharmacy
Pharmaceutical and Medicinal Chemistry,
Saarbrücken, Germany

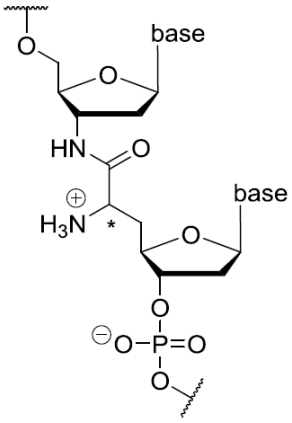
"*From Nucleoside-Derived Antibiotics to Novel Oligonucleotide Modifications*"

Web: http://www.ducholab.de/

Abstract:

The emerging resistances of bacterial strains towards established antibiotics cause an urgent need for the development of novel antibacterial agents. One approach to achieve this goal is the systematic investigation of naturally occurring antibiotics with new or previously unexploited modes of action.
Muraymycins (*e.g.* **1**-**3**, see Figure) belong to the class of naturally occurring nucleoside-peptide antibiotics and were isolated from a *Streptomyces* sp. as a collection of 19 compounds.[1,2] They inhibit the bacterial membrane protein translocase I (MraY), a key enzyme in the intracellular part of peptidoglycan biosynthesis and therefore an attractive target for new antibacterial drugs.[2]
We have developed modular synthetic approaches for the preparation of muraymycins and their analogues, *e.g.* 5'-deoxy muraymycin C4 **4** (see Figure).[3] In combination with biological assays,[4,5] the stage is thus set for detailed structure-activity relationship studies, which might potentially lead to novel antibacterial drug candidates. The 5'-deoxy nucleoside core of muraymycin analogues such as **4** has furthermore inspired the design of the novel nucleosyl amino acid (NAA) modification of oligonucleotides, which furnishes nucleic acid analogues of type **5** with partially zwitterionic backbone structures (see Figure).[6,7] In this talk, the synthesis and properties of muraymycin analogues as well as of NAA-modified oligonucleotides will be presented.





NAA-modified oligonucleotide **5**

References

[1] L. A. McDonald *et al.*, *J. Am. Chem. Soc.* **2002**, *124*, 10260-10261. [2] D. Wiegmann, S. Koppermann, M. Wirth, G. Niro, K. Leyerer, C. Ducho, *Beilstein J. Org. Chem.* **2016**, *12*, 769-795. [3] A. P. Spork, M. Büschleb, O. Ries, D. Wiegmann, S. Boettcher, A. Mihalyi, T. D. H. Bugg, C. Ducho, *Chem. Eur. J.* **2014**, *20*, 15292-15297. [4] O. Ries, C. Carnarius, C. Steinem, C. Ducho, *Med. Chem. Commun.* **2015**, *6,* 879-886. [5] S. Wohnig, A. P. Spork, S. Koppermann, G. Mieskes, N. Gisch, R. Jahn, C. Ducho, *Chem. Eur. J.* **2016**, *22*, 17813-17819. [6] B. Schmidtgall, A. P. Spork, F. Wachowius, C. Höbartner, C. Ducho, *Chem. Commun.* **2014**, *50*, 13742-13745. [7] B. Schmidtgall, C. Höbartner, C. Ducho, *Beilstein J. Org. Chem.* **2015**, *11*, 50-60.