



University of Groningen

#### Metabolic adaptations in models of fatty liver disease

Hijmans, Brenda

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: 2017

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA): Hijmans, B. (2017). *Metabolic adaptations in models of fatty liver disease: Of mice and math.* [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

#### 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/taverneamendment.

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.

## Metabolic adaptations in models of fatty liver disease

Of mice and math





The work described in this thesis was performed at the Department of Pediatrics, Center for Liver, Digestive and Metabolic Diseases, University of Groningen, University Medical Center Groningen, the Netherlands. This research was performed within the framework of CTMM, the Center for Translational Molecular Medicine (www.ctmm.nl), project PREDICCt (grant 01C-104), and supported by the Dutch Heart Foundation, Dutch Diabetes Research Foundation and Dutch Kidney Foundation. The work was also supported by research grants from de Agence Nationale de la Recherche (ANR11-BSV1-009-01), the Association Francophone des Glycogénoses, and the University of Groningen.

Printing of this dissertation was financially supported by:



Cover design by Sander Onur Cover graphic was designed by Brenda Hijmans

Printed by Ipskamp Drukkers, Enschede, the Netherlands

ISBN: 978-90-367-9500-5 (printed version) ISBN: 978-90-367-9499-2 (electronic version)



# Metabolic adaptations in models of fatty liver disease

Of mice and math

## Proefschrift

ter verkrijging van de graad van doctor aan de Rijksuniversiteit Groningen op gezag van de rector magnificus prof. dr. E. Sterken en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

woensdag 22 februari 2017 om 14.30 uur

door

### Brenda Samantha Hijmans

geboren op 21 januari 1985 te Amersfoort

#### **Promotores**

Prof. dr. A.K. Groen Prof. dr. D.J. Reijngoud

**Copromotor** Dr. ir. M.H. Oosterveer

# **Beoordelingscommissie** Prof. dr. A.J.W. Scheurink

Prof. dr. B.M. Bakker Prof. dr. R.J.A. Wanders

# Contents

1	General introduction	7
2	A systems biology approach reveals the origin of hepatic steatosis induced by liver X receptor activation	25
3	Integration of transcriptional data into ADAPT improves its esti- mation on changes in lipid metabolism induced by liver X receptor activation	49
4	Perturbed lipid metabolism in a mouse model of glycogen storage disease type Ia: differential contributions of <i>de novo</i> lipogenesis to liver steatosis in fed and fasted states	59
5	Hepatocytes contribute to residual glucose production in a mouse model for glycogen storage disease type Ia	81
6	Zonation of glucose and fatty acid metabolism: mechanism and metabolic consequence	103
7	General discussion	123
A	Appendices	
$\mathbf{A}$	Taqman qPCR primer and probe sequences.	141
В	ADAPT methodology	145
С	Lipolytic enzymes in L- $G6pc^{+/+}$ and L- $G6pc^{-/-}$ mice	155
Bi	Bibliography	
W	Wetenschappelijke samenvatting	
Da	Dankwoord	