

University of Groningen

## Environment-host-microbe interactions shape human metabolism

Chen, L; Fu, Jingyuan

DOI:  
[10.33612/diss.171839167](https://doi.org/10.33612/diss.171839167)

**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):*  
Chen, L., & Fu, J. (2021). *Environment-host-microbe interactions shape human metabolism*. University of Groningen. <https://doi.org/10.33612/diss.171839167>

### 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.

# **Environment-host-microbe interactions shape human metabolism**

Lianmin Chen

Cover designed by Stella Ilchenko

Printing of this thesis was financially supported by:  
The University of Groningen (RUG)  
The University Medical Center Groningen (UMCG)  
Graduate School of Medical Science (GSMS)  
The Groningen University Institute for Drug Exploration (GUIDE)

**Copyright © 2021 Lianmin Chen**

All right reserved. No part of this thesis may be reproduced, 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.



university of  
 groningen

# **Environment-host-microbe interactions shape human metabolism**

## **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  
 Tuesday 22 June 2021 at 12.45 hours

by

**Lianmin Chen**

born on 23 November 1991  
 in Jiangsu, China

**Supervisors**

Prof. J. Yang-Fu

Prof. F. Kuipers

Prof. A.P. Zhernakova

**Assessment Committee**

Prof. V.V.A.M. Knoers

Prof. M. Nieuwdorp

Prof. O.P. Kuipers

## Propositions

Inter-individual variations in gut microbial composition associate with host health status. (*Zhernakova et al., Science, 2016*)

Gut microbial pathways can be linked to the cardiometabolic risk of the host. (*this thesis*)

Plasma bile acid profiles show large inter-individual variability in individuals with obesity. (*this thesis*)

Gut microbial genetic makeup shows long-term stability and individual specificity that can serve as a host fingerprint. (*this thesis*)

Gut microbial changes over time are related to changes in plasma metabolite levels in the host. (*this thesis*)

The levels of specific plasma metabolites are dominantly driven by different factors, including diet, microbiome and genetics, that vary from metabolite to metabolite. (*this thesis*)

Gut microbial interactions that are reflected by co-abundances show specificity in inflammatory bowel disease and obesity. (*this thesis*)

Research is what I'm doing when I don't know what I'm doing. (*Wernher von Braun*)

We cannot solve problems with the same thinking we used to create them. (*Albert Einstein*)

# Content

<b>Chapter 1</b>	Introduction ..... 1 <i>(Human Molecular Genetics, 2018)</i>
<b>Chapter 2</b>	Gut microbial associations to plasma metabolites linked to cardiovascular phenotypes and risk ..... 15 <i>(Circulation Research, 2019, Cover story)</i>
<b>Chapter 3</b>	Genetic and microbial associations to plasma and fecal bile acids in obesity relate to plasma lipids and liver fat content ..... 41 <i>(Cell Reports, 2020, Cover story)</i>
<b>Chapter 4</b>	Diet, genetics and gut microbiome determine human plasma metabolome. .... 64 <i>(Submitted, 2021)</i>
<b>Chapter 5</b>	The long-term genetic stability and individual specificity of the human gut microbiome ..... 93 <i>(Cell, 2021, Cover story)</i>
<b>Chapter 6</b>	Gut microbial co-abundance networks show specificity in inflammatory bowel disease and obesity ..... 124 <i>(Nature Communications, 2020, with “behind the paper”)</i>
<b>Chapter 7</b>	Discussion and perspective ..... 151
<b>Appendices</b>	Summary ..... 172 Acknowledgement ..... 175 Curriculum vitae ..... 177 Publications ..... 178