Targeting keystone species helps restore the dysbiosis of butyrate-producing bacteria in non-alcoholic fatty liver disease

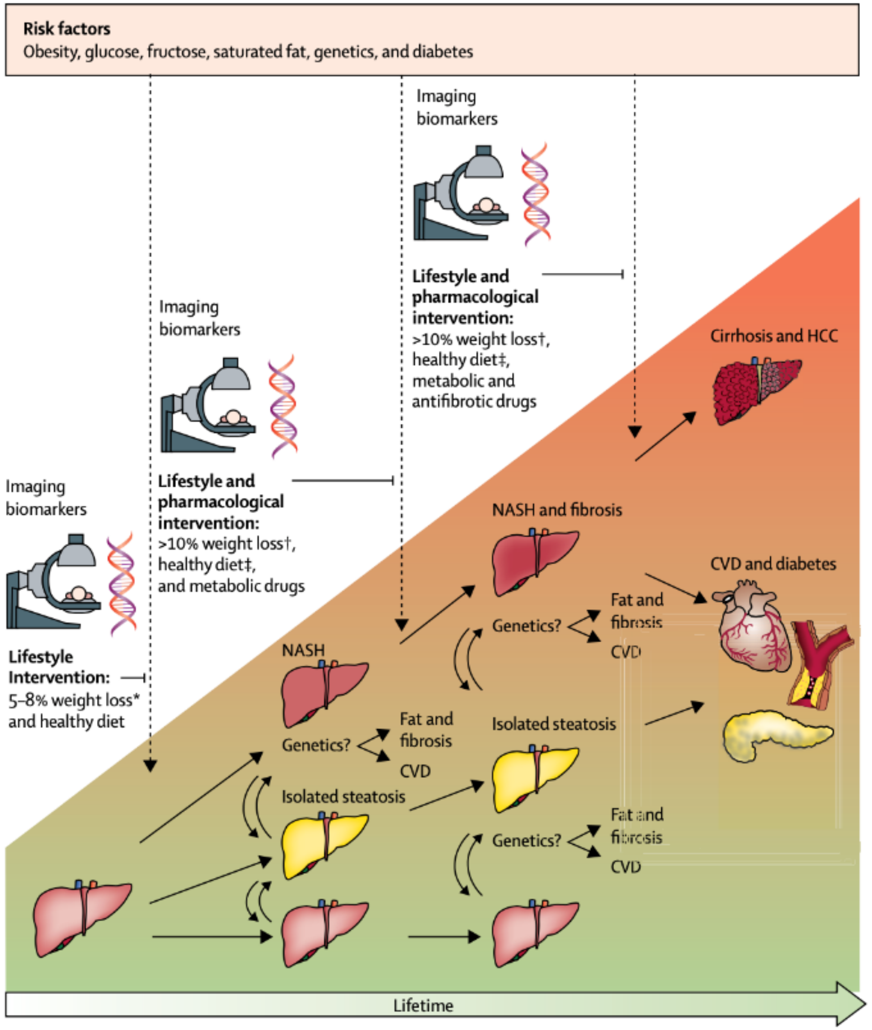
Dingfeng Wu[1, 2, #], Lei Liu[2, #], Na Jiao[1, 3, #], Yida Zhang[4], Li Yang[5], Chuan Tian[2], Ping Lan[3, 6], Lixin Zhu[3, 6, 7, *], Rohit Loomba[8, *], Ruixin Zhu[2, 9, *]

[1]National Clinical Research Center for Child Health, the Children's Hospital, Zhejiang University School of Medicine, Hangzhou 310058, Zhejiang, P. R. China.
[2]The Shanghai Tenth People's Hospital, School of Life Sciences and Technology, Tongji University, Shanghai 200072, P. R. China.
[3]Guangdong Institute of Gastroenterology, Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Diseases, the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou 510655, P.R. China.
[4]Department of Biomedical Informatics, Harvard Medical School, Boston, MA 02215, United States.
[5]State Key Laboratory of Biotherapy, West China Hospital, Sichuan University and Collaborative Innovation Center, Chengdu, Sichuan, P.R.China.
[6]Department of Gastroenterology, the Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou 510655, P.R.China.
[7]Digestive Diseases and Nutrition Center, Department of Pediatrics, the State University of New York at Buffalo, Buffalo, NY14214, United States.
[8]NAFLD Research Center, Division of Gastroenterology and Epidemiology, Department of Medicine, University of California San Diego, La Jolla, California 92093, United States.
[9]Research Institute, GloriousMed Clinical Laboratory Co., Ltd., Shanghai 201318, P. R.China.

Wu, Dingfeng, Lei Liu, Na Jiao, Yida Zhang, Li Yang, Chuan Tian, Ping Lan, Lixin Zhu, Rohit Loomba, Ruixin Zhu. 2022. Targeting keystone species helps restore the dysbiosis of butyrate-producing bacteria in non-alcoholic fatty liver disease. ***iMeta***. e61. https://doi.org/10.1002/imt2.61

