



Universiteit
Leiden
The Netherlands

Preclinical validation and mechanistic understanding of drug repurposing candidates for polycystic kidney disease

Kanhai, A.A.

Citation

Kanhai, A. A. (2025, October 28). *Preclinical validation and mechanistic understanding of drug repurposing candidates for polycystic kidney disease*. Retrieved from <https://hdl.handle.net/1887/4280870>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/4280870>

Note: To cite this publication please use the final published version (if applicable).

Preclinical validation and mechanistic understanding of drug repurposing candidates for polycystic kidney disease

Anish August Kanhai

Preclinical validation and mechanistic understanding of drug repurposing candidates for polycystic kidney disease

Anish August Kanhai

Leiden University Medical Center, The Netherlands

ISBN: 978-94-6510-909-1

Layout & cover design: Anish Kanhai and Chiara Formica

Printing: ProefschriftMaken www.proefschriftmaken.nl

© 2025, Anish Kanhai. Copyright of the published material in chapters 2-4 lies with the publisher of the journal listed at the beginning of each chapter.

All rights reserved. No part of this thesis may be reprinted, reproduced or utilized in any form by electronic, mechanical, or other means now known or hereafter invented, including photocopying and recording in any information storage or retrieval system without prior written permission of the author.

Preclinical validation and mechanistic understanding of drug repurposing candidates for polycystic kidney disease

PROEFSCHRIFT

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof.dr.ir. H. Bijl,
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 28 oktober 2025
klokke 14.30 uur

door

Anish August Kanhai

geboren te Leiden
in 1992

Promotor:

Prof.dr. D.J.M. Peters

Co-promotor:

Dr. W.N. Leonhard

Promotiecommissie:

Prof.dr.ir. J.A.P. Willems van Dijk

Prof.dr. I. Meulenbelt

Prof.dr. G.J.P. van Westen¹

Prof.dr. E.J. Hoorn²

¹Computational Drug Discovery, Division of Medicinal Chemistry, Leiden Academic Centre for Drug Research, Leiden University, the Netherlands

²Department of Internal Medicine, Division of Nephrology and Transplantation, Erasmus Medical Center Rotterdam, the Netherlands

The studies described in this thesis have been performed at the department of Human Genetics, Leiden University Medical Center, the Netherlands.

Table of contents

Chapter 1	General introduction	7
Chapter 2	Renal cyst growth is attenuated by a combination treatment of tolvaptan and pioglitazone, while pioglitazone treatment alone is not effective	47
Chapter 3	Salsalate, but not metformin or canagliflozin, slows kidney cyst growth in an adult-onset mouse model of polycystic kidney disease	77
Chapter 4	Short salsalate administration affects cell proliferation, metabolism and inflammation in polycystic kidney disease	113
Chapter 5	Targeted analysis of salicylate binding partners in renal epithelial cells reveals major AMPK dependency	159
Chapter 6	Fiboflapon reduces cyst swelling <i>in vitro</i> , but does not affect cyst growth <i>in vivo</i>	201
Chapter 7	Summarizing discussion	223
Appendix		239
	Nederlandse samenvatting	241
	Curriculum vitae	244
	List of publications	245
	Dankwoord	246