

University of Groningen

The role of accelerated ageing in aberrant lung tissue repair and remodelling in COPD

Woldhuis, Roy

DOI:
[10.33612/diss.155044507](https://doi.org/10.33612/diss.155044507)

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):
Woldhuis, R. (2021). *The role of accelerated ageing in aberrant lung tissue repair and remodelling in COPD*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.
<https://doi.org/10.33612/diss.155044507>

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.

**The role of accelerated ageing in
aberrant lung tissue repair and remodelling in COPD**

Roy R. Woldhuis

The studies presented in this thesis were performed within the framework of the Groningen University Institute for Drug Exploration (GUIDE), the Groningen Research Institute for Asthma and COPD (GRIAC), Woolcock Institute of Medical Research and University of Technology Sydney (UTS). The studies presented in this thesis were financially supported by the Australian National Health and Medical Research Council (NHMRC; grant number: APP1104704) and the Lung Foundation Netherlands (Longfonds; grant number: 3.2.12.044).

Printing of this thesis was financially supported by the University of Groningen, Graduate School of Medical Sciences Groningen (GSMS).

Cover design by Gildeprint and Vecteezy.com

Layout design by Roy R. Woldhuis

Printed by Gildeprint

© 2021, Roy R. Woldhuis, The Netherlands

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



university of
 groningen

**The role of accelerated ageing in
 aberrant lung tissue repair and remodelling in COPD**

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

Tuesday 29 June 2021 at 11:00 hours

by

Roy Rolf Woldhuis

born on 23 June 1992
 in Assen, the Netherlands

Supervisors

Prof. C.A. Brandsma

Prof. B.G. Oliver

Prof. W. Timens

Prof. H.I. Heijink

Assessment committee

Prof. S. Meiners

Prof. P.M. Hansbro

Prof. R. Gosens

Prof. H.A.M. Kerstjens

Paranimfen

Mirjam P. Roffel

Wierd Kooistra

TABLE OF CONTENTS

CHAPTER 1	General introduction & scope of this thesis	9
CHAPTER 2	Lung ageing and COPD: is there a role for ageing in abnormal tissue repair? <i>Eur Respir Rev. 2017 Dec 6;26(146):170073</i>	23
CHAPTER 3	Age-related gene and miRNA expression changes in airways of healthy individuals <i>Sci Rep. 2019 Mar 6;9(1):3765</i>	49
CHAPTER 4	Link between increased cellular senescence and extracellular matrix changes in COPD <i>Am J Physiol Lung Cell Mol Physiol. 2020 Jul 1;319(1):L48-L60</i>	67
CHAPTER 5	COPD-derived fibroblasts secrete higher levels of senescence-associated secretory phenotype proteins <i>Thorax. 2020 Dec 3;thoraxjnl-2020-215114</i>	95
CHAPTER 6	High levels of cellular senescence in airway smooth muscle cells; no increase in COPD <i>In revision, Am J Physiol Lung Cell Mol Physiol.</i>	117
CHAPTER 7	E-cigarette vapour induces cellular senescence in lung fibroblasts and may contribute to lung pathology <i>Research letter submitted</i>	145
CHAPTER 8	Summary, general discussion & future perspectives	153
CHAPTER 9	Dutch summary / Nederlandse samenvatting	173
APPENDIX 1	Acknowledgements / dankwoord	183
APPENDIX 2	List of publications	197