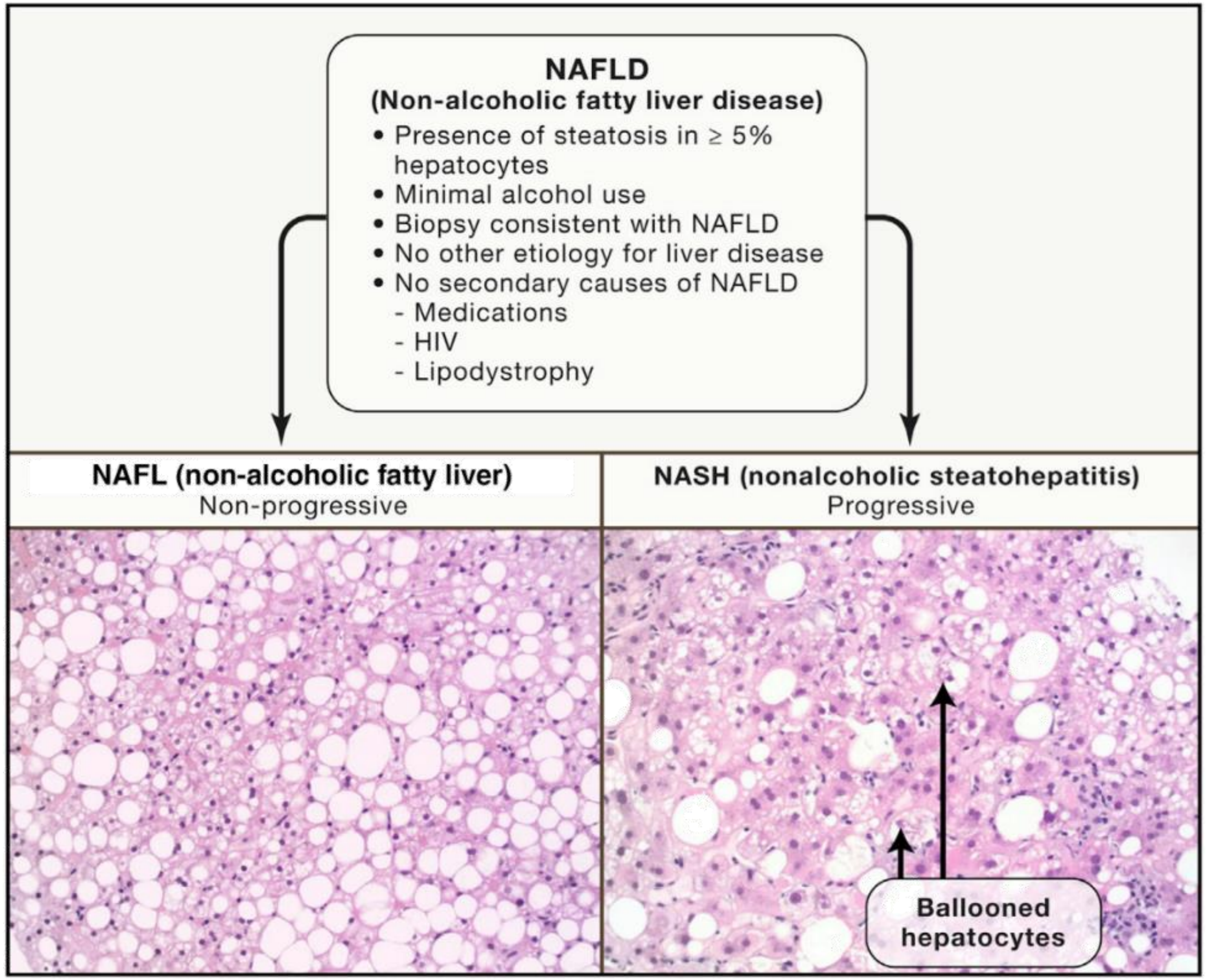
Introduction

Natural history of NAFLD



Stefan, N., et al. The Lancet Diabetes & Endocrinology. 2019.

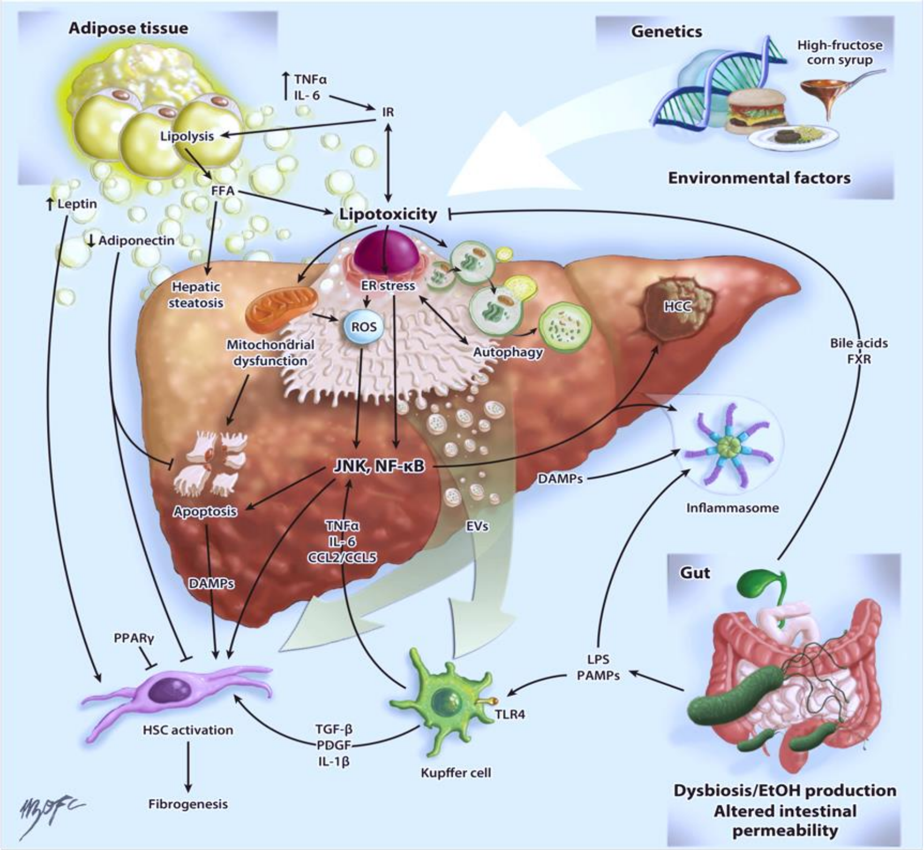
Histologic features of NAFLD



Loomba R, et al. Cell. 2021.

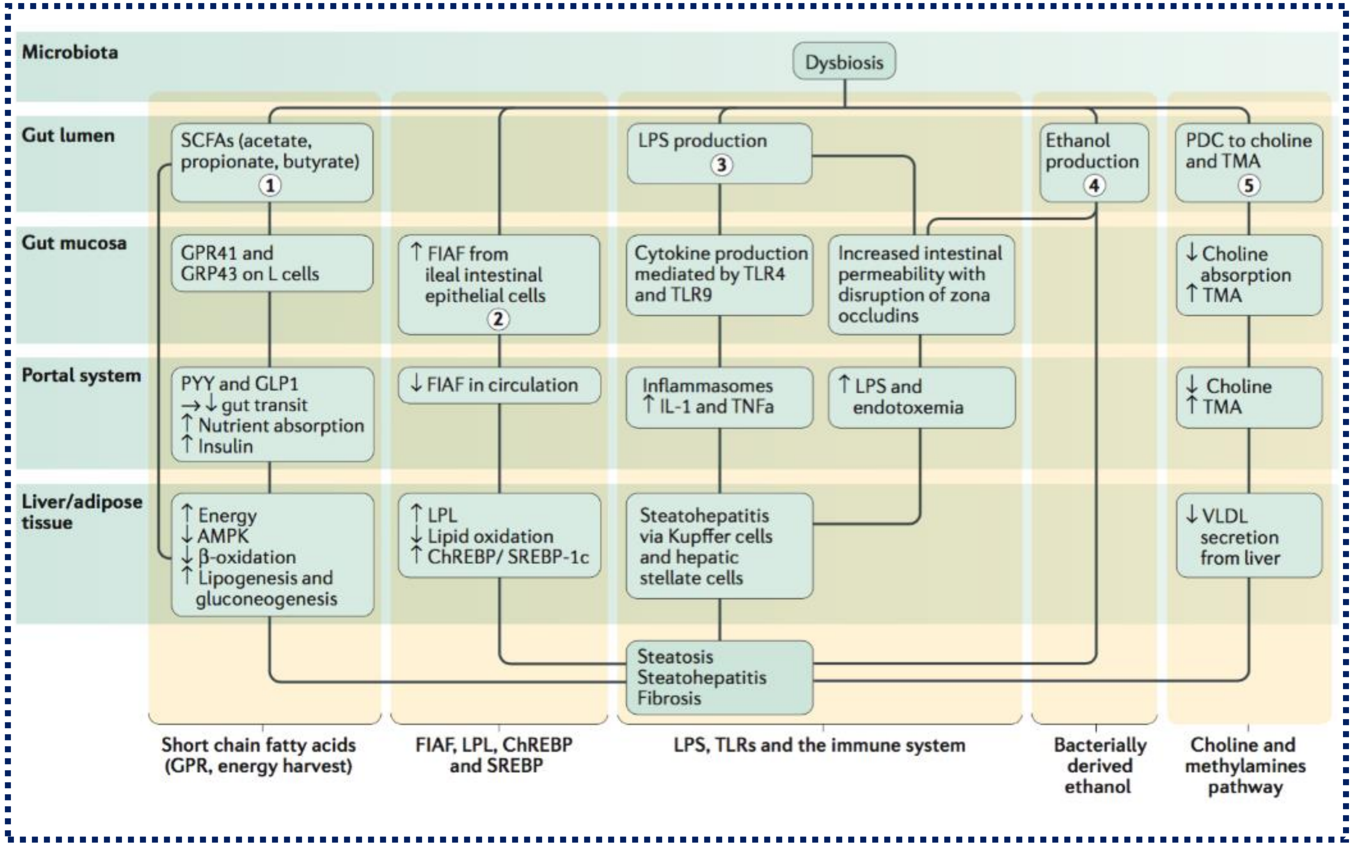
Introduction

Multiple hit hypothesis for the development of NAFLD



Buzzetti E, et. al. Metabolism, 2016.

