

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/42675> holds various files of this Leiden University dissertation.

Author: Thijsen, P.E.

Title: Genetics and epigenetics of repeat derepression in human disease

Issue Date: 2016-09-01

Genetics and epigenetics of repeat derepression in human disease

Peter E. Thijssen

Lay out & cover design: Peter Thijssen

Printing: Publisher BOXPress | | Proefschriftmaken.nl

ISBN: 9789462954250

© **Copyright by Peter E. Thijssen**

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

Publication of this thesis was financially supported by the department of Human Genetics and the Leiden University Medical Center

Genetics and epigenetics of repeat derepression in human disease

Proefschrift

ter verkrijging van de graad van Doctor aan de Universiteit Leiden
op gezag van Rector Magnificus prof.dr.C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op donderdag 1 september 2016
klokke 13:45

door

Peter Evert Thijssen

geboren te Zoetermeer in 1983

Promotores:

Prof. Dr. Ir. S.M. van der Maarel
Prof. Dr. P.E. Slagboom

Leden promotiecommissie:

Prof. Dr. A.M. Aartsma-Rus
Prof. Dr. J.H.L.M. van Bokhoven¹
Prof. S. Tapscott, MD, PhD²

1: UMC Radboud, Nijmegen, The Netherlands

2: Fred Hutchinson Cancer Research Center, Seattle, WA, USA

A grayscale photograph of a river flowing through a forest. The river is in the center, surrounded by large, dark rocks. The background is filled with tall, thin trees, and the overall scene is dimly lit, creating a somber and quiet atmosphere.

- Voor papa -

Table of Contents

Chapter 1:	General introduction	9
Chapter 2:	Correlation analysis of clinical parameters with epigenetic modifications in the <i>DUX4</i> promoter in FSHD.	35
Chapter 3:	Chromatin remodeling of human subtelomeres and TERRA promoters upon cellular senescence: commonalities and differences between chromosomes.	47
Chapter 4:	Increased <i>DUX4</i> expression during muscle differentiation correlates with decreased <i>SMCHD1</i> protein levels at <i>D4Z4</i> .	67
Chapter 5:	<i>DUX4</i> promotes transcription of <i>FRG2</i> by directly activating its promoter in Facioscapulohumeral muscular dystrophy.	89
Chapter 6:	Intrinsic epigenetic regulation of the <i>D4Z4</i> macrosatellite repeat in a transgenic mouse model for FSHD.	105
Chapter 7:	Mutations in <i>CDCA7</i> and <i>HELLS</i> cause immunodeficiency, centromeric instability and facial anomalies syndrome.	135
Chapter 8:	General discussion	149
Chapter 9:	Appendices	171
	Summary	
	Samenvatting	
	Curriculum vitae	
	List of publications	
	Dankwoord	