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The metabolic and developmental role of FXR in adipose tissue and proximal small intestine

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DOI:
[10.33612/diss.202786503](https://doi.org/10.33612/diss.202786503)

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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):

Yang, J. (2022). *The metabolic and developmental role of FXR in adipose tissue and proximal small intestine*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.
<https://doi.org/10.33612/diss.202786503>

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The metabolic and developmental role of FXR in adipose tissue and proximal small intestine

Jiufang Yang

The research described in this thesis was conducted at the Department of Pediatrics, section Molecular Metabolism and Nutrition, University Medical Center Groningen (UMCG), The Netherlands.

This work was financially supported by the China Scholarship Council (CSC), Graduate School of Medical Science (GSMS), University of Groningen (RUG) and De Stichting De Cock-Hadders.

The author gratefully acknowledges the financial support of the University of Groningen (RUG), Graduate School of Medical Science (GSMS), Groningen University Institute for Drug Exploration (GUIDE) and Netherlands Association for the Study of the Liver (NVH/NASL).

Cover design: Jiufang Yang and Qinfei Zhou

Layout design: Jiufang Yang

Printed by: Ipskamp Drukkers B.V

ISBN: 978-94-6421-652-3

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university of
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The metabolic and developmental role of FXR in adipose tissue and proximal small intestine

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

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Preface

To those who may find directly diving into this scientific thesis a bit daunting, here is some interesting information related to the keywords of this thesis, which might spark your curiosity about bile acids and FXR.

Gallbladder: 1. People can still live a perfectly normal life without a gallbladder. For example, for patients who suffer a lot from gallstones, surgical removal of the gallbladder is probably the most effective treatment. However, the Chinese culture attaches special importance to the gallbladder. It is believed that the gallbladder is associated with courage. Maybe the brave prehistorical men who were able to hunt more animals needed more bile acids stored in their gallbladder to facilitate fat digestion. Even now, some sayings and expressions related to the gallbladder are still commonly used in our daily lives. For example: “浑身是胆” (whole-body is gall) means “be every inch a hero”; “狐胆英雄” (single-gall hero) means “a lone fighter”; “七头八胆” (seven-heads eight-galls) means “extremely bold” ¹.

2. The name gall comes from the Greek word ‘cholè’ referring to its green or yellow color. The terms such as cholesterol, cholecystitis and cholecystectomy were named after gall. Interestingly, ancient Greeks believed that human personalities could be reflected by the four humors (blood, phlegm, yellow bile and black bile), which were located in the heart, brain, gallbladder and spleen respectively. Yellow bile is represented as irritability ².

The Farnesoid X receptor (FXR): In 1995, FXR was isolated and identified as an orphan nuclear receptor ³. FXR got its name because rat FXR can be activated by high concentrations of farnesol, which can be found in both plants and animals. In 1999, FXR was finally adopted and endogenous bile acids are its natural ligands. It is quite amazing to find a lot of progress about FXR within the last 20 years. You will find more detailed information in Chapter 1.

The small intestine: The length of the small intestine in humans is around 7 meters and finger-like structures called villi help increase the absorptive surface area of the small intestine. Different from humans, some fish such as sharks have spiral intestines and this spiral arrangement of the mucosa also increases the surface area of their short intestine ⁴.

White adipose tissue (WAT): WAT expands by increasing the size of adipocytes (hypertrophy) and increasing the number of adipocytes (hyperplasia). Weight loss induces shrinkage of adipocytes; however, quite unfortunately, the number of adipocytes will not change ⁵. It means that those adipocytes are ready to store lipids for you if you start to take in more calories than you need.

Brown adipose tissue (BAT): 1. You will find many references about BAT in mice and humans in this thesis. Before exploring those, BAT also exists in many other animals. Delphinoid BAT in blubber might function like an electric blanket, allowing marine animals to maintain body temperature in cool waters ⁶. Animals living in polar environments also equipped themselves with BAT to defend themselves against the cold. For example, massive deposits of BAT surround the internal organs like the heart in newborn muskoxen ⁷.

2. After seeing the striking difference of thermogenic gene expression changes of BAT from mice before and after cold exposure in this thesis, I hope you will be convinced to join one of the Dutch traditions, diving into ice cold sea water on New Year's Day ("Nieuwjaarsduik"), to activate your BAT!

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Table of contents

Chapter 1:	General introduction	9
Chapter 2:	Emerging roles of bile acids in control of intestinal functions	39
Chapter 3:	Intestinal Farnesoid X Receptor modulates duodenal surface area but does not control glucose absorption in mice	51
Chapter 4:	Farnesoid X Receptor overexpression alters adipose tissue architecture and limits its storage capacity leading to ectopic fat deposition and insulin resistance	83
Chapter 5:	Role of bile acid receptor FXR in development and function of brown adipose tissue	117
Chapter 6:	Metabolic characterization of a mouse model with Farnesoid X receptor deficiency in adipocytes	149
Chapter 7:	General discussion & conclusion	181
Appendices:	English summary Nederlandse samenvatting Curriculum vitae Acknowledgements / Dankwoord / 致谢	197