



Universiteit
Leiden
The Netherlands

Inherited retinal degenerations: clinical characterization on the road to therapy

Talib, M.

Citation

Talib, M. (2022, January 25). *Inherited retinal degenerations: clinical characterization on the road to therapy*. Retrieved from <https://hdl.handle.net/1887/3250802>

Version: Publisher's Version

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

License: <https://hdl.handle.net/1887/3250802>

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

**INHERITED RETINAL DEGENERATIONS:
CLINICAL CHARACTERIZATION ON THE ROAD TO THERAPY**

by

Mays Talib

ISBN | 978-94-6423-566-1

Design Cover | Véronique Baur – www.veerillustratie.nl

Lay-out | Bregje Jaspers – www.ProefschriftOntwerp.nl

Printing | ProefschriftMaken, Vianen, The Netherlands

The research described in this thesis was financially supported by
Curing Retinal Blindness Foundation, Janivo Stichting, Bayer, Stichting Blindenhulp

Financial support for the printing of this thesis was kindly provided by
Stichting Leids Oogheelkundig Ondersteuningsfonds, Rotterdamse Stichting Blindenbelangen,
Stichting Blindenhulp, Landelijke Stichting voor Blinden en Slechtzienden, Universitaire
Bibliotheken Leiden, Vitaminen op Recept, Oculenti Contactlenspraktijken, Revoir/Ergra Low
Vision, Laservision Instruments B.V., Medical Workshop B.V., Bayer, Theapharma, Santen, Syngenta
Medical, Tramedico B.V., Santen Pharmaceutical, D.O.R.C., ChipSoft, Low Vision Totaal.

All funding organizations provided unrestricted grants and had no role in the design or conduct
of this research described.

© Mays Talib (maystal@gmail.com), 2022

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

**INHERITED RETINAL DEGENERATIONS:
CLINICAL CHARACTERIZATION ON THE ROAD TO THERAPY**

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 25 januari 2022
klokke 13:45
door

Mays Talib

Geboren te Al-Karg, Irak
In 1990

Promotoren:

Prof. dr. C.J.F. Boon

Prof. dr. N.E. Schalij-Delfos

Copromotor:

Dr. J. Wijnholds

Promotiecommissie:

Prof. dr. M.J. Jager (secretaris)

Prof. dr. A.M. Aartsma-Rus

Prof. dr. R.E. MacLaren (*University of Oxford, UCL Institute of Ophthalmology*)

Prof. dr. R.W.J. Collin (*Radboud universitair medisch centrum*)

Voor mijn ouders

LIST OF ABBREVIATIONS

ACD	anterior chamber depth
ADRP	autosomal dominant retinitis pigmentosa
AF	autofluorescence
ARRP	autosomal recessive retinitis pigmentosa
AZOOOR	acute zonal occult outer retinopathy
BCVA	best-corrected visual acuity
BCEA	bivariate contour ellipse area
CF	counting fingers
CFC	cystoid fluid collections
CFT	central foveal thickness
CHM	choroideremia
CI	confidence interval
CME	cystoid macular edema
COD	cone dystrophy
CORD	cone-rod dystrophy
CRB1	Crumbs 1
CRISPR	clustered regularly interspaced short palindromic repeats
CRT	central retinal thickness
CSL	cone sensitivity loss
DA	dark-adapted
dB	decibel
DNA	deoxyribonucleic acid
ELM	external limiting membrane
EMA	European Medicines Association
ERG	electroretinography
ERM	epiretinal membrane
ETDRS	Early Treatment Diabetic Retinopathy Study
EZ	ellipsoid zone
FAF	fundus autofluorescence
FAZ	foveal avascular zone
FD	flow density
FDA	Food and Drug Administration
FfERG	full-field electroretinography
FST	full-field stimulus testing
FTMH	full-thickness macular hole
GCL	ganglion cell layer
GI	genetic isolate
GVF	Goldmann visual field
HM	hand motion

ILM	inner limiting membrane
INL	inner nuclear layer
IPL	inner plexiform layer
iPSC	induced pluripotent stem cells
IQR	interquartile range
IRD	inherited retinal dystrophy
ISCEV	International Society for Clinical Electrophysiology of Vision
IZ	interdigitation zone
LA	light-adapted
LCA	Leber congenital amaurosis
LogMAR	logarithm of the minimal angle of resolution
LP	light perception
LRAT	Lecithin:retinol acetyltransferase
MAIA	macular integrity assessment
MD	mean deviation
MP	microperimetry
NLP	no light perception
OCT	optical coherence tomography
OCTA	optical coherence tomography angiography
ONL	outer nuclear layer
OPL	outer plexiform layer
ORF15	open reading frame 15
P-AI	participation and activity inventory
PPRPE	para-arteriolar preservation of the retinal pigment epithelium
PSD	pattern standard deviation
RD	retinal dystrophy
REP-1	Rab escort protein 1
RHO	rhodopsin
RP	retinitis pigmentosa
RPA	retinitis punctata albescens
RPE	retinal pigment epithelium
RPE65	RPE specific protein 65 kDa
RPGR	retinitis pigmentosa GTPase regulator
SD	standard deviation
SD-OCT	spectral domain optical coherence tomography
SE	standard error
SER	spherical equivalent of the refractive error
SPC	subcapsular posterior cataract
VA	visual acuity
VF	visual field
XLRP	X-linked retinitis pigmentosa

CONTENTS

Chapter 1. General introduction	11
Chapter 2. CRB1-associated retinal dystrophies	49
2.1 Genotypic and phenotypic characteristics of <i>CRB1</i> -associated retinal dystrophies: A long term follow-up study <i>Ophthalmology</i> 2017;124(6):884-895	51
2.2 <i>CRB1</i> -associated retinal dystrophies in a Belgian cohort: Genetic characteristics and long-term clinical follow-up <i>Br J Ophthalmol</i> 2021; online ahead of print	85
2.3 Defining inclusion criteria and endpoints for clinical trials: A prospective cross-sectional study in <i>CRB1</i> -associated retinal dystrophies <i>Acta Ophthalmol</i> 2021;99(3):e403-e414	115
Chapter 3. Choroideremia	147
3.1 Long-term follow-up of patients with choroideremia with scleral pits and tunnels as a novel observation <i>Retina</i> 2018;38(9):1713-1724	149
3.2 Outcome of full-thickness macular hole surgery in choroideremia <i>Genes</i> 2017;8(7):187	171
Chapter 4. RPGR-associated retinal dystrophies	183
4.1 Clinical and genetic characteristics of male patients with <i>RPGR</i> -associated retinal dystrophies: A long-term follow up study <i>Retina</i> 2019;39(6):1186-1199	185
4.2 The spectrum of structural and functional abnormalities in female carriers of pathogenic variants in the <i>RPGR</i> gene <i>Invest Ophthalmol Vis Sci</i> 2018;59(10):4123-4133	215

Chapter 5. LRAT-associated retinal dystrophies	245
5.1. Long-term follow-up of retinal degenerations associated with <i>LRAT</i> mutations and their comparability to phenotypes associated with <i>RPE65</i> mutations	247
<i>Transl Vis Sci Technol</i> 2019;8(4):24	
Chapter 6. RHO-associated retinitis pigmentosa	273
6.1. Clinical characteristics and natural history of <i>RHO</i> -associated retinitis pigmentosa: A long-term follow-up study	275
<i>Retina</i> 2021;41(1):213-223	
Chapter 7. General Discussion	299
Chapter 8.	
English Summary	355
Dutch Summary (Nederlandse samenvatting)	363
Acknowledgments	371
About the author	377
List of publications	381

