



Universiteit
Leiden
The Netherlands

Personalized treatment for von Willebrand disease by RNA-targeted therapies

Jong, A. de

Citation

Jong, A. de. (2020, April 7). *Personalized treatment for von Willebrand disease by RNA-targeted therapies*. Retrieved from <https://hdl.handle.net/1887/136853>

Version: 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/1887/136853>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/136853> holds various files of this Leiden University dissertation.

Author: Jong, A. de

Title: Personalized treatment for von Willebrand disease by RNA-targeted therapies

Issue date: 2020-04-07

Personalized treatment for von Willebrand disease

by RNA-targeted therapies

Annika de Jong

Personalized treatment for von Willebrand disease by RNA-targeted therapies

ISBN: 978-94-6375-766-9

Cover design: Marilou Maes (persoonlijkproefschrift.nl)

Printing: Ridderprint BV

Copyright © Annika de Jong, Leiden 2020

All rights are reserved. No parts of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, without permission of the copyright owners

Personalized treatment for von Willebrand disease

by RNA-targeted therapies

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden
op gezag van de Rector Magnificus Prof. mr. C.J.J.M. Stolker
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 7 april 2020
klokke 16.15 uur

door

Annika de Jong
Geboren te Spijkenisse in 1988

Promotor

Prof. dr. H.C.J. Eikenboom

Copromotor

Dr. B.J.M. van Vlijmen

Leden promotiecommissie

Prof. dr. H.H. Versteeg

Prof. dr. F.W.G. Leebeek

Prof. dr. J.J. Voorberg

Dr. C.V. Denis

Erasmus Universiteit Rotterdam

Universiteit van Amsterdam

Inserm U1176, Parijs, Frankrijk

The research described in this thesis was funded by a grant of The Landsteiner Foundation for Blood Transfusion Research (LSBR 1504) and by a research grant from CSL Behring.

Financial support by the Dutch Heart Foundation for the publication of this thesis is gratefully acknowledged.



Table of contents

Chapter 1:	General introduction and outline of the thesis	9
Chapter 2:	Developments in the diagnostic procedures for von Willebrand disease	23
Chapter 3:	Von Willebrand disease mutation spectrum and associated mutation mechanisms	47
Chapter 4:	Correction of a dominant-negative von Willebrand factor multimerization defect by small interfering RNA-mediated allele-specific inhibition of mutant von Willebrand factor	73
Chapter 5:	Variability of von Willebrand factor-related parameters in endothelial colony forming cells	99
Chapter 6:	Defective von Willebrand factor multimerization in endothelial colony forming cells with low von Willebrand factor production	127
Chapter 7:	<i>Ex vivo</i> improvement of a von Willebrand disease type 2A phenotype using an allele-specific small interfering RNA	141
Chapter 8:	Amelioration of the murine von Willebrand disease type 2B phenotype using an allele-specific small interfering RNA	161
Chapter 9:	General discussion and perspectives	179
Chapter 10:	English summary	207
	Nederlandse samenvatting	212
Appendix:	Dankwoord	220
	Curriculum Vitae	221
	Publication list	222
	PhD portfolio	223