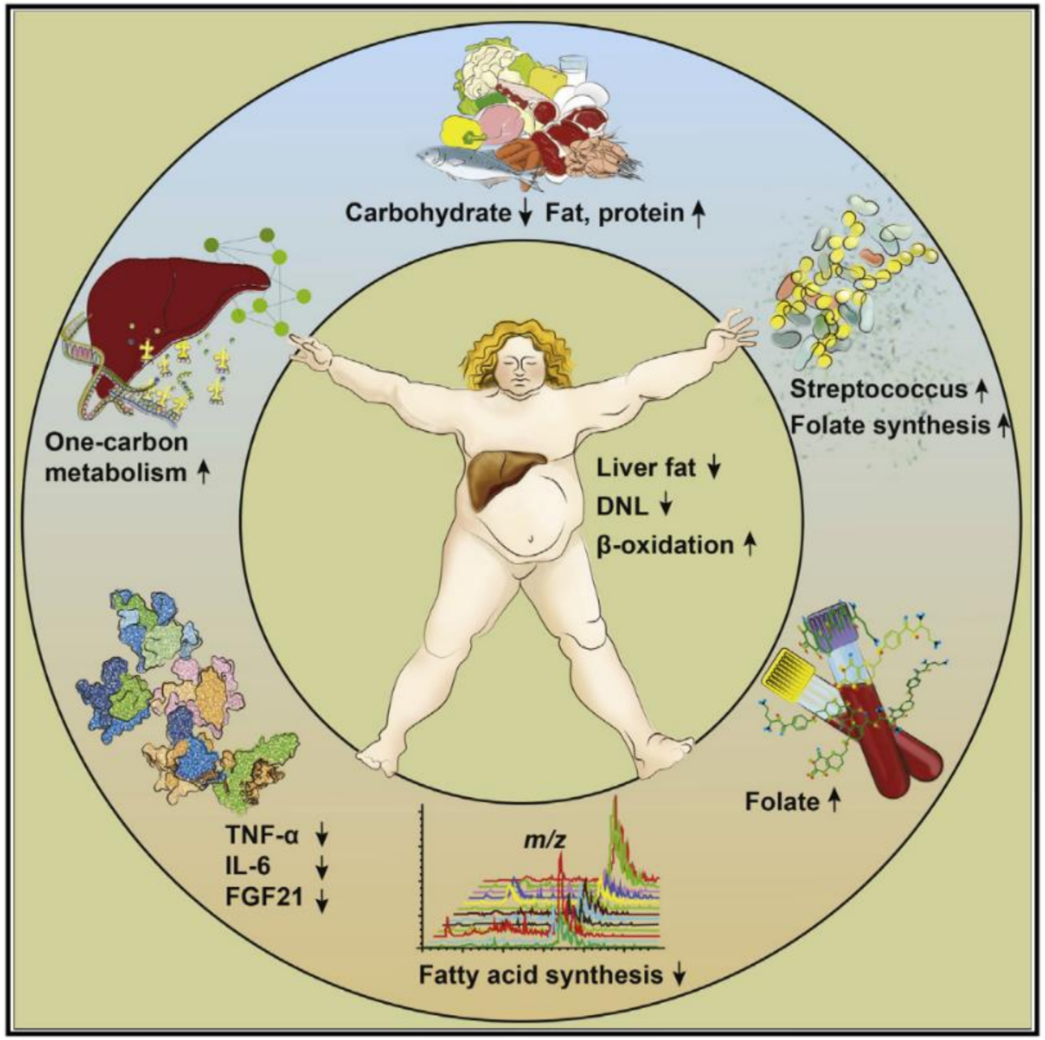
Key mechanistic pathways involved in the gut–liver axis in NAFLD progression



Leung C, et. al. Nature Reviews Gastroenterology & Hepatology, 2016.

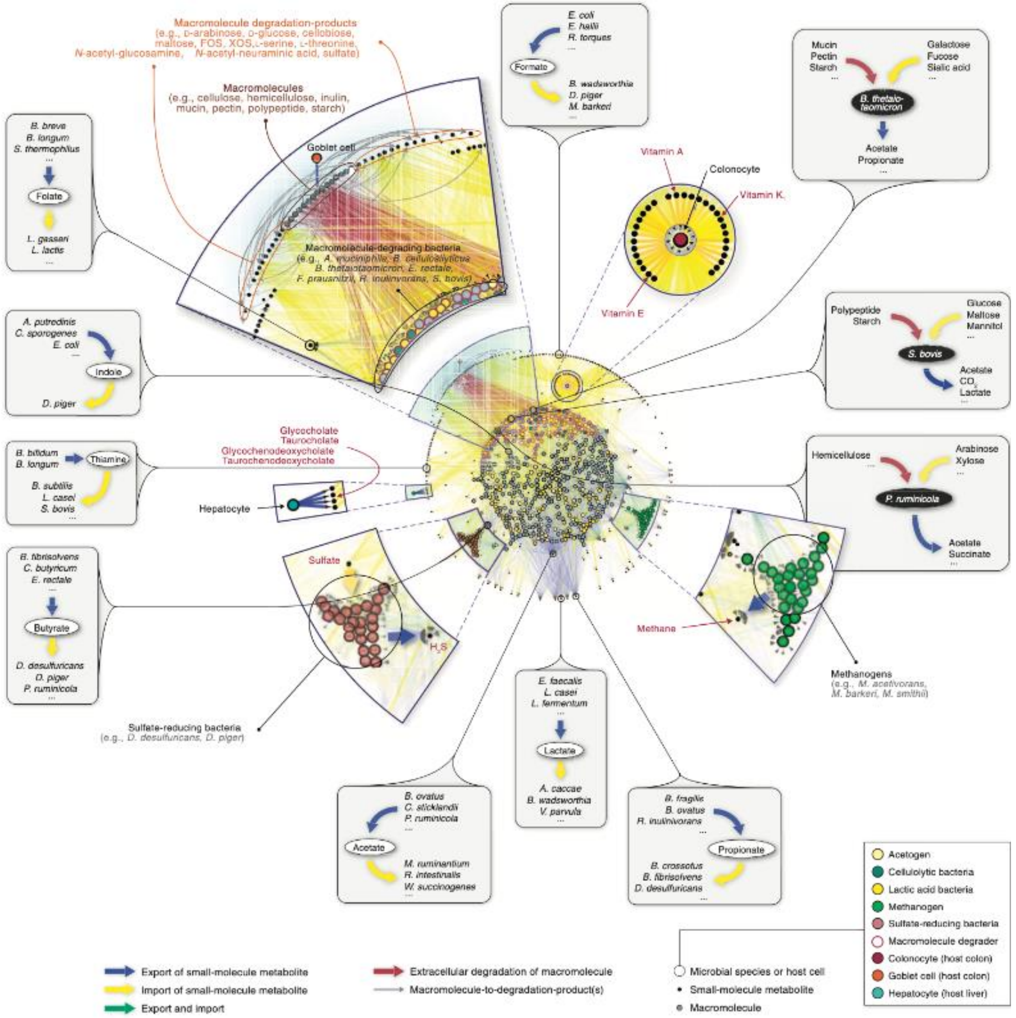
Introduction

Treatment targeted gut microbiota



Mardinoglu A, et. al. Cell Metab. 2018.

