



University of Groningen

### Brain dead donor graft deterioration and attenuation with N-octanoyl dopamine preconditioning

Hottenrott, Christina Maximilia Valentina

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: 2016

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA): Hottenrott, C. M. V. (2016). Brain dead donor graft deterioration and attenuation with N-octanoyl dopamine preconditioning: Emphasis on lung and kidney grafts [Groningen]: University of Groningen

#### 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).

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.

## Brain dead donor graft deterioration and attenuation with N-octanoyl dopamine preconditioning:

With emphasis on lung and kidney grafts

Christina Maximilia Valentina Hottenrott

This Ph.D.-thesis was supported by:

Research Training Group GRK 880, German Research Foundation (DFG) Medical Faculty Mannheim, University of Heidelberg, Germany Groningen Institute for Drug Exploration (GUIDE) University Medical Center Groningen, University of Groningen, The Netherlands

Printing of this thesis was financially supported by: University of Groningen Groningen Institute for Drug Exploration (Guide) University Medical Center Groningen Organ Assist

Cover design and lay-out: Nicole Nijhuis - Gildeprint Printed: Gildeprint, The Netherlands

© Copyright 2015, Christina Maximilia Hottenrott

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means without permission of the author. ISBN (printed): 978-90-367-8589-1 ISBN (digitally): 978-90-367-8588-4



# Brain dead donor graft deterioration and attenuation with N-octanoyl dopamine preconditioning:

With emphasis on lung and kidney grafts

#### PhD thesis

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

This thesis will be defended in public on

Monday 13 January 2015 at 11.00 hours

by

#### Christina Maximilia Valentina Hottenrott

born on 30 September 1983 in Frankfurt am Main, Germany **Supervisors** Prof. Dr. H.G.D. Leuvenink Prof. Dr. B.A.Yard Prof. Dr. M.A. Mariani

#### **Co-Supervisor**

Dr. M.E. Erasmus

#### Assessment committee

Prof. Dr. H.A.M. Kerstjens Prof. Dr. J.L. Hillebrands Prof. Dr. H.-P. Hammes

#### Paranimfen

M.E. Hottenrott S.L. Meyer

#### Table of contents

Introduction		9
Chapter 1	N-octanoyl dopamine is an agonist at the capsaicin receptor TRPV1 and mitigates ischemia-induced acute kidney injury in rat	29
Chapter 2	Dopamine and lipophilic derivates protect cardiomyocytes against cold preservation injury	53
Chapter 3	N-octanoyl dopamine inhibits the expression of a subset of κB regulated genes: potential role of p65 Ser276 phosphorylation	71
Chapter 4	Brain dead donor preconditioning with N-octanoyl dopamine to attenuate ischemia/ reperfusion injury in a rat lung transplantation model	95
Chapter 5	Open lung approach with low tidal volume mechanical ventilation attenuates lung injury in rats with massive brain damage	111
Chapter 6	Influence of ventilation strategies on gene expression profiles in kidneys from brain dead donor rats	131
Chapter 7	Quality of donor lungs: A comparative study between explosive and gradual brain death induction models in rats	153
Chapter 8	Slow brain death induction leads to more pronounced donor kidney and liver deterioration than a fast induction model	169
Chapter 9	Summary, discussion and future perspectives	189
Chapter 10	Nederlandse samenvatting	213
Appendix	Acknowledgments	217

Introduction