



Universiteit
Leiden

The Netherlands

Scientific and clinical implications of heterogeneity in uveal melanoma

Lange, M.J. de

Citation

Lange, M. J. de. (2024, June 13). *Scientific and clinical implications of heterogeneity in uveal melanoma*. Retrieved from <https://hdl.handle.net/1887/3762814>

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/1887/3762814>

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

SCIENTIFIC AND CLINICAL IMPLICATIONS OF HETEROGENEITY IN UVEAL MELANOMA

Mark Johan de Lange

Cover design: Michelle de Lange

Printed by Proefschriftspecialist | proefschriftspecialist.nl

Layout and design: Puck Paassen, persoonlijkproefschrift.nl

ISBN: 978-94-93330-89-4

The research presented in this thesis was performed at the department of Ophthalmology of the Leiden University Medical Center, The Netherlands. The research was supported by grant UL 2011-4991 from the Dutch Cancer Society (KWF).

Scientific and clinical implications of heterogeneity in uveal melanoma

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 13 juni 2024

klokke 15.00 uur

door

Mark Johan de Lange

Promotiecommissie

Promotors Prof. Dr. G.P.M. Luyten

Prof. Dr. M.J. Jager

Copromotor Dr. P.A. van der Velden

Overige leden Prof. Dr. C.J.F. Boon

Prof. Dr. A.B. Maier (Vrije Universiteit, Amsterdam)

Prof. Dr. A.W. Langerak (Erasmus MC, Rotterdam)

Dr. T.H.K. Vu

Dr. N.A. Gruis

Aan Magnus, Sif en Trine

CONTENTS

Chapter 1:	Introduction: Scientific and clinical implications of genetic and cellular heterogeneity in uveal melanoma (<i>Published: Molecular Biomedicine, 2021</i>)	9
Chapter 2:	Digital PCR validates 8q dosage as prognostic tool in uveal melanoma (<i>Published: PLoS one, 2015</i>)	33
Chapter 3:	Heterogeneity revealed by integrated genomic analysis uncovers a molecular switch in malignant uveal melanoma (<i>Published: Oncotarget, 2015</i>)	55
Chapter 4:	Digital PCR-based T-cell quantification-assisted deconvolution of the microenvironment reveals that activated macrophages drive tumor inflammation in uveal melanoma (<i>Published: Molecular Cancer Research, 2018</i>)	99
Chapter 5:	Distribution of <i>GNAQ</i> and <i>GNA11</i> mutation signatures in uveal melanoma points to a light dependent mutation mechanism (<i>Published: PLoS one, 2015</i>)	125
Chapter 6:	Pre-clinical analysis of Dasatinib in uveal melanoma xenografts	139
Chapter 7:	Summary and Discussion	159
Chapter 8:	Nederlandse samenvatting	170
	List of publications	174
	Dankwoord	176
	Curriculum vitae	178