University of Groningen

Hibernating mitochondria, the cool key to cellular protection and transplant optimization

Hendriks, Koen

DOI:
[10.33612/diss.160451743](https://doi.org/10.33612/diss.160451743)

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):

Hendriks, K. (2021). *Hibernating mitochondria, the cool key to cellular protection and transplant optimization: Mitochondrial aspects of hibernators and non-hibernators in hypothermia*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.160451743>

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.

HIBERNATING MITOCHONDRIA

THE COOL KEY TO CELLULAR
PROTECTION AND TRANSPLANT
OPTIMIZATION

*Mitochondrial aspects of hibernators
and non-hibernators in hypothermia*

Koen Derk Willem Hendriks

The research presented in this thesis was mainly conducted at the department of Clinical Pharmacy and Pharmacology and the Department of Experimental Transplant Surgery of the University of Groningen. This thesis would not have existed without the help of many collaborators and sponsors.

This MD/PhD project and printing of this thesis were financially supported by:

University Medical Center Groningen

NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Author: Koen D.W. Hendriks
Cover: Maaïke M. van der Meulen
Lay-out: Maaïke M. van der Meulen
Print by: Gildeprint
ISBN: 978-94-641-9138-7

© K.D.W. Hendriks, Groningen, the Netherlands, 2021.

All rights reserved. No part of this thesis may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording or any information storage retrieval system, without prior permission of the author.

Hibernating mitochondria, the cool key to cellular protection and transplant optimization

Mitochondrial aspects of hibernators
and non-hibernators in hypothermia

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. C. Wijmenga
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

maandag 22 maart 2021 om 12.45 uur

door

KOEN DERK WILLEM HENDRIKS

Geboren op 4 september 1994 te Eemsum

Promotores

Prof. dr. R.H. Henning
Prof. dr. H.G.D. Leuvenink
Prof. dr. H. van Goor

Beoordelingscommissie

Prof. dr. M.M.R.F. Struys
Prof. dr. P. Dutkowski
Prof. dr. J.L. Hillebrands

Paranimfen

Dr. D. Nakladal
H. Maassen

Mens, op tafel
De nier gisteravond koud
in een piepschuimen doos
weggezet en expres ingevlogen

*De herfst loopt op zijn eind,
de voorraadkast vol eikeltjes
Het holletje op slot en rustig slapen*

Nier, weggerukt
in een bak ijs gedrukt
Met de energieketen verbroken krijgen
de radicalen vrij spel

*In totale ontspanning
vertraagt het leven
Zo nu en dan even strekken
Metabolisme 1 procent*

Koud in het nieuwe lichaam
Bruut weer tot leven gewekt komt de genade als een klap
overcompensatie, reperfusie, inflammatie
Op de laatste adem, net gehaald

*De kou verdwenen
en de fysiologie weer op stoom
Is zonder incidenten en als vanzelf
De hamster
als herboren*

TABLE OF CONTENTS

Chapter 1	General introduction	9
Chapter 2	Renal temperature reduction progressively favors mitochondrial ROS production over respiration in hypothermic kidney preservation	19
Chapter 3	Differences in mitochondrial function and morphology during cooling and rewarming between hibernator and non-hibernator derived epithelial cells	43
Chapter 4	Hibernator-derived cells show superior protection and survival in hypothermia compared to non-hibernator cells	67
Chapter 5	Oxidative stress and ATP depletion confer extensive DNA strand breaks during cell and organ cooling	89
Chapter 6	Gasotransmitters in health and disease: a mitochondria-centered view	111
Chapter 7	Hydrogen sulphide-induced hypometabolism in human-sized porcine kidneys	127
Chapter 8	Perioperative mild hypothermia is associated with optimal 5-year survival after cardiopulmonary bypass assisted CABG operations	141
Chapter 9	General discussion	163
Chapter 10	Appendices <i>Nederlandse samenvatting (Dutch summary)</i> <i>List of contributing authors</i> <i>About the author</i> <i>Dankwoord / Acknowledgements</i> <i>List of publications</i>	181