University of Groningen

The ECM as a driver of fibroblast senescence and disrupted epithelial repair in IPF

Blokland, Kaj

DOI:
[10.33612/diss.177953737](https://doi.org/10.33612/diss.177953737)

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):

Blokland, K. (2021). *The ECM as a driver of fibroblast senescence and disrupted epithelial repair in IPF*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.
<https://doi.org/10.33612/diss.177953737>

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 ECM as a driver of fibroblast senescence and disrupted epithelial repair in IPF

Kaj Erik Cornelis Blokland

The research in this thesis was performed at the School of Biomedical Sciences and Pharmacy at the University of Newcastle and at the Graduate School of Medical Sciences at the University of Groningen.

Printing of this thesis was generously supported by the University of Groningen, University Medical Center Groningen and the Centre of Research Excellence in Pulmonary Fibrosis.

Centre of Research Excellence in
Pulmonary Fibrosis

Cover design: Kaj E.C. Blokland

Lay-out: Kaj E.C. Blokland

Printed by IPSKAMP printing

© Copyright 2021 K.E.C. Blokland

All rights reserved. No part of this thesis may be reproduced, stored on a retrieval system, or transmitted in any form or by any means, without written permission of the author.

university of
groningen

THE UNIVERSITY OF
NEWCASTLE
AUSTRALIA

The ECM as a driver of fibroblast senescence and disrupted epithelial repair in IPF

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

and

to obtain the degree of PhD at the
University of Newcastle
in Immunology and Microbiology

Double PhD degree

This thesis will be defended in public on
Wednesday 8 September 2021 at 09.00 hours

by

Kaj Erik Cornelis Blokland

Born on 16 October 1986
in Apeldoorn, The Netherlands

Supervisors

Prof. J.K. Burgess

Prof. D.A. Knight

Co-supervisors

Dr. C.L. Grainge

Dr. S.D. Pouwels

Dr. M. Schuliga

Assessment committee

Prof. G. Westergren-Thorsson

Prof. K.N Faber

Prof. P. Olinga

Prof. C. Samuel

Paranymph

Jolien Fledderus

Mehmet Nizamoglu

You only fail when you choose to quit

Table of contents

PREFACE	8
CHAPTER 1 General introduction	9
CHAPTER 2 Regulation of cellular senescence by extracellular matrix during chronic fibrotic diseases	21
CHAPTER 3 Stiff matrices induce a profibrotic response but not cellular senescence in primary lung fibroblasts	67
CHAPTER 4 Regulation of cellular senescence is independent from profibrotic fibroblast-deposited ECM	93
CHAPTER 5 Senescence of IPF lung fibroblasts disrupt alveolar epithelial cell proliferation and promote migration in wound healing	131
CHAPTER 6 Summary, general discussion and future directions	147
CHAPTER 7 Dutch summary	167
APPENDICES Statement of contributions Acknowledgements Curriculum vitae List of publications	173

PREFACE

STATEMENT OF ORIGINALITY

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. I confirm that the thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution, with the exception of the approved partner university associated with this Dual Award Doctoral Degree. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University of Newcastle Digital Repository and its equivalent at the partner university, subject to the provisions of the Copyright Act 1968 and any approved embargo.

Kaj E.C Blokland

THESIS BY PUBLICATION

I hereby certify that this thesis is in the form of a series of papers. I have included as part of the thesis a written declaration from each co-author, endorsed in writing by the Faculty Assistant Dean (Research Training), attesting to my contribution to any jointly authored papers.