

University of Groningen

Reversible Suppression of Hemostasis in Hibernation and Hypothermia

de Vrij, Edwin

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:

2019

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

Citation for published version (APA):

de Vrij, E. (2019). *Reversible Suppression of Hemostasis in Hibernation and Hypothermia*. 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.

Reversible Suppression of Hemostasis in Hibernation and Hypothermia

Edwin L. de Vrij

Reversible Suppression of Hemostasis in Hibernation and Hypothermia

The research presented in this thesis was mainly conducted at the Department of Clinical Pharmacy and Pharmacology 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:



De Cock en Hadders Foundation

Author: Edwin L. de Vrij
Cover: Edwin L. de Vrij, Miller Figueroa
Lay-out: Ilse Modder, www.ilsemodder.nl
Print by: Gildeprint – Enschede, www.gildeprint.nl
ISBN: 978-94-034-1407-2 (printed version)
978-94-034-1406-5 (electronic version)



© E.L. de Vrij, Groningen, the Netherlands, 2019.

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 or retrieval system, without prior permission of the author.

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

Wednesday 27 February 2019 at 16.15 hours

by

Edwin Lammert de Vrij

born on 28 November 1988
in Leeuwarderadeel

Supervisor

Prof. R.H. Henning

Paranymphs

M. Goris

Co-supervisor

Dr. H.R. Bouma

Dr. R. Mulder

Assessment Committee

Prof. S. Cooper

Prof. K. Meijer

Prof. N.P. Juffermans

CONTENTS

Chapter 1	General introduction	11	Appendices	Nederlandse samenvatting	208
	Thrombosis: a major cause of death and global disease burden	12		List of contributing authors	214
	Normal hemostasis	12		About the author	219
	Pathological hemostasis	16		List of publications	220
	Hemostasis in hypothermia	19		Acknowledgements	222
	Mammalian hibernation: a unique natural model of suppressing hemostasis	20			
	Aim of this thesis	23			
Chapter 2	Platelet dynamics during natural and pharmacologically induced torpor and forced hypothermia	31			
Chapter 3	Mechanisms and dynamics of anticoagulation in hibernation - a cool way to suppress hemostasis	61			
Chapter 4	Reversible thrombocytopenia during hibernation originates from storage and release of platelets in liver sinusoids	85			
Chapter 5	Hypothermia associated thrombocytopenia is governed in rodents by reversible platelet storage in liver sinusoids	109			
Chapter 6	Temperature dependent platelet shape changes through tubulin polymerization in hibernating and non-hibernating mammals	139			
Chapter 7	General Discussion	169			
	Summary	170			
	Suppression of hemostasis in hibernating hamster compared with other hibernators	174			
	Suppression of hemostasis in hypothermia in non-hibernators	187			
	Future perspectives	191			
	Conclusions	197			