



Universiteit  
Leiden  
The Netherlands

## Weibel-Palade body formation and exocytosis in von Willebrand disease

Wang, J.W.

### Citation

Wang, J. W. (2013, January 17). *Weibel-Palade body formation and exocytosis in von Willebrand disease*. Retrieved from <https://hdl.handle.net/1887/20418>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/20418>

**Note:** To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/20418> holds various files of this Leiden University dissertation.

**Author:** Wang, Jiong-Wei

**Title:** Weibel-Palade body formation and exocytosis in von Willebrand disease

**Issue Date:** 2013-01-17

# Weibel-Palade body formation and exocytosis in von Willebrand disease

Jiong-Wei Wang

The research described in this thesis was financially supported by the Netherlands Organisation for Scientific Research (NWO, grant 91209006) and the China Scholarship Council and was performed at the Einthoven Laboratory for Experimental Vascular Medicine, Department of Thrombosis and Hemostasis of the Leiden University Medical Center in Leiden, the Netherlands.

Financial support by the Department of Thrombosis and Hemostasis of the Leiden University Medical Center for the publication of this thesis is gratefully acknowledged.

Cover illustration: von Willebrand factor strings derived from neighboring Weibel-Palade bodies run into bundles and networks.

Printed by: Uitgeverij BOXPress, Oisterwijk

Copyright © 2013 J.W. Wang

ISBN: 978-90-8891-535-2

All rights reserved. No part of this book may be reproduced or transmitted, in any form or by any means, without written permission of the author, or when appropriate, of the publishers of publications.

# **Weibel-Palade body formation and exocytosis in von Willebrand disease**

## **Proefschrift**

ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus prof.mr. P.F. van der Heijden,  
volgens besluit van het College voor Promoties  
te verdedigen op donderdag 17 januari 2013  
klokke 16.15 uur

door

**Jiong-Wei Wang**

geboren te Shangcai, Henan, China  
in 1982

## **Promotiecommissie**

### **Promotores:**

Prof. dr. P.H. Reitsma

Prof. dr. H.C.J. Eikenboom

### **Overige leden:**

Prof. dr. A.J. van Zonneveld

Prof. dr. F.W.G. Leebeek (Erasmus Universitair Medisch Centrum)

Dr. P.J. Lenting (Inserm U770, Paris, France)

*Curiosity and dream power my life.*



## Table of Contents

Chapter 1	General introduction and outline of thesis	9
Chapter 2	Von Willebrand disease and Weibel-Palade bodies	17
Chapter 3	Intracellular storage and regulated secretion of von Willebrand factor in quantitative von Willebrand disease	35
Chapter 4	Biogenesis of Weibel-Palade bodies in von Willebrand disease variants with impaired von Willebrand factor intrachain or interchain disulfide bond formation	65
Chapter 5	Biogenesis and exocytosis of Weibel-Palade bodies is affected by naturally occurring variants within the von Willebrand factor A1-A3 domains	89
Chapter 6	Analysis of von Willebrand factor storage and secretion in blood outgrowth endothelial cells derived from von Willebrand disease patients	109
Chapter 7	Formation of platelet binding von Willebrand factor strings on non-endothelial cells	139
Chapter 8	Severity of bleeding tendency in von Willebrand disease is associated with von Willebrand factor string formation	171
Chapter 9	Summary Samenvatting 总结	197
Acknowledgement		221
Curriculum Vitae		223
Publications		225

