University of Groningen

Opportunities and Challenges of Epigenetic Editing in Human Diseases

Goubert, Désirée

DOI:
[10.33612/diss.173201281](https://doi.org/10.33612/diss.173201281)

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:
2021

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

Citation for published version (APA):

Goubert, D. (2021). *Opportunities and Challenges of Epigenetic Editing in Human Diseases: Towards the Curable Genome*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.
<https://doi.org/10.33612/diss.173201281>

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).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

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.

Opportunities and Challenges of Epigenetic Editing in Human Diseases

-

Towards the Curable Genome

Désirée Goubert

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 642691.

Horizon2020
European Union Funding
for Research & Innovation

Paranymphs: Joana Saldida

Anita E. Niemarkt

Cover Illustration: Falke Bogaerts,

M.Sc. Biomedical Sciences

Printing: Ridderprint BV, the Netherlands

Copyright © Désirée Goubert, 2020

All rights reserved. No parts of this thesis may be reproduced or transmitted in any form or by any means without prior permission of the author, or, when appropriate, of the publisher of the publications.

Contact: desiree.goubert@gmail.com

university of
 groningen

Opportunities and Challenges of Epigenetic Editing in Human Diseases

Towards the Curable Genome

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. C. Wijmenga
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on

Monday 28 June 2021 at 12.45 hours

by

Désirée Goubert

born on 15 May 1991
in Hasselt, Belgium

Supervisors

Prof. M.G. Rots

Prof. P.J. Verschure

Assessment Committee

Prof. S. Wiemann

Prof. G.A.P. Hospers

Prof. G. Molema

Table of Contents

Chapter 1: General introduction	7
Chapter 2: Epigenetic Editing: towards realization of the curable genome concept	25
Chapter 3: Rewriting DNA Methylation Signatures at Will: The Curable Genome within reach?	39
Chapter 4: Functional validation of the putative oncogenic activity of <i>PLAU</i>	61
Chapter 5: KRAB-Induced Heterochromatin Effectively Silences <i>PLOD2</i> Gene Expression in Somatic Cells and is Resilient to TGF β 1 Activation	89
Chapter 6: Towards sustained silencing of the <i>UCHL1</i> gene by recruiting both M.SssI and SKD: improving CRISPR tools	137
Chapter 7: Establishment of Cell Lines Stably Expressing dCas9-Fusions to Address Kinetics of Epigenetic Editing	169
Chapter 8: General Discussion and Future Perspectives	191
Appendices: English Summary	221
Nederlandse Samenvatting	225
List of Publications	229
List of Outreach Activities	231
Acknowledgements	233