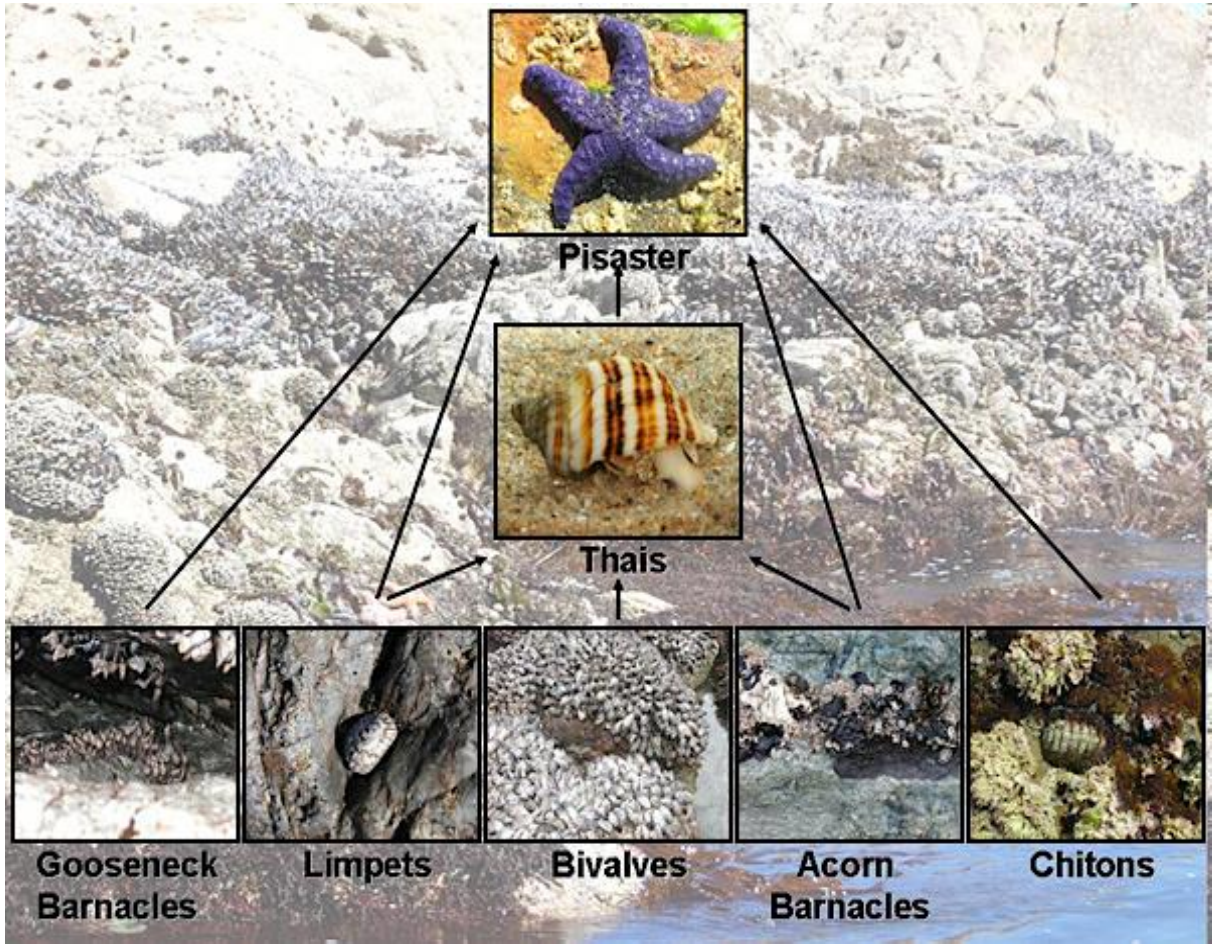
Structural complexity of the microecosystem



Sung J, et. al. Nat Commun. 2017.
Tarantino G, et. al. Future Microbiol. 2015.

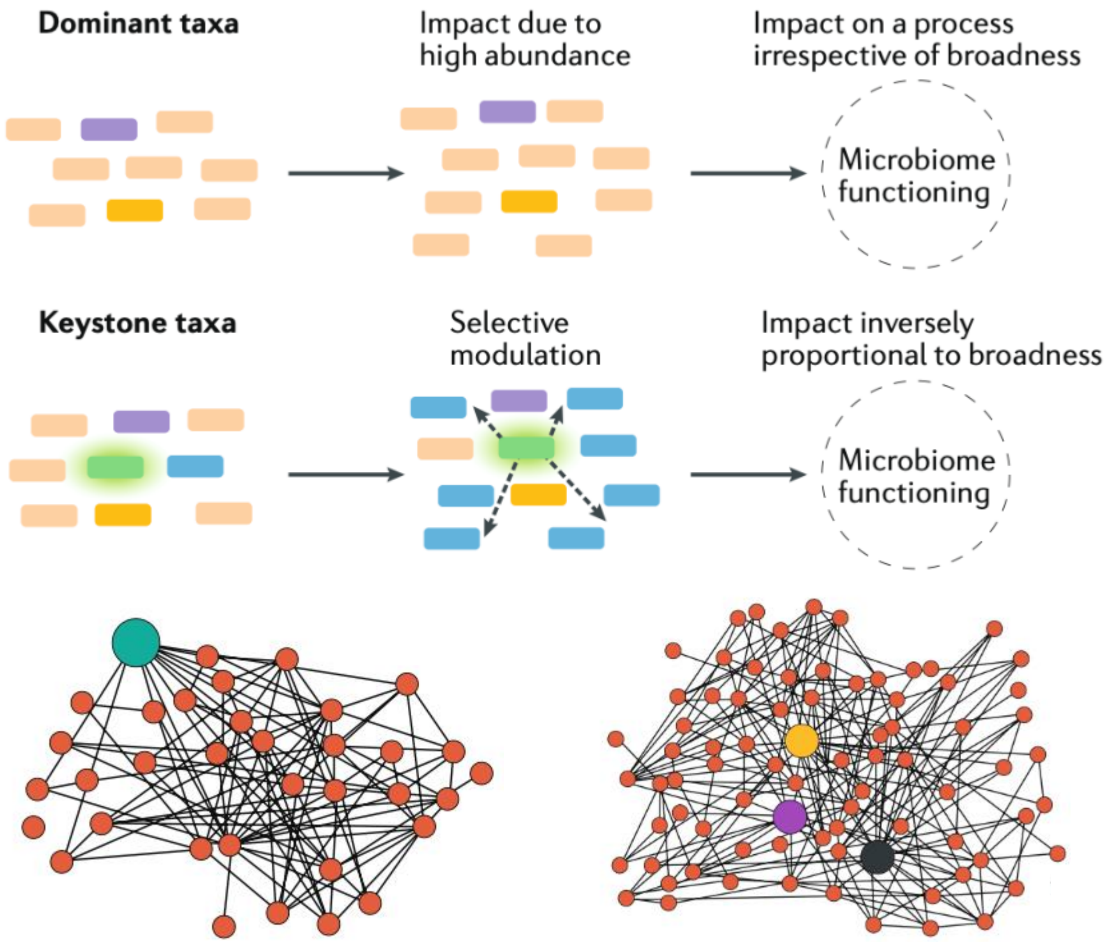
Introduction

Keystone species in food web



Stephen C. et. al. Nature Education Knowledge. 2010

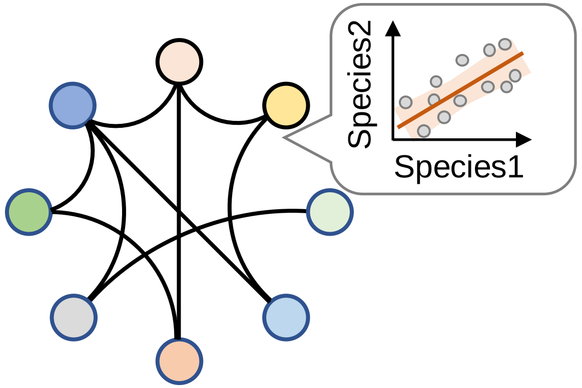
Keystone species in microbial interaction network



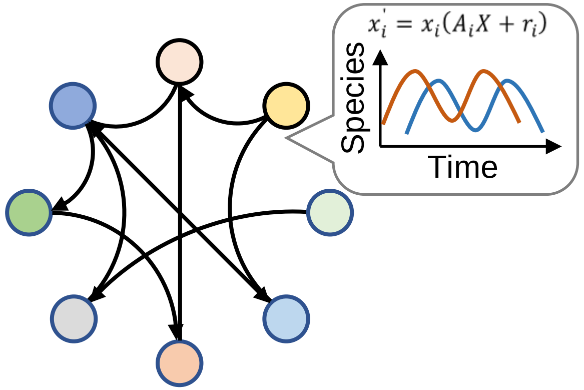
Banerjee S. et. al. Nat Rev Microbiol. 2018.

