

University of Groningen

Site-selective modification of aminoglycoside antibiotics for therapeutic and diagnostic applications

Warszawik, Eliza

DOI:

[10.33612/diss.154330217](https://doi.org/10.33612/diss.154330217)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Warszawik, E. (2021). *Site-selective modification of aminoglycoside antibiotics for therapeutic and diagnostic applications*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.154330217>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Site-selective modification of aminoglycoside antibiotics for therapeutic and diagnostic applications

Eliza M. Warszawik

Site-selective modification of aminoglycoside antibiotics for therapeutic and diagnostic applications

Eliza Maria Warszawik
University of Groningen
Groningen, The Netherlands

The research described in this thesis was carried out in the Polymer Chemistry and Bioengineering group at the Zernike Institute of Advanced Materials, University of Groningen, The Netherlands and financially supported by The European Research Council and the Zernike Institute for Advanced Materials.

Zernike Institute PhD thesis: 2021-02
ISSN: 1570-1530

Copyright © 2020 by Eliza Maria Warszawik
Cover design: Eliza Maria Warszawik
Print: Ridder Print | www.ridderprint.nl



university of
 groningen

Site-selective modification of aminoglycoside antibiotics for therapeutic and diagnostic applications

PhD thesis

to obtain the degree of PhD at the
 University of Groningen
 on the authority of the
 Rector Magnificus Prof. C. Wijmenga
 and in accordance with
 the decision by the College of Deans.

This thesis will be defended in public on

Friday 8 January 2021 at 16.15 hours

by

Eliza Maria Warszawik

born on 2 February 1989
 in Warsaw, Poland

Promotor:

Prof. A. Herrmann

Co-promotor:

Dr. P. van Rijn

Assessment Committee:

Prof. J. M. van Dijk

Prof. A. S. S. Dömling

Prof. N. I. Martin

*"Nothing in life is to be feared, it is only to be understood.
Now is the time to understand more, so that we may fear less. "*

Maria Skłodowska-Curie

CONTENTS

Chapter 1

General Introduction

1.1. General introduction	9
1.2. Aminoglycosides as therapeutics	13
1.3. Structures and terminology of aminoglycosides	14
1.4. Mode of action of aminoglycosides	16
1.5. Bacterial resistance to aminoglycosides	20
1.6. Strategies to overcome bacterial resistance to aminoglycosides	25
1.7. Motivation and thesis overview	35
1.8. References	37

Chapter 2

3-N-alkylation in 2-DOS ring of Aminoglycoside Antibiotics Overcomes Bacterial Resistance Mediated by Acetyltransferase (3)IIIa

2.1. Introduction	44
2.2. Results and discussion	48
2.3. Conclusions	59
2.4. Experimental section	61
2.5. Supplementary data	71
2.6. References	73

Chapter 3

Photocontrolled activity of Aminoglycoside Antibiotics

3.1. Introduction	78
3.2. Results and discussion	83
3.3. Conclusions and further perspectives	88
3.4. Experimental section	89
3.5. Supplementary data	92
3.6. References	94

Chapter 4

Uptake and Localization of Fluorescent Aminoglycoside Conjugates in Live *Escherichia coli*

4.1. Introduction	98
4.2. Results and discussion	103
4.3. Conclusions	133
4.4. Experimental section	135
4.5. Supplementary data	149
4.6. References	160

Chapter 5

Selective Identification of Gram-negative Bacterial Infections with Fluorescent Aminoglycoside Probes

5.1. Introduction	166
5.2. Results and discussion	169
5.3. Conclusions	184
5.4. Experimental section	185
5.5. Supplementary data	191
5.6. References	202

Chapter 6

Summary

6.1. English summary	206
6.2. Nederlandse samenvatting	208
6.3. Polskie streszczenie	210

Chapter 7

Author Contributions and Acknowledgements

7.1. Author contributions	217
7.2. Acknowledgements	218