University of Groningen

Genetic and Environmental Effects on Liver Diseases

Li, Yanni

DOI:
[10.33612/diss.182480991](https://doi.org/10.33612/diss.182480991)

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:
2021

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

Citation for published version (APA):
Li, Y. (2021). *Genetic and Environmental Effects on Liver Diseases*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.182480991>

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.

Genetic and Environmental Effects on Liver Diseases

**Yanni Li
2021.10**

Genetic and Environmental Effects on Liver Diseases

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 27 October 2021 at 9.00 hours

Printing of this thesis was financially supported by the university of Groningen (RUG), the University Medical Center Groningen (UMCG), the Graduate School of Medical Science (GSMS), the Groningen University Institute for Drug Exploration (GUIDE), and Chinese Scholarship Council (CSC).

Cover design: Yue Zhang and Yanni Li

Layout and printing: Guus Gijben, Proefschrift-AIO

© Copyright 2021, Y. Li, the Netherlands

All rights reserved. No part of this thesis may be produced, distributed, or transmitted in any form or by any means without the prior permission of the author or, where applicable, the publisher holding the copyright on the published articles.

by

Yanni Li

born on 03 July 1990
in Tianjin, P.R. China

Promoter

Prof. R.K. Weersma

Co-supervisors

Dr. E.A.M. Festen

Dr. V.E. de Meijer

Assessment committee

Prof. J.P. Drenth

Prof. I.P.J. Alwayn

Prof. S.P. Berger

Paranymphs

Dr. W.T.C. Uniken Venema

Dr. C. Qi

Propositions**Belonging to PhD thesis****Genetic and Environmental Effects on Liver Diseases**

1. Complications of liver transplantation such as rejection or allograft dysfunction are likely influenced by multiple genetic polymorphisms. (this thesis)
2. Investigation of multiple risk factors, including demographics, environmental risk factors, and genetic risk factors enables a better understanding of the complications of liver transplantation. (this thesis)
3. The presence of reported thrombosis risk loci in liver donors did not increase thrombosis risk in liver transplant recipients, suggesting that it is not necessary to exclude liver donors solely based on thrombosis-susceptible polymorphisms. (this thesis)
4. Quantification of the genetic mismatch between the liver donor and recipient could potentially identify those recipients at increased risk for acute cellular rejection. (this thesis)
5. High genetic correlations between Metabolic Associated Fatty Liver Disease (MAFLD) phenotypes (MRI-PDFF vs. Fatty Liver Index) supports the notion that non-invasive serum biomarkers can be used as phenotypes in epidemiological and genetic studies for MAFLD. (this thesis)
6. Beyond GWAS, the potential of “multi-omics” studies in liver disease provide a framework for future fundamental research and translational medicine. (this thesis)
7. Data sharing between consortia and the creation of tissue biobanks which include deeply phenotyped samples, is the key to well-powered genetic and translational research. (this thesis)
8. The clinical implementation of rapidly developing technologies and the interpretation of the accumulating genetic data are challenging, but the combination of genetic studies and functional studies unveil pathogenetic processes in complex liver diseases. (this thesis)
9. “There are, in effect, two things: to know and to believe one knows. To know is science; to believe one knows is ignorance.” (Hippocrates)
10. “Remember to look up at the stars and not down at your feet. Try to make sense of what you see.” (Stephen Hawking)

Table of contents

Chapter 1	General introduction	9
Chapter 2	The impact of donor and recipient genetic variation on outcomes after solid organ transplantation: a scoping review and future perspectives <i>Under review at Transplantation</i>	21
Chapter 3	Donor tobacco smoking is associated with postoperative thrombosis after primary liver transplantation <i>J Thromb Haemost. 2020 Oct;18(10):2590-2600</i>	41
Chapter 4	Donor genetic variants as risk factors for thrombosis after liver transplantation: a genome-wide association study <i>Am J Transplant. 2021;10.1111/ajt.16490</i>	61
Chapter 5	Donor-recipient genetic mismatch is associated with acute cellular rejection after liver transplantation <i>Under review at Am J Transplant.</i>	89
Chapter 6	Gut microbiome dysbiosis is associated with increased mortality following solid organ transplantation <i>Under review at Nature Microbiology</i>	109
Chapter 7	Large scale genome-wide studies reveal novel risk factors for Metabolic Associated Fatty Liver Disease <i>Under review at J Hepatology</i>	139
Chapter 8	Discussion and future perspectives	173
Appendices	Summary Nederlandse samenvatting Acknowledgements List of publications Curriculum Vitae	189