Introduction

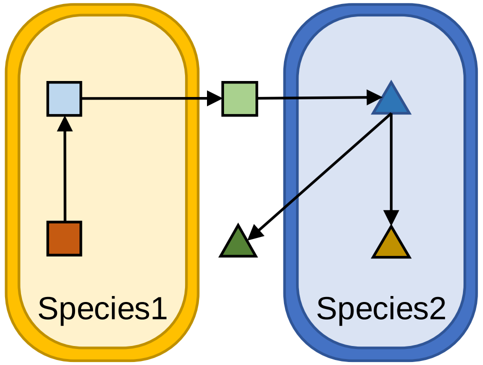
Common microecosystem modeling methods



Co-occurrence networks

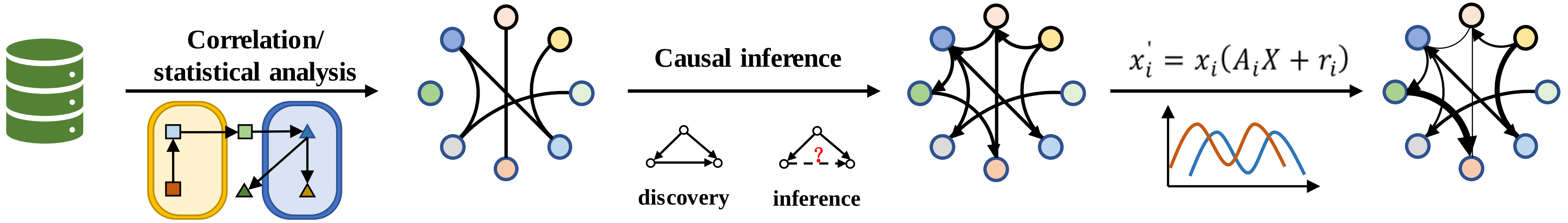


Population dynamic models



Metabolic models

Microecosystem modeling based on causality theory

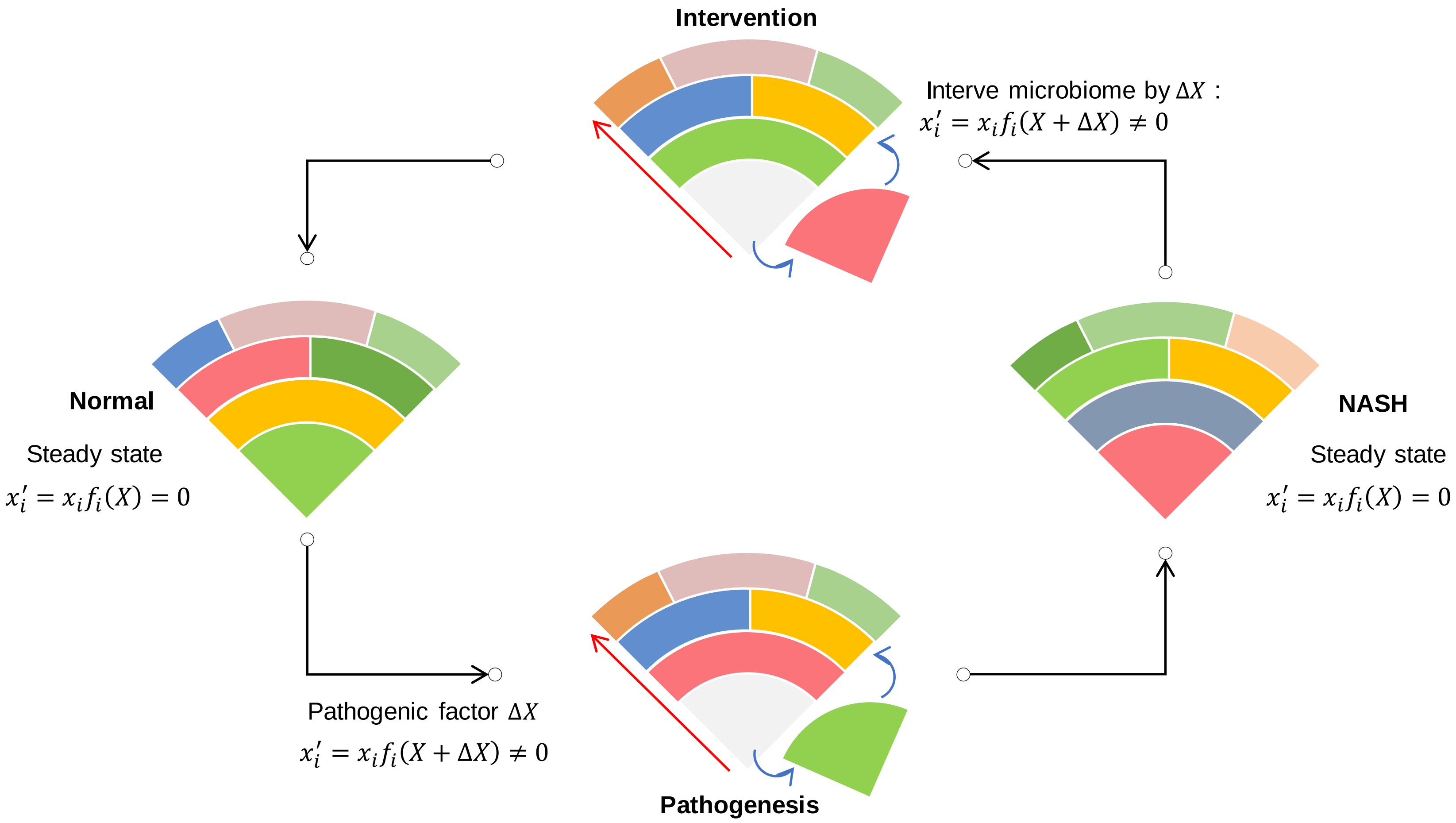


Prior knowledge — Prior knowledge network — Microbial interaction — Microecosystem model

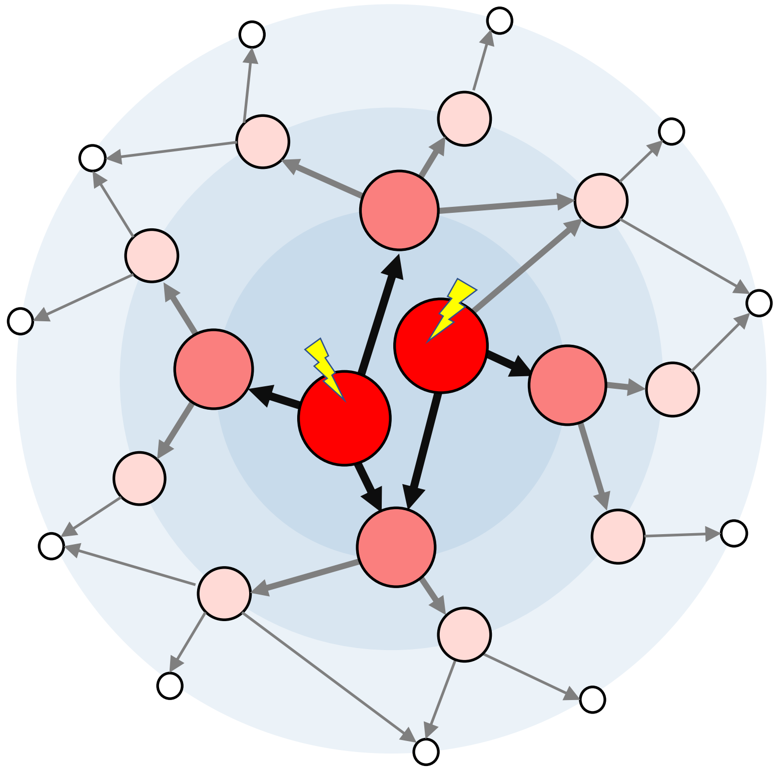
Faust K, et al. PLoS computational biology, 2012.
Judea Pearl, et. al. 《The Book of Why》. 2020

