

## University of Groningen

### The cardiac fetal gene program in heart failure

van der Pol, Atze

**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:*  
2018

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

*Citation for published version (APA):*

van der Pol, A. (2018). The cardiac fetal gene program in heart failure: From OPLAH to 5-oxoproline and beyond [Groningen]: Rijksuniversiteit 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).

**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 cardiac fetal gene program in heart failure**

from OPLAH to 5-oxoproline and beyond

Atze van der Pol

2018

Financial support by the Groningen University Institute for Drug Exploration (GUIDE) and University of Groningen is gratefully acknowledged.

Financial support by the Dutch Heart Foundation for the publication of this thesis is gratefully acknowledged.

Financial support for the publication of this thesis is gratefully acknowledged:

Pfizer Nederland B.V.

Servier Nederland Frama B.V.

Cover design: Atze van der Pol

Lay-out: Atze van der Pol

Printed by: Gildepring, Enschede

ISBN: 978-94-034-0712-8; printed version

ISBN: 978-94-034-0711-1; electronic version

The cardiac fetal gene program in heart failure: from OPLAH to 5-oxoproline and beyond

**© Copyright 2018 Atze van der Pol**

All rights reserved.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, without permission of the author.



rijksuniversiteit  
groningen

# The cardiac fetal gene program in heart failure

From OPLAH to 5-oxoproline and beyond

## Proefschrift

ter verkrijging van de graad van doctor aan de  
Rijksuniversiteit Groningen  
op gezag van de  
Rector Magnificus prof. dr. E. Sterken  
en volgens besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op

woensdag 4 juli 2018 om 9:00

door

**Atze van der Pol**

geboren op 28 april 1986  
te Yaoundé, Kameroen

**Promotores:**

Prof. dr. P. van der Meer  
Prof. dr. W.H. van Gilst  
Prof. dr. R.A. de Boer

**Beoordelingscommissie:**

Prof. dr. J.P.G. Sluijter  
Prof. dr. E.A.A. Nollen  
Prof. dr. G.J. Navis

**Paranimfen:**

Martijn Hoes

Jasper Tromp



Para mi Familia

Foar myn Famylje

For my Family

Voor mijn Familie



<b>Chapter 1</b>	Introduction and Aims	11
<b>Chapter 2</b>	Cardiac fetal reprogramming: a tool to exploit novel treatment targets for the failing heart	15
<b>Chapter 3</b>	Accumulation of 5-oxoproline in myocardial dysfunction and the protective effects of OPLAH	39
<b>Chapter 4</b>	OPLAH ablation leads to accumulation of 5-oxoproline, oxidative stress, fibrosis and elevated filling pressures in a murine model for heart failure with a preserved ejection fraction	91
<b>Chapter 5</b>	LC-MS Analysis of Key Components of the $\gamma$ -Glutamyl Cycle in Tissues and Body Fluids from Mice with Myocardial Infarction	123
<b>Chapter 6</b>	Treating oxidative stress in heart failure: past, present and future	143
<b>Chapter 7</b>	Discussion and future perspectives	161
<b>Chapter 8</b>	Summary	175
<b>Chapter 9</b>	Nederlandse samenvatting	181
<b>Appendices:</b>		187
	Curriculum vitae & publications	189
	Acknowledgments	193

