University of Groningen

Imaging of Infections: switch on the light

Lopez Alvarez, Marina

DOI:
[10.33612/diss.175224336](https://doi.org/10.33612/diss.175224336)

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):

Lopez Alvarez, M. (2021). *Imaging of Infections: switch on the light: Development and evaluation of novel tracers for optical molecular fluorescence imaging*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.175224336>

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.

Imaging of Infections: switch on the light

Development and evaluation of novel tracers for
optical molecular fluorescence imaging

Marina López-Álvarez

The research described in this thesis was conducted at the Molecular Bacteriology lab at the Department of Medical Microbiology of the University Medical Center Groningen and the University of Groningen, the Netherlands.

This research was funded by Marie Skłodowska-Curie Actions Grant number 713660 PRONKJEWAIL.

Printing of this thesis was financially supported by the University of Groningen, the Graduate School of Medical Sciences of the University Medical Center Groningen, PerkinElmer and Noord Negentig.

Cover design by   Ayşegül Öktem and Marina López-Álvarez

Printed by   Ipskamps Printing
                             Enschede, the Netherlands

ISBN   978-94-6421-401-7 (print)
                             978-94-6421-405-5 (digital)

Copyright © 2021 Marina López-Álvarez

All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted in any form or by any means without prior written permission of the author.

university of
 groningen

Imaging of Infections: switch on the light

Development and evaluation of novel tracers for optical
molecular fluorescence imaging

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

Monday 23 August 2021 at 9.00 hours

by

Marina López Álvarez

born on 11 July 1990
in Gijón, Spain

Supervisors

Prof. dr. J.M. van Dijk

Co-supervisor

Dr. M. van Oosten

Assessment Committee

Prof. dr. P.H. Elsinga

Prof. dr. H.C. van der Mei

Prof. dr. B. Bröker

*“Never let the fear of striking out
Keep you from playing the game.”*

-Babe Ruth

Para güelito

Paranymphs

Natalia Ortí Casañ

Bimal Prajapati

Lisanne Braams

Table of contents

Chapter 1	General introduction and scope of the thesis	11

PART I – FLUORESCENTLY-LABELED ANTIBODIES AS TRACERS FOR IMAGING OF INFECTIONS

Chapter 2	<i>Staphylococcus aureus</i> exposure and elimination with a fully human Protein A-specific monoclonal antibody Manuscript in preparation	29
Chapter 3	First-time <i>in situ</i> visualization of the fungal pathogen <i>Aspergillus fumigatus</i> in the alveolar space using confocal laser endomicroscopy Manuscript submitted for publication	69

PART II – FLUORESCENTLY-LABELED ANTIBIOTICS FOR DETECTION AND TREATMENT OF INFECTIONS

Chapter 4	A facile and reproducible synthesis of NIR-fluorescent conjugates with small targeting molecules for microbial infection imaging ACS Omega, 2020	93
Chapter 5	Image-guided <i>in situ</i> detection of bacterial biofilms in a human prosthetic knee infection model: a feasibility study for clinical diagnosis of prosthetic joint infections European Journal of Nuclear Medicine and Molecular Imaging, 2020	121
Chapter 6	Bacteria-targeted fluorescence imaging for visualization of fracture-related infections in orthopaedic trauma surgery Manuscript submitted for publication	143
Chapter 7	Busting the staphylococcal biofilm with a photo-activatable vancomycin-phthalocyanine conjugate Manuscript in preparation	161

PART III – SMART-ACTIVATABLE TRACERS FOR DETECTION OF INFECTIONS

Chapter 8	The smart activatable P2&3TT probe allows accurate, fast, and highly sensitive detection of <i>Staphylococcus aureus</i> in clinical blood culture samples <i>Scientific Reports, 2020</i>	183
Chapter 9	Summary, conclusions and future perspectives	199
Appendix	Nederlandse samenvatting	217
	Resumen en español	229
	Deutsche Zusammenfassung	241
	List of publications	253
	Acknowledgements	255