



Universiteit  
Leiden  
The Netherlands

## **Mineralocorticoid receptor gene variants : implications for stress, blood pressure and personality**

Leeuwen, N. van

### **Citation**

Leeuwen, N. van. (2010, November 9). *Mineralocorticoid receptor gene variants : implications for stress, blood pressure and personality*. Retrieved from <https://hdl.handle.net/1887/16122>

Version: Corrected 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/1887/16122>

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

**MINERALOCORTICOID  
RECEPTOR GENE VARIANTS**  
**Implications for stress, blood pressure  
and personality**

**Nienke van Leeuwen**

## **Promotie commissie**

- Promotores: Prof. dr. ER de Kloet  
Prof. dr. FG Zitman
- Co-promotor: Dr. RH de Rijk
- Overige leden: Prof.dr. W Hoogendijk (VUmc, Amsterdam)  
Prof.dr. AJW van der Does  
Prof.dr. P Slagboom  
Prof.dr. JWA Smit  
Dr. JW Koper (Erasmus Universiteit, Rotterdam)  
Dr. S Wüst (Central Institute of Mental Health, Mannheim, Duitsland)  
Prof.dr. M Danhof (secretaris)

ISBN: 978-90-8891-198-9

Print: Boxpress BV, [www.proefschriftmaken.nl](http://www.proefschriftmaken.nl)

Cover: Representation of DNA strands (Les Contamines, France)

The research described in this thesis was performed at the division of Medical Pharmacology of the Leiden/ Amsterdam Center for Drug Research and the Leiden University Medical Center. This work was financially supported by Psychiatric Hospital Rivierduinen and the Royal Netherlands Academy of Arts and Sciences (KNAW).

Financial support from the Netherlands Heart Foundation and the DFG-NWO International Research Training group (IRTG) Leiden-Trier (NWO-DN 95-420) for the publication of this thesis is gratefully acknowledged.

Printing of this thesis was also sponsored by:  
Leiden/Amsterdam Center for Drug Research (LACDR)  
J.E. Jurriaanse stichting  
Berthold

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

**MINERALOCORTICOID  
RECEPTOR GENE VARIANTS**  
**Implications for stress, blood pressure  
and personality**

**Proefschrift**

ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus Prof. mr. P.F. van der Heijden,  
volgens besluit van het College voor Promoties  
te verdedigen op dinsdag 9 november 2010  
klokke 13.45 uur

door

**Nienke van Leeuwen**

geboren te Haarlem  
in 1975



# Contents

<b>Chapter 1</b>	<b>7</b>
General Introduction	
<b>Chapter 2</b>	<b>31</b>
Identification of genetic variation in the Mineralocorticoid Receptor	
<b>Chapter 3</b>	
In vitro functional polymorphisms in the human Mineralocorticoid Receptor gene are associated with morning cortisol levels after 0.25mg DEX	<b>35</b>
<b>Chapter 4</b>	<b>51</b>
The functional -2 G variant of the mineralocorticoid receptor modulates basal and salt-dependent renin and aldosterone levels and associates with higher blood pressure	
<b>Chapter 5</b>	<b>69</b>
Human Mineralocorticoid Receptor (MR) gene haplotypes modulate MR expression and transactivation: implication for the stress response	
<b>Chapter 6</b>	<b>85</b>
Two haplotype blocks in the Mineralocorticoid Receptor (MR) associate with neuroticism but not with mood and anxiety disorders	
<b>Chapter 7</b>	<b>95</b>
General discussion	
<b>Summary in English</b>	<b>111</b>
<b>Samenvatting in het Nederlands</b>	<b>115</b>
<b>Reference list</b>	<b>119</b>
<b>Publications &amp; Presentations</b>	<b>131</b>
<b>Curriculum vitae</b>	<b>133</b>
<b>Dankwoord</b>	<b>134</b>