New polymyxin antibiotics for old problems: addressing nephrotoxicity and resistance

Slingerland, C.J.

Curriculum Vitae

Jaco (formally: Cornelis Jacob) Slingerland was born in December 1990, in Lekkerkerk, NL. He obtained his bachelor in Molecular Life Sciences at Wageningen University, NL in 2013. For his Masters in Molecular Life Sciences, he completed dual specializations, both in *Physicial Chemistry* as well as in *Biomedical Research*. He did his thesis work on the biophysical characterization of silk-like proteins interacting with heparins for cell growth support under supervision of Dr. Marleen Kamperman. Under supervision of Dr. Gosia Teodorowicz, he studied effects of whey protein hydrolysates on diverse immune cells. Under late professor Huib Ovaa, he was involved in the synthesis and evaluation of a ubiquitin-based probe for metallo-deubiquitinase RPN11.

In late 2017, Jaco started his PhD research under supervision of Dr. Nathaniel Martin. Initially, Jaco worked on the semisynthesis and characterization of polymyxin analogues with a reductively labile tail for reduced nephrotoxicity. *In vitro* nephrotoxicity evaluation was done in close collaboration with Dr. Roos Masereeuw (Utrecht University).

The scope of Jaco's PhD work was expanded by work on hybrid compounds with a polymyxin nonapeptide motif, as well as by investigations on the mechanism of actions of polymyxins. In addition, Jaco initiated projects on the total syntheses of macolacin and paenilipoheptin (both natural products from *P. polymyxa*).

Publications

From this thesis:

Wood, T. M.*; Slingerland, C. J.*; Martin, N. I. A Convenient Chemoenzymatic Preparation of Chimeric Macrocyclic Peptide Antibiotics with Potent Activity against Gram-Negative Pathogens.
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Slingerland, C. J.; Kotsogianni, I.; Wesseling, C. M. J.; Martin, N. I. Polymyxin Stereochemistry and Its Role in Antibacterial Activity and Outer Membrane Disruption.
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Slingerland, C. J.; Martin, N. I. Recent Advances in the Development of Polymyxin Antibiotics: 2010 – 2023.
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Bakker, A.T.; Kotsogianni, I.; Avalos, M.; Punt, J.M.; Liu, B.; Piermarini, D.; Gagestein, B.; Slingerland, C.J.; Zhang, L.; Willemse, J.J.; Ghimire, L.; Van den Berg, R.J.H.B.N.; Janssen, A.P.A.; Ottenhoff, T.H.M.; Van Boeckel, C.A.A.; Van Wezel, G.P.; Ghilarov, D.; Martin, N.I.; Van der Stelt, M. Discovery of isoquinoline sulfonamides as allosteric gyrase inhibitors active against fluoroquinolone-resistant bacteria.
Nature Chemistry – accepted for publication.

Javed, A.; Slingerland, C. J.; Wood, T. M.; Martin, N. I.; Broere, F.; Weingarth, M. H.; Veldhuizen, E. J. A. Chimeric Peptidomimetic Antibiotic Efficiently Neutralizes Lipopolysaccharides (LPS) and Bacteria-Induced Activation of RAW Macrophages.
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Wade, N.; Wesseling, C. M. J.; Innocenti, P.; Slingerland, C. J.; Koningstein, G. M.; Luirink, J.; Martin, N. I. Synthesis and Structure–Activity Studies of β-Barrel Assembly Machine Complex Inhibitor MRL-494.
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Other publications

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Biomacromolecules 2016, 17 (6), 2063–2072.

*: denotes equal contributions

Patents

WO2023/153932 - *Antibiotic compounds, formulations and methods of use.*
Slingerland, C.J.; Martin, N.I. Priority date: 11-02-2022