Introduction

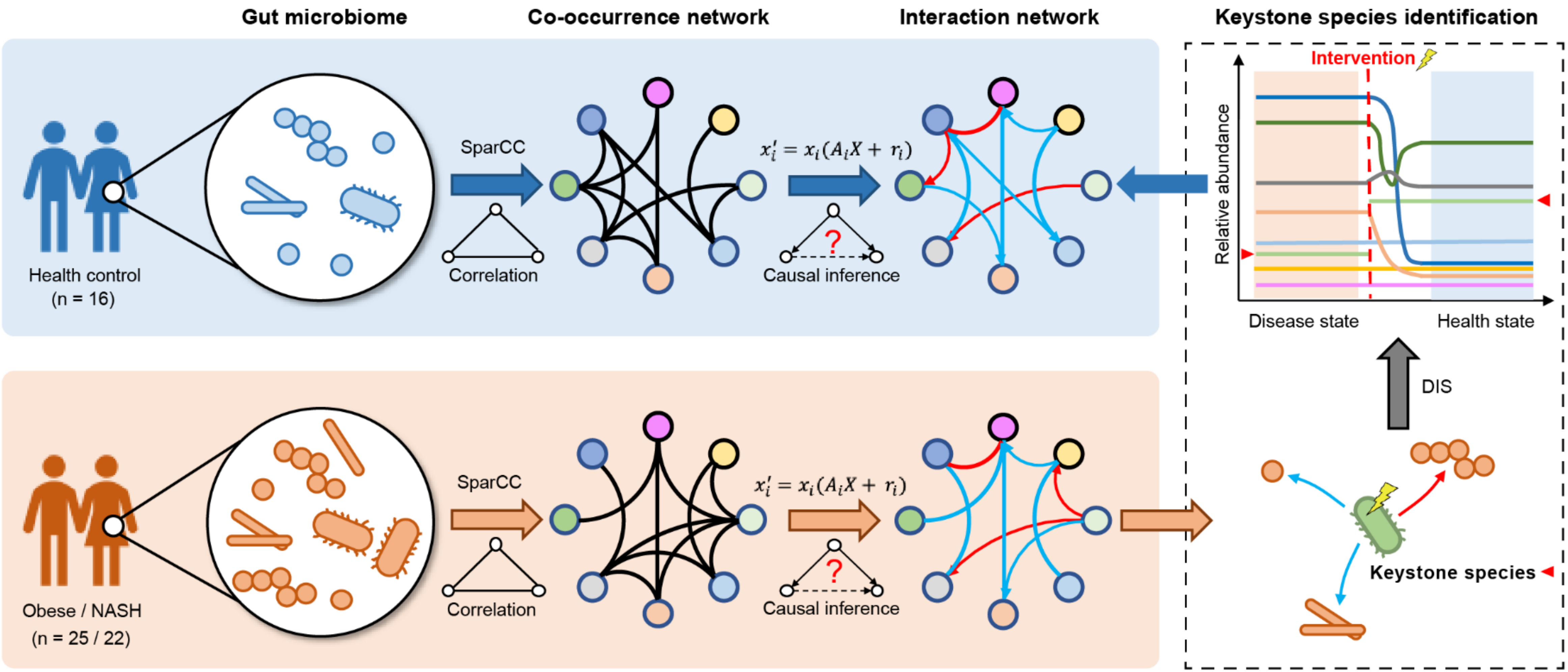
Dynamic intervention simulation



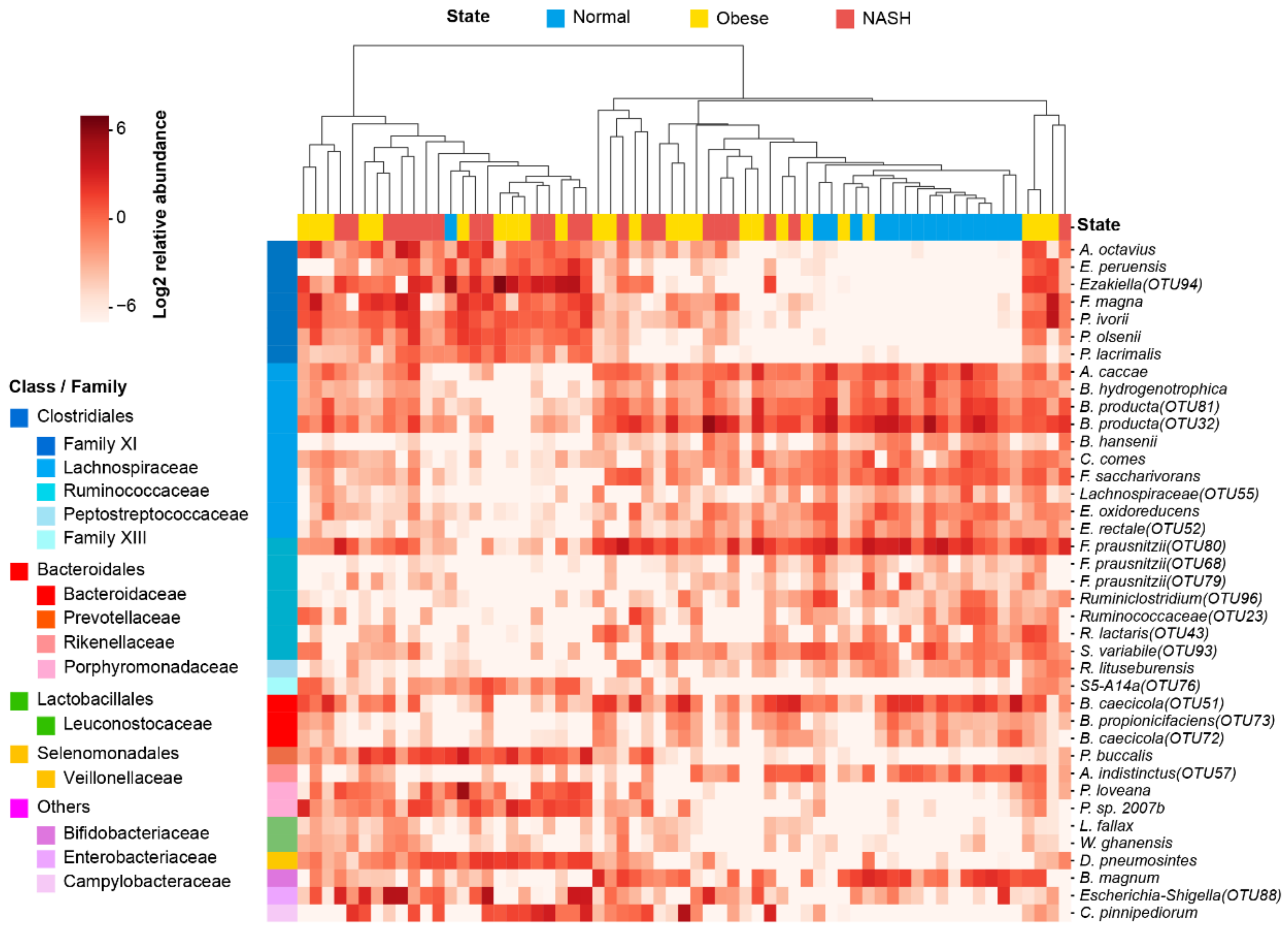
Dynamic changes during intervention

