



Universiteit
Leiden
The Netherlands

Glucocorticoid receptor knockdown and adult hippocampal neurogenesis

Hooijdonk, L.W.A. van

Citation

Hooijdonk, L. W. A. van. (2010, April 20). *Glucocorticoid receptor knockdown and adult hippocampal neurogenesis*. Retrieved from <https://hdl.handle.net/1887/15275>

Version: Corrected Publisher's Version

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

License: <https://hdl.handle.net/1887/15275>

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

Glucocorticoid receptor knockdown and adult hippocampal neurogenesis

Lenneke van Hooijdonk

Lenneke van Hooijdonk

Glucocorticoid receptor knockdown and adult hippocampal neurogenesis

Thesis, Leiden University

April 20, 2010

ISBN: 978-90-8891-152-1

Cover: Box Press (design); Carlos Fitzsimons, Dirk-Jan Saaltink (photo's)

Printing: Box Press, proefschriftmaken.nl

© 2010, L.W.A. van Hooijdonk

No part of this thesis may be reproduced or transmitted in any form or by any means without written permission of the author

Glucocorticoid receptor knockdown and adult hippocampal neurogenesis

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van de Rector Magnificus Prof. Mr. P.F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 20 april 2010
klokke 13.45 uur

door

Leonarda Wilhelmina Antonia van Hooijdonk
geboren te Dordrecht
in 1980

Promotiecommissie

Promotor: Prof. Dr. E.R. de Kloet

Copromotor: Dr. E. Vreugdenhil

Overige leden: Prof. Dr. M. Danhof

Prof. Dr. R.R. Frants

Prof. Dr. R.C. Hoeben

Prof. Dr. R. Adan (UMCU, RMI of Neuroscience, Utrecht)

Dr. P. Lucassen (UvA, SILS-CNS, Amsterdam)

Dr. J.A. Morrow (Merck, Scotland)

Dr. M.J.M. Schaaf

The studies described in this thesis have been performed at the Division of Medical Pharmacology of the Leiden/ Amsterdam Center for Drug Research (LACDR) and Leiden University Medical Center (LUMC), The Netherlands. This research was financially supported by a program grant from the Dutch Technology Foundation (STW, LFA 6332).

Financial support for the printing of this thesis was kindly provided by:

- Leiden/ Amsterdam Center for Drug Research (LACDR)
- NWO-DFG International Research and Training Program (IRTG) Leiden-Trier (NWO-DN 95-420)
- J.E. Jurriaanse Stichting
- Internationale Stichting Alzheimer Onderzoek

Shoot for the moon. Even if you miss, you'll land among the stars.

Les Brown

Voor mijn ouders

List of abbreviations	8
CHAPTER 1 General introduction	9
CHAPTER 2 <i>In vitro validation of glucocorticoid receptor silencing by RNA-interference</i>	47
CHAPTER 3 Lentivirus-mediated transgene delivery to the hippocampus reveals sub-field specific differences in expression	65
CHAPTER 4 Glucocorticoid receptor regulates functional integration of newborn neurons in the hippocampus	89
CHAPTER 5 Glucocorticoid receptor knockdown in newborn neurons results in impaired fear memory	111
CHAPTER 6 General discussion	129
CHAPTER 7 Summary Samenvatting	145
CHAPTER 8 Curriculum vitae Publications	153
CHAPTER 9 Reference list	157

LIST OF ABBREVIATIONS

ACTH	adrenocorticotrophic hormone
ADX	adrenalectomy
AGLV	advanced generation lentiviral vector
AVP	argentine-vasopressin
BBB	Blood-Brain Barrier
CA	cornu ammonis (part of hippocampal formation)
CamKII	Ca ²⁺ /calmodulin dependent protein kinase
CMV	cytomegalovirus
CNS	central nervous system
CORT	corticosterone
CRH	corticotrophin releasing hormone
DBD	DNA binding domain
DCLK	double cortin like kinase
DCL	double cortin like
DCX	double cortin
DG	dentate gyrus
EGFP	enhanced green fluorescent protein
GC	glucocorticoid hormone (corticosterone, cortisol)
GCL	granular cell layer (of the dentate gyrus)
GFAP	Glial Fibrillar Acidic Protein
GR	Glucocorticoid Receptor
GRE	glucocorticoid response element
HPA axis	hypothalamo-pituitary-adrenal axis
LBD	ligand binding domain
LV	lentivirus
mRNA	messenger RNA
miRNA	micro RNA
mm-shGR	mismatch-shRNA
MMLV	Murine Maloney Leukemia Virus
ML	Molecular Layer
MR	Mineralocorticoid Receptor
mRNA	messenger RNA
NeuN	Neuron-specific Nuclear marker
NPC	Neuronal Progenitor Cell
Ns-1 PC12	Neuroscreen-1 Pheochromocytoma 12
PI	post- injection (time)
pm-shGR	perfect match shRNA against the GR
POMC	pro-opiomelanocortin
PTSD	post-traumatic stress disorder
PVN	Paraventricular nucleus
RISC	RNA induced silencing complex
RNAi	RNA-interference
SD	standard deviation
SEM	standard error of the mean
shGR	shRNA against GR, [shRNA] mouse model
siRNA	short interfering RNA
shRNA	short hairpin RNA
SGZ	sub granular zone (of the dentate gyrus)
SR	stratum radiatum
Syn	synapsin I
VSVg	Vesicular stomatitis virus glycoprotein