



Universiteit
Leiden
The Netherlands

Shepherding precision gene editing with CRISPR-Cas9 variants and adenoviral vectors

Tasca, F.

Citation

Tasca, F. (2023, June 15). *Shepherding precision gene editing with CRISPR-Cas9 variants and adenoviral vectors*. Retrieved from <https://hdl.handle.net/1887/3620378>

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/1887/3620378>

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

Shepherding precision gene editing with CRISPR-Cas9 variants and adenoviral vectors

Francesca Tasca

Shepherding precision gene editing with CRISPR-Cas9 variants and adenoviral vectors

Francesca Tasca

Cover: Modified immunofluorescence picture of patient-derived myotube showing the rescue of dystrophin expression upon treatment, taken by Francesca Tasca. Technical details on the immunostaining can be found in Chapter 3.

Layout: Francesca Tasca

Printing: GildePrint

The research presented in this thesis was performed at the Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, the Netherlands. This research was supported by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement no. 765269 (IMGENE - Improving Genome Editing Efficiency), the Prinses Beatrix Spierfonds (W.OR16-13 and W.OR21-01), the China Scholarship Council-Leiden University Joint Scholarship Programme, and the DutchDuchenne Parent Project (17.012).

Copyright © Francesca Tasca, 2023, Leiden, the Netherlands. All rights reserved. No part of this thesis may be reproduced or transmitted in any form or by any means without written permission of the copyright owner.

Shepherding precision gene editing with CRISPR-Cas9 variants and adenoviral vectors

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 donderdag 15 juni 2023
klokke 13.45 uur

door

Francesca Tasca

geboren te Marostica, Italie
in 1993

Promotor: Prof. Dr. R.C. Hoeben

Co-promotor: Dr. M.A.F.V. Gonçalves

Leden Promotiecommissie:

Prof. Dr. A.M. Aartsma-Rus

Prof. Dr. M.J.T.H. Goumans

Prof. Dr. N. Geijsen

Prof. Dr. F. Larcher (Universidad Carlos III de Madrid, Spain)

Prof. Dr. J.G. Mikkelsen (Aarhus University Department of Biomedicine, Denmark)

Prof. Dr. E. Mastrobattista (University of Utrecht, Netherlands)

Contents

Chapter 1 General Introduction

Chapter 2 Adenoviral vectors meet gene editing: a rising partnership for the genomic engineering of human stem cells and their progeny

Chapter 3 High-capacity adenovector delivery of forced CRISPR-Cas9 heterodimers fosters precise chromosomal deletions in human cells

Chapter 4 Large-scale genome editing based on high-capacity adenovector particles and CRISPR-Cas9 nucleases rescues full-length dystrophin synthesis in DMD muscle cells

Chapter 5 Expanding the editable genome and CRISPR-Cas9 versatility using DNA cutting-free gene targeting based on *in trans* paired nicking

Chapter 6 Conclusions and Final remarks

Chapter 7 Nederlandse Samenvatting

Curriculum Vitae

List of Publications

Acknowledgements