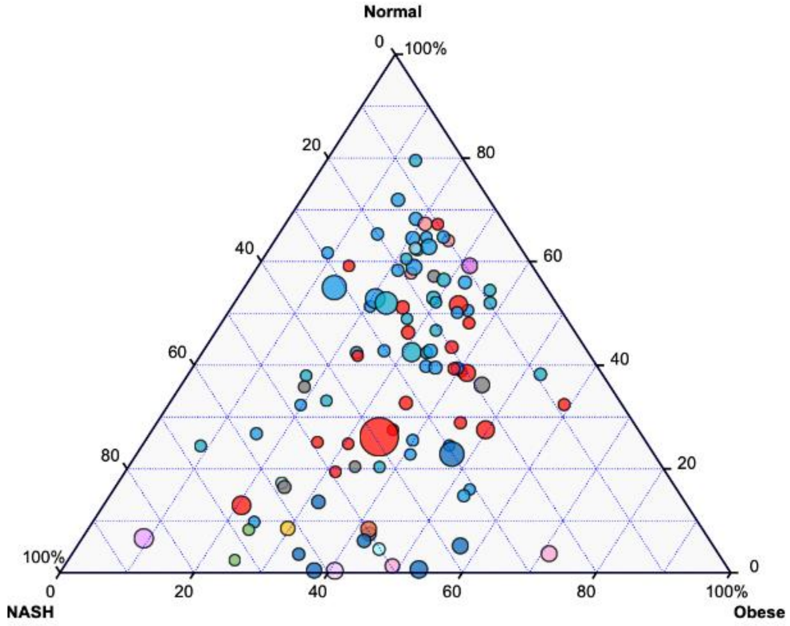


Study design



Abundance changes of the gut microbial species in obesity and NASH.



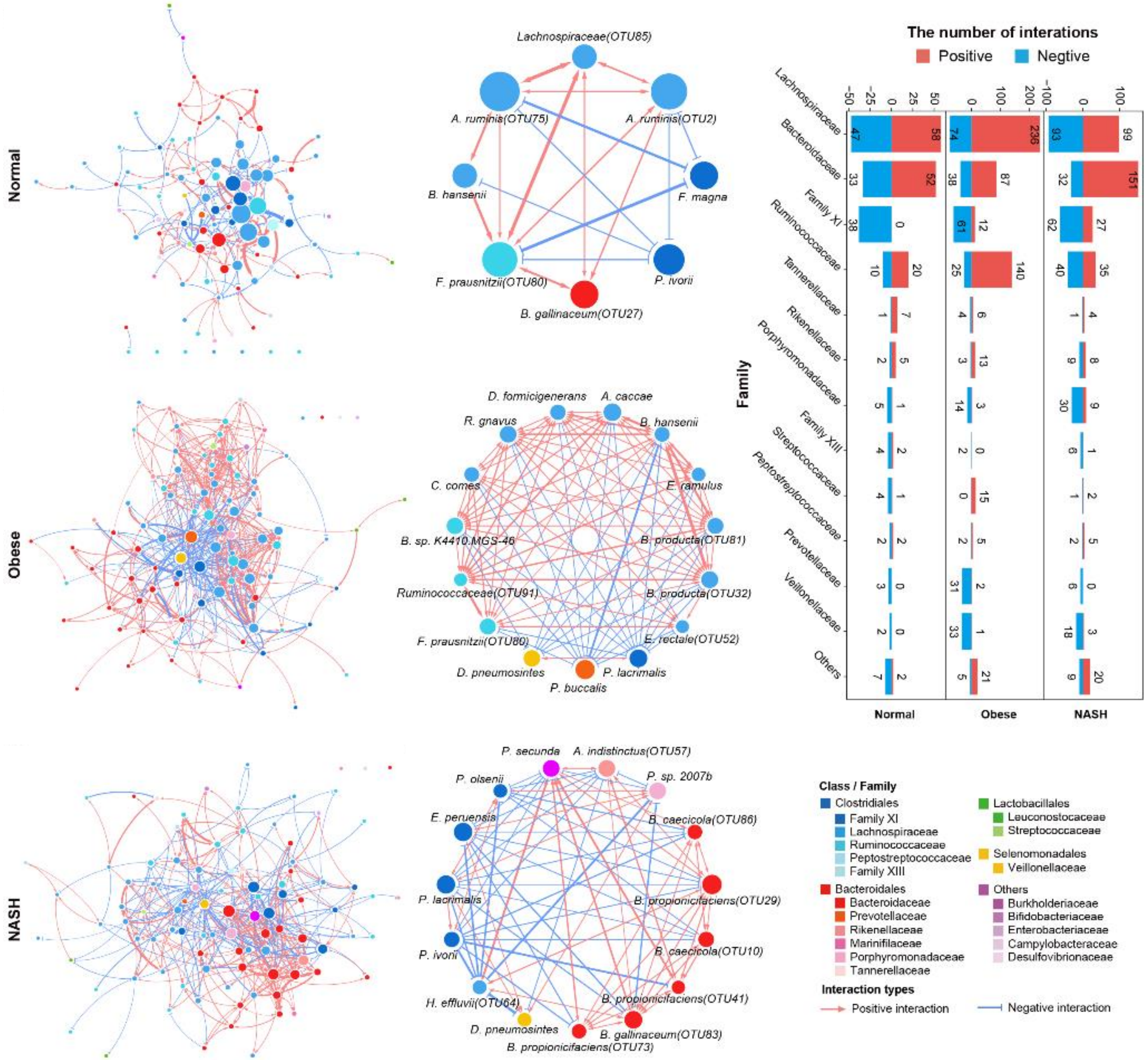


Decreased abundances in family:

