

## University of Groningen

### Cell-specific targeting of renal fibrosis

Poosti, Fariba

**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:*

2015

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

*Citation for published version (APA):*

Poosti, F. (2015). *Cell-specific targeting of renal fibrosis*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.

**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.

# **Cell-specific targeting of renal fibrosis**

**Fariba Poosti**

This project was financially supported by:  
University Medical Center Groningen  
Research Institute GUIDE  
Jan Kornelis de Cock Foundation

The printing of this thesis was financially supported by BiOrion Technologies BV, a Dutch bio-pharmaceutical company located in Groningen developing targeted therapeutics and companion imaging diagnostics for human fibrotic, inflammatory and neoplastic diseases. [www.biorion.com](http://www.biorion.com).

The logo for BiOrion, featuring the word "BiOrion" in a sans-serif font. The "Bi" is in dark grey, the "O" is a light green circle, and "rion" is in a medium green color.

Financial support by the Dutch Kidney Foundation, University of Groningen, University Medica Center of Groningen, Graduate School of Medical Science for the publication of this thesis is gratefully acknowledged

Cover: Dr Mojtaba Sadeghi  
Lay-out: Legatron Electronic Publishing, Rotterdam, the Netherlands  
Publication: IPSKAMP Drukkers, Enschede, the Netherlands

Copyright: Fariba Pootsi, 2015

All rights reserved. No part of this publication may be reproduced, stored or transmitted in any form or by any means, electronically or mechanically, including photocopy, recording or otherwise without the written permission of the author.

ISBN/EAN: 978-94-6259-957-4



rijksuniversiteit  
 groningen

# Cell-specific targeting of renal fibrosis

## PhD thesis

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

This thesis will be defended in public on  
2<sup>nd</sup> December 2015

by

**Fariba Poosti**

born on 21 March 1981  
in Ghom, Iran

**Supervisors**

Prof. J.L. Hillebrands

Prof. H. van Goor

**Co-supervisor**

Dr. M.H. de Borst

**Assessment committee**

Prof. R.A. Bank

Prof. S. Florquin

Prof. G.M.M. Groothuis

*Dedicated to my parents  
and  
my husband  
with great affection and love*

**PARANINFEN**

Rik Mencke  
and  
Marian Bulthuis

## CONTENTS

<b>Chapter 1</b>	General introduction & Scope of the thesis	<b>9</b>
<b>Chapter 2</b>	Targeted renal delivery of protein kinase inhibitors for the treatment of chronic kidney disease	<b>15</b>
<b>Chapter 3</b>	Targeted inhibition of renal Rho kinase reduces macrophage infiltration and lymphangiogenesis in acute renal allograft rejection	<b>37</b>
<b>Chapter 4</b>	Selective delivery of interferon gamma to renal interstitial myofibroblasts: A novel strategy for the treatment of renal fibrosis	<b>55</b>
<b>Chapter 5</b>	IFN $\gamma$ peptidomimetic targeted to interstitial myofibroblasts attenuates renal fibrosis in unilateral ureteral obstruction in mice	<b>81</b>
<b>Chapter 6</b>	Precision-cut kidney slices (PCKS) to study development of renal fibrosis and efficacy of drug targeting <i>ex vivo</i>	<b>103</b>
<b>Chapter 7</b>	Proteinuria triggers renal lymphangiogenesis prior to the development of interstitial fibrosis	<b>121</b>
<b>Chapter 8</b>	Summary and General discussion	<b>143</b>
<b>Chapter 9</b>	Samenvatting en Discussie	<b>153</b>
<b>Chapter 10</b>	Acknowledgments	<b>163</b>