

University of Groningen

## Investigating the genetic complexity of glaucoma

Lo Faro, Valeria

DOI:  
[10.33612/diss.216689872](https://doi.org/10.33612/diss.216689872)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2022

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Lo Faro, V. (2022). *Investigating the genetic complexity of glaucoma*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.216689872>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

UNIVERSITY OF GRONINGEN

Investigating the genetic complexity of glaucoma

Valeria Lo Faro

The research described in this thesis was supported by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant No.675033 (EGRET plus). Additional funding was provided by the Rotterdamse Stichting Blindenbelangen (grant ID B20150036).

Financial support for publication of this thesis was kindly provided by the University of Groningen, BCN, GSMS and Professor Mulder Stichting.



Cover design Danilo Recchia | [danilo.recc@gmail.com](mailto:danilo.recc@gmail.com)

Layout Danilo Recchia | [danilo.recc@gmail.com](mailto:danilo.recc@gmail.com)

Printed Gildeprint, Enschede | [www.gildeprint.nl](http://www.gildeprint.nl)



Copyright © 2022 by Valeria Lo Faro

All rights reserved. Any unauthorised reprint or use of this material is prohibited. No part of this thesis may be reproduced, stored or transmitted in any form or by any means, without written permission of the copyright owner.



**university of  
groningen**

# Investigating the genetic complexity of glaucoma

**PhD thesis**

to obtain the degree of PhD at the  
University of Groningen  
on the authority of the  
Rector Magnificus Prof. C. Wijmenga  
and in accordance with  
the decision by the College of Deans.

This thesis will be defended in public on

Wednesday 1 June 2022 at 11:00 hours

by

**Valeria Lo Faro**

born on 24 December 1988  
in Catania, Italy

## **Supervisors**

Prof. N.M. Jansonius

Prof. A.A.B. Bergen

Prof. H. Snieder

## **Assessment Committee**

Prof. J. Wiggs

Prof. V. Guryev

Prof. J. Neidhardt

# Table of Contents

## Chapter 1

Introduction .....	09
Glaucoma.....	10
Prevalence of glaucoma.....	10
Glaucoma classification.....	11
Risk factors for POAG.....	12
Genetics of POAG .....	13
Gene discovery methods in POAG.....	14
Missing heritability in POAG.....	16
Clinical features and gene discovery of congenital glaucoma .....	17
Scope of the thesis .....	19

## Chapter 2

Differences in clinical presentation of primary open-angle glaucoma between African and European population .....	25
---	----

## Chapter 3

Novel mutations in the <i>PITX2</i> gene in Pakistani and Mexican families with Axenfeld-Rieger syndrome .....	41
--	----

## Chapter 4

Genome-wide CNV investigation suggests a role for cadherin, Wnt, and p53 pathways in primary open-angle glaucoma .....	53
--	----

## Chapter 5

Mitochondrial genome study identifies association between primary open-angle glaucoma and variants in <i>MT-CYB</i> , <i>MT-ND4</i> genes and haplogroups.....	85
--	----

## Chapter 6

Genome-wide association meta-analysis identifies novel ancestry-specific primary open-angle glaucoma loci and shared biology with vascular mechanisms and cell proliferation.....	103
---	-----

## Chapter 7

General Discussion.....	131
Main Findings .....	132
Monogenic diseases can provide insights into more common forms of glaucoma	132
Impact of copy number variants in glaucoma .....	134
Mitochondrial genome: another actor responsible for glaucoma complexity.....	135
The era of multi-ancestry studies in glaucoma .....	136
Future Perspectives: toward personalised medicine in glaucoma.....	139
Advances in the field of genetics that lead up to personalised medicine in glaucoma .....	139
What it is still needed to make possible personalised medicine for glaucoma.....	141
Final remarks .....	142

## Chapter 8

Summary .....	148
Samenvatting .....	150

## Appendix

Acknowledgements.....	155
-----------------------	-----





