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Potentiation of Gram-positive specific antibiotics against Gram-negative bacteria through outer membrane disruption

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Sources of bacterial strains

Utrecht University Medical Center (UMC), Microbiology department, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

E. coli BW25113
E. coli 552060.1
E. coli mcr-1
S. aureus USA300
E. faecium E7314
E. faecium E155

Utrecht University, Molecular Pharmacy, Universiteitsweg 99, 3584 CG Utrecht, the Netherlands

S. aureus ATCC29213

Leiden University Medical Center (LUMC), Department of Medical Microbiology, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

A. baumannii ATCC17978
E. coli ATCC25922
K. pneumoniae ATCC13883
P. aeruginosa ATCC27853

Wageningen Bioveterinary Research, Bacteriology and Epidemiology, Houtribweg 39, 8221 RA Lelystad, The Netherlands

E. coli EQASmcr-1/EQAS 2016 412016126
E. coli EQASmcr-2/EQAS 2016 KP37
E. coli EQASmcr-3/EQAS 2017 2013-SQ352

BEI resources

S. aureus COL
S. aureus LIM2
S. aureus VRS3b

List of publications

From this thesis:

Al Ayed;, K.;‡ Ballantine, R.D.;‡ Hoekstra, M.; Bann, S.J.; Wesseling, C.M.J.; Bakker, A.T.; Zhong, Z.; Li, Y.; Brüchle, N.C.; Stelt, M. van der; Cochrane, S.A.; Martin, N.I. (2022) Synthetic studies with the brevicidine and laterocidine lipopeptide antibiotics including analogues with enhanced properties and in vivo efficacy, *Chem. Sci.*, **2022**,13, 3563-3570.
‡denotes shared first authorship

Wesseling, C.M.J.; Slingerland, C.J.; Veraar, S.; Lok, S.; Martin, N.I. (2021) Structure-activity studies with bis-amidines that potentiate Gram-positive specific antibiotics against Gram-negative pathogens, *ACS Infect. Dis.* **2021**, 7, 12, 3314−3335.

Wesseling, C.M.J.;‡ Wood, T.M.;‡ Slingerland, C.J.; Bertheussen, K.; Lok, S.; Martin, N.I. (2021) Thrombin-Derived Peptides Potentiate the Activity of Gram-Positive-Specific Antibiotics against Gram-Negative Bacteria, *Molecules* **2021**, 26, 1954.
‡denotes shared first authorship

Other

Bruin, G. de; Rooden, E.J. van; Ward, D.; Wesseling, C.M.J.; Nieuwendijk, A.M.C.H. van den; Boeckel, C.A.A. van; Driessen, C.; Kisselev, A.F.; Florea, B.I.; Stelt, M. van der; Overkleeft, H.S. (2017) Asymmetric synthesis of lysine analogues with reduced basicity, and their incorporation into proteasome inhibitors, *Eur. J. Org. Chem.* **2017**(39): 5921-5934.

Manuscripts in preparation

Wesseling, C.M.J.; Martin, N.I. Synergy by perturbing the outer membrane: access for Gram-positive specific antibiotics. (submitted)

Curriculum Vitae

Charlotte Marie José Wesseling was born in Woerden, the Netherlands on the 3rd of April, 1990. She attended secondary school at the Coornhert Gymnasium in Gouda, during which she followed the extracurricular pre-university program of Leiden University, LAPP-TOP. After graduating from secondary school in 2008 she spend a year in Spain where she learned to speak Spanish, passed the DELE Inicial and Intermedio exams, and worked at the winery Elias Mora.

Back in the Netherlands, she started her Bachelor degree in Molecular Science & Technology at both Leiden University and TU Delft in 2009. During her bachelor, she elected a minor in Latin American Studies and she performed a research internship on the "Synthesis of a new diacylglycerol lipase-β inhibitor building block based on the structure of tetrahydrolipstatin" under the supervision of prof. dr. Mario van der Stelt.

After obtaining her BSc in 2013, she continued her studies with a Research Master in Chemistry at Leiden University, specializing in Design & Synthesis and Biochemistry which she successfully completed in 2016. She performed a research internship for both specializations. In the first internship she worked on the "Synthesis of selective inhibitors of the catalytically active subunits of the proteasome" under the supervision of prof. dr. Hermen Overkleeft. She also performed a research internship in Berlin on the "Total synthesis of dehydroalanine containing lanthipeptides" under the supervision of prof. dr. Roderich Süßmuth.

In 2017, Charlotte joined the research group of prof. dr. Nathaniel Martin at Utrecht University as a PhD candidate, where she worked on several projects including the synergistic activity of pentamidine and thrombin-derived peptides. In July 2018 the research group transferred to the Institute of Biology Leiden at Leiden University, where she continued her PhD. Her chapter on the synergistic combinations of serum with conventional Gram-positive specific antibiotics was performed in the department of Microbiology in the group of prof. dr. Suzan H.M. Rooijakkers at the UMC. Charlotte has published two research papers and a review article has been submitted for publication. Parts of her work have been presented as a poster during Chains 2017, 2018, 2019, 2020, HIPS symposium 2021 and an oral presentation at the IBL cluster meeting.

“Als je goed
om je heen kijkt
zie je dat alles
gekleurd is”

- *K. Schippers*