



Universiteit
Leiden

The Netherlands

Combinatorial testing of viral vector and CRISPR systems for precision genome editing

Li, Z.

Citation

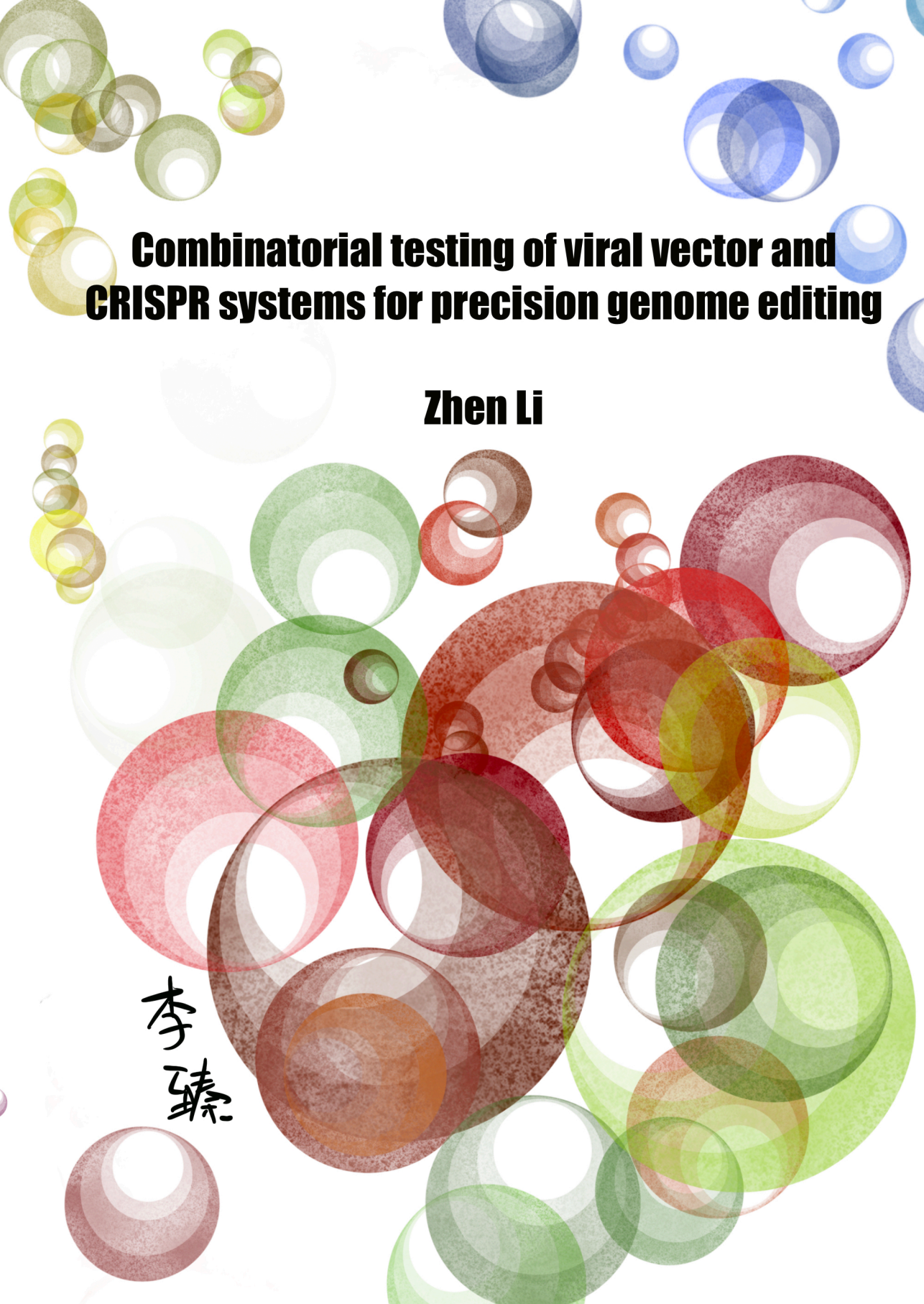
Li, Z. (2025, October 8). *Combinatorial testing of viral vector and CRISPR systems for precision genome editing*. Retrieved from <https://hdl.handle.net/1887/4262567>

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/1887/4262567>

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



Combinatorial testing of viral vector and CRISPR systems for precision genome editing

Zhen Li

李臻

**Combinatorial testing of viral vector and
CRISPR systems for precision genome editing**

Zhen Li

Combinatorial testing of viral vector and CRISPR systems for precision genome editing

Zhen Li

ISBN: 978-94-6522-568-5

The research presented in this thesis was supported by the China Scholarship Council - Leiden University joint program, the Prinses Beatrix Spierfonds, the Duchenne Parent Project NL, the Dutch Research Council (NWO) - Open Technology Program, and EU Marie Skłodowska-Curie Doctoral Network Actions.

Cover: concept and design by Zhen Li

Layout: Zhen Li

Printing: Ridderprint, www.ridderprint.nl

Copyright © Zhen Li, 2025, Leiden, the Netherlands. 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 copyright owner.

Combinatorial testing of viral vector and CRISPR systems for precision genome editing

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op woensdag 8 oktober 2025
klokke 10:00 uur

door

Zhen Li

geboren te Sanya, Hainan, China

in 1993

Promotor:

Prof. Dr. R.C. Hoeben

Co-promotor:

Dr. M.A.F.V. Gonçalves

Leden Promotiecommissie:

Prof. Dr. S.M. Chuva de Sousa Lopes

Prof. Dr. W.W.M. Pijnappel (Erasmus MC, Rotterdam)

Prof. Dr. M.H.M. Heemskerk

Prof. Dr. P. ten Dijke

Dr. Z.Y. Lei (University Medical Center Utrecht)

敬谢家人长久相伴

愿春祺夏安，秋绥冬禧

To my family for their love and trust

Contents

Chapter 1	General introduction	9
Chapter 2	“Soft” genome editing using CRISPR nickases as a potential source of safer cell products	15
Chapter 3	AAV-vectored base editor <i>trans</i> -splicing delivers dystrophin repair	31
Chapter 4	Precision genome editing using combinatorial viral vector delivery of CRISPR-Cas9 nucleases and donor DNA constructs	39
Chapter 5	Selector AAV-CRISPR vectors purge off-target chromosomal insertions and promote precise genome editing	97
Chapter 6	Summary and general discussion	151
Chapter 7	Nederlandse Samenvatting <i>Curriculum Vitae</i> <i>List of Publications</i> <i>Acknowledgements</i>	161