



Universiteit
Leiden

The Netherlands

Anthracycline biosynthesis in *Streptomyces*: engineering, resistance and antimicrobial activity

Hulst, M.B.

Citation

Hulst, M. B. (2024, June 20). *Anthracycline biosynthesis in Streptomyces: engineering, resistance and antimicrobial activity*. Retrieved from <https://hdl.handle.net/1887/3764194>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3764194>

Note: To cite this publication please use the final published version (if applicable).

Anthracycline biosynthesis in *Streptomyces*: engineering, resistance and antimicrobial activity

Mandy B. Hulst

Cover illustration: Naomi Hulst

Layout and design: Hans Schaapherder, persoonlijkproefschrift.nl

Printed by: Ridderprint, ridderprint.nl

Copyright © 2024, Mandy B. Hulst

All rights reserved. No part of this thesis may be reproduced, distributed, sorted in a retrieval system, or transmitted in any form or by any means without prior permission of the author or, where applicable, the publisher holding the copyright on the published articles.

Anthracycline biosynthesis in *Streptomyces*: engineering, resistance and antimicrobial activity

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op donderdag 20 juni 2024
klokke 10:00 uur

door

Mandy B. Hulst

geboren te Rotterdam, Nederland
in 1994

Promotoren:

Prof.dr. G.P. van Wezel

Prof.dr. J.J.C. Neefjes

Promotiecommissie:

Prof.dr. A.H. Meijer

Prof.dr. N.I. Martin

Prof.dr. J. den Hertog

Prof.dr. J.T. Pronk (Delft University of Technology)

Dr. E. Nybo (Ferris State University)

Contents

Chapter 1	Thesis outline	7
Chapter 2	Anthracyclines: biosynthesis, engineering and clinical applications	11
Chapter 3	Metabolic engineering of <i>Streptomyces peucetius</i> for biosynthesis of <i>N,N</i> -dimethylated anthracyclines	47
Chapter 4	Cryptic transporter genes that confer resistance to anthracyclines in <i>Streptomyces</i>	81
Chapter 5	<i>N,N</i> -dimethylated anthracyclines with improved antibiotic activity	125
Chapter 6	Integrated proteomics and metabolomics analysis of small-scale <i>Streptomyces peucetius</i> cultures	143
Chapter 7	General discussion	160
	Nederlandse samenvatting	166
	References	172
	Curriculum vitae	190
	Publications	192