- **Lachnospiraceae**
- **Ruminococcaceae**

Results

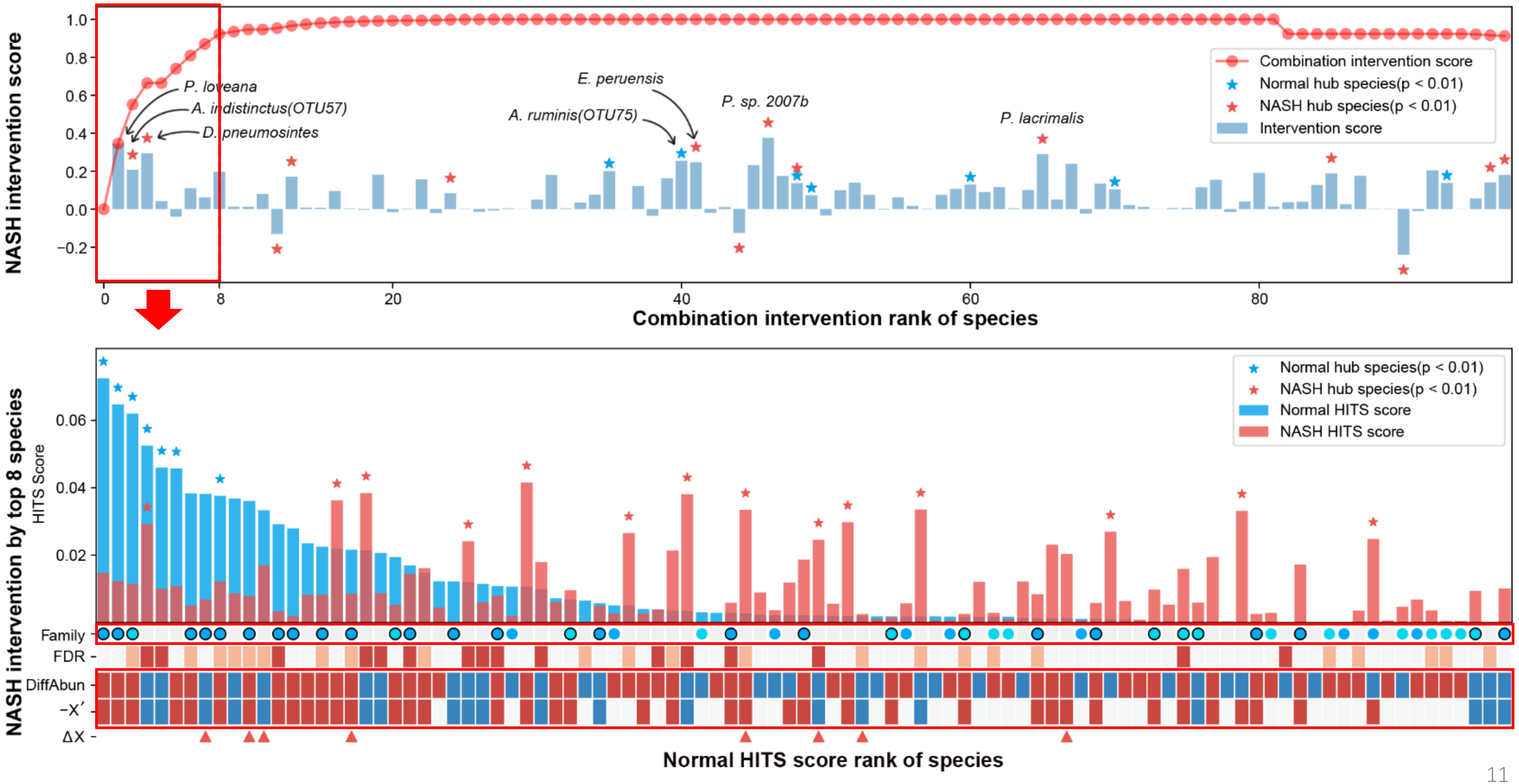
Distinct patterns of the microbial interactions in the gut of normal, obese and NASH subjects.



The gut microbiome of normal, obese and NASH groups exhibited distinct patterns of microbial interactions.

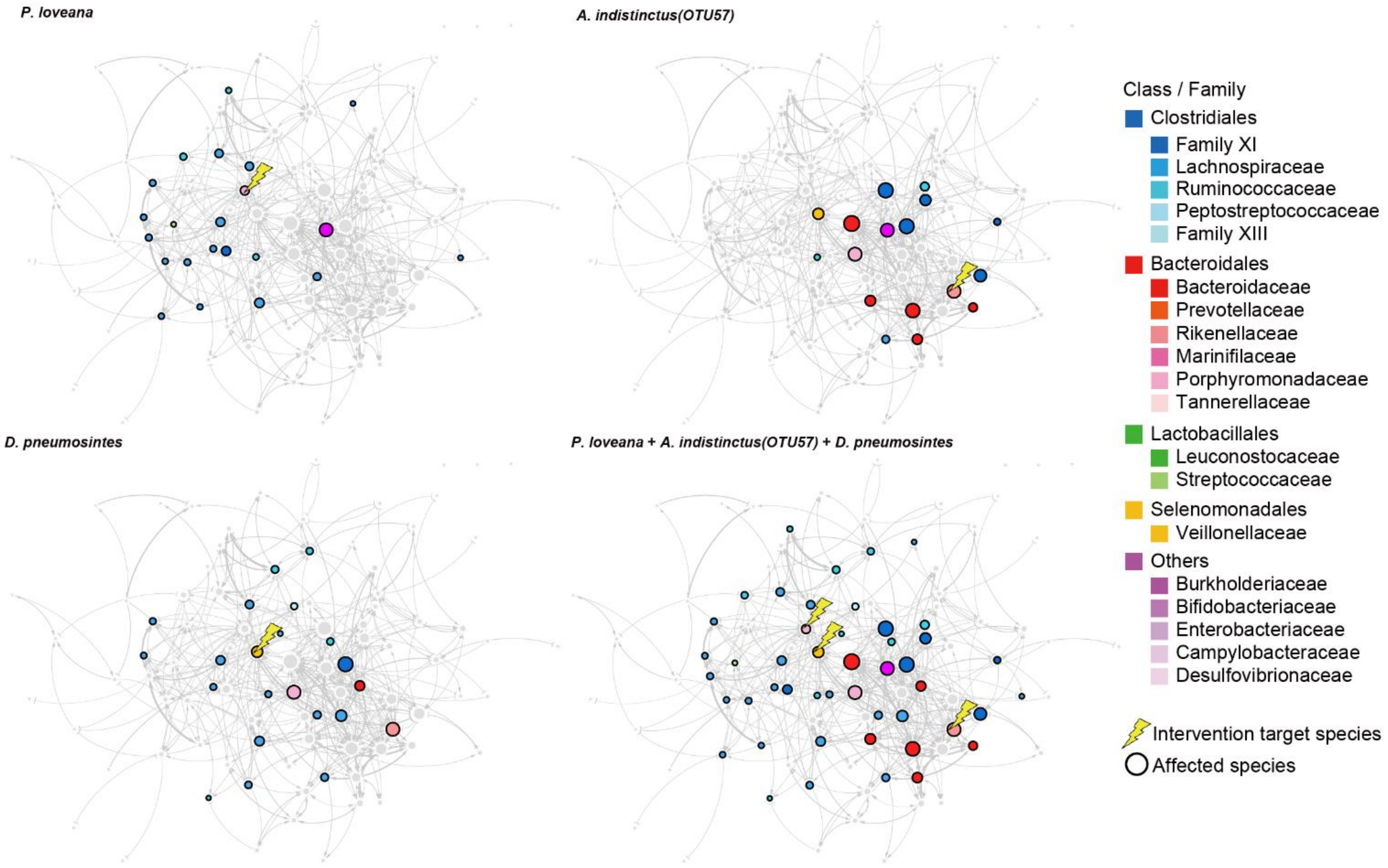
Results

Keystone species of NASH drive the changes of the diseased gut microbiome toward a normal microbiome.



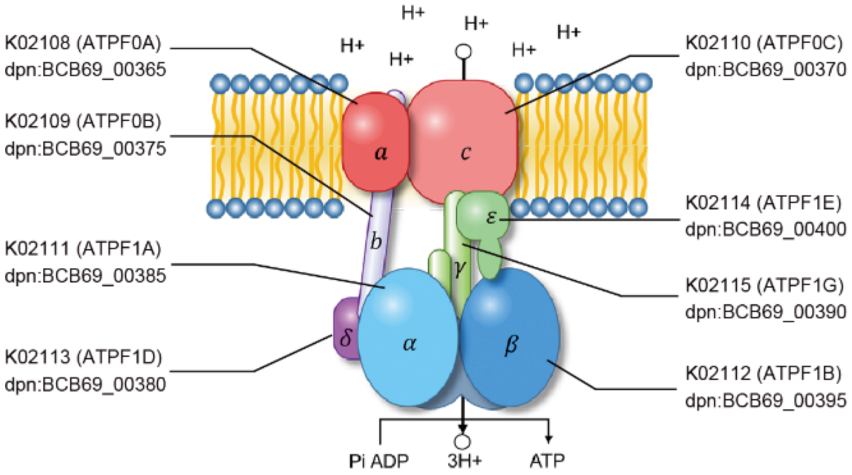
Results

