



Universiteit  
Leiden  
The Netherlands

## **Diversity of glucocorticoid receptor signaling: molecular mechanisms and therapeutic implications**

Viho, E.M.G.

### **Citation**

Viho, E. M. G. (2023, September 7). *Diversity of glucocorticoid receptor signaling: molecular mechanisms and therapeutic implications*. Retrieved from <https://hdl.handle.net/1887/3638839>

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/1887/3638839>

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

# **DIVERSITY OF GLUCOCORTICOID RECEPTOR SIGNALING**

Molecular mechanisms and therapeutic implications

**Eva Viho**

*'When it all comes together'*

## **Diversity of glucocorticoid receptor signaling**

Molecular mechanisms and therapeutic implications

© 2023, Eva M. G. Viho

The work described in this thesis was performed at the Department of Medicine, Division of Endocrinology of the Leiden University Medical Center, Leiden, The Netherlands, and at the Einthoven Laboratory for Experimental Vascular Medicine, Leiden, The Netherlands.

The research described in this thesis was supported by Corcept Therapeutics.

Cover illustration: Marie Viho  
Design & Layout: Anke Muijsers | [www.persoonlijkproefschrift.nl](http://www.persoonlijkproefschrift.nl)  
Printing: Ridderprint | [www.ridderprint.nl](http://www.ridderprint.nl)  
ISBN: 978-94-6458-959-7

All rights reserved. No part of this thesis may be transformed, reproduced, stored, or transmitted in any form and by any means without permission in writing from the author.

# **Diversity of glucocorticoid receptor signaling**

Molecular mechanisms and therapeutic implications

## **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 donderdag 7 september 2023  
klokke 15:00 uur

door

**Eva Myriam Goussivi Viho**

geboren te Rennes, Frankrijk  
in 1995

**Promotor** Prof. Dr. O.C. Meijer

**Copromotor** Dr. J. Kroon

**Leden promotiecommissie** Prof. Dr. B. Heijmans  
Dr. E. M. Winter  
Prof. Dr. W. Zwart (NKI, Amsterdam)  
Prof. Dr. V. Dubois (Ghent University, Belgium)

À ma famille,



## TABLE OF CONTENTS

<b>Chapter 1</b>	General introduction and outline	1
<b>Chapter 2</b>	The development of novel glucocorticoid receptor antagonists: from rational chemical design to therapeutic efficacy in metabolic disease models	21
<b>Chapter 3</b>	Peripheral glucocorticoid receptor antagonism by relacorilant with modest HPA axis disinhibition	53
<b>Chapter 4</b>	The glucocorticoid receptor modulator CORT118335 induces a unique interactome associated with altered chromatin dynamics	85
<b>Chapter 5</b>	Corticosteroid action in the brain: the potential of selective receptor modulation	119
<b>Chapter 6</b>	Cell type specificity of glucocorticoid signaling in the adult mouse hippocampus	141
<b>Chapter 7</b>	The hippocampal response to acute corticosterone elevation is altered in a mouse model for Angelman syndrome	185
<b>Chapter 8</b>	General discussion and perspectives	221
<b>Chapter 9</b>	Appendices	243
	Summary.....	245
	Samenvatting.....	249
	Résumé.....	253
	List of publications.....	257
	Curriculum Vitae.....	259
	Acknowledgements.....	261