



### University of Groningen

WNT and β-catenin signalling in airway smooth muscle: emerging concepts for asthma Koopmans, Tim

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: 2017

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Koopmans, T. (2017). WNT and β-catenin signalling in airway smooth muscle: emerging concepts for asthma. University of Groningen.

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/taverneamendment.

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.

Download date: 26-08-2022

WNT and β-catenin signalling in airway smooth muscle: emerging concepts for asthma

Tim Koopmans

Institute for Drug Exploration (GUIDE) and the Groningen Research Institute for Asthma and COPD

(GRIAC), and was financially supported by a NWO Vidi grant (016.126.307).

Graduate School of Science and Engineering (GSSE)

Stichting Astma Bestrijding (SAB)

☑ thesis.defense.t.koopmans@gmail.com

Cover and lay-out by Tim Koopmans

Printed by Ipskamp Printing, Enschede, The Netherlands

Printed on FSC certified paper

© 2017 by Tim Koopmans

All rights reserved. No part of this book may be reproduced or transmitted in any form, or by any

means, electronic, by print, or otherwise, without permission in writing from the author, or when

ISBN: 978-94-028-0743-1



# WNT and β-catenin signalling in airway smooth muscle: emerging concepts for asthma

#### 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

Friday 20 October 2017 at 12.45 hours

by

**Tim Koopmans** 

born on 31 October 1986 in Leeuwarden

# **Supervisors**

Prof. R. Gosens

Prof. H. Meurs

## **Assessment Committee**

Prof. M.C. Harmsen

Prof. P.S. Hiemstra

Prof. S. Bellusci

"As the material came on I felt that I was being enveloped, and my attention had to be directed to it. I became quite fearful, and my face felt cold and ashen. I felt that I wanted to go back, but I knew there was no turning back. Then the fear started to leave me, and I could try taking little baby steps, like taking first steps after being reborn. The woodpile is so beautiful, about all the joy and beauty that I can stand. I am afraid to turn around and face the mountains, for fear they will overpower me. But I did look, and I am astounded. Everyone must get to experience a profound state like this. I feel totally peaceful. I have lived all my life to get here, and I feel I have come home. I am complete."

Alexander Shulgin

# Table of contents

1	Chapter 1 General Introduction	8-39
2	Chapter 2 – review manuscript  'Revisiting asthma therapeutics: focus on WNT signal transduction'	40-77
3	Chapter 3 – review manuscript  'Ca <sup>2+</sup> handling and sensitivity in airway smooth muscle: emerging comechanistic understanding and therapeutic targeting'	78-115 Incepts for
4	Chapter 4 – research manuscript  'Regulation of actin dynamics by wnt-5a: implications for human airw muscle contraction'	116-141 ay smooth
5	<b>Chapter 5</b> – research manuscript  'Cooperative signaling by tgf-β1 and wnt-11 drives sm-α-actin exp smooth muscle via rho kinase-actin-mrtf-a signalling'	142-165 pression in
6	Chapter 6 – research manuscript  'Characterization of smooth-muscle-derived wnt-5a in allergic asthmating effects on th2-cell activation'	166-193 : modulat-

	Chapter 7 – research manuscript	194-225
7	'Selective targeting of cbp/β-catenin inhibits growth of and extracely	lular matrix
/	remodelling by airway smooth muscle'	
0	Chapter 8 – research manuscript	226-255
8	'β-catenin directs nf-κb p65 output via cbp/p300 in human airw	ay smooth
	muscle'	
	Chapter 9	256-279
9	General Discussion	200 27 7
•	Certici di Discussioni	
10	Chapter 10	280-305
10	Chapter 10  Nederlandse samenvatting (Dutch summary)	280-305
10		280-305
		280-305
<ul><li>10</li><li>11</li></ul>	Nederlandse samenvatting (Dutch summary)	
	Nederlandse samenvatting (Dutch summary)  Chapter 11  Acknowledgements	306-313
11	Nederlandse samenvatting (Dutch summary)  Chapter 11 Acknowledgements  Chapter 12	
	Nederlandse samenvatting (Dutch summary)  Chapter 11  Acknowledgements	306-313
11	Nederlandse samenvatting (Dutch summary)  Chapter 11 Acknowledgements  Chapter 12 Curriculum vitae	306-313
11	Nederlandse samenvatting (Dutch summary)  Chapter 11 Acknowledgements  Chapter 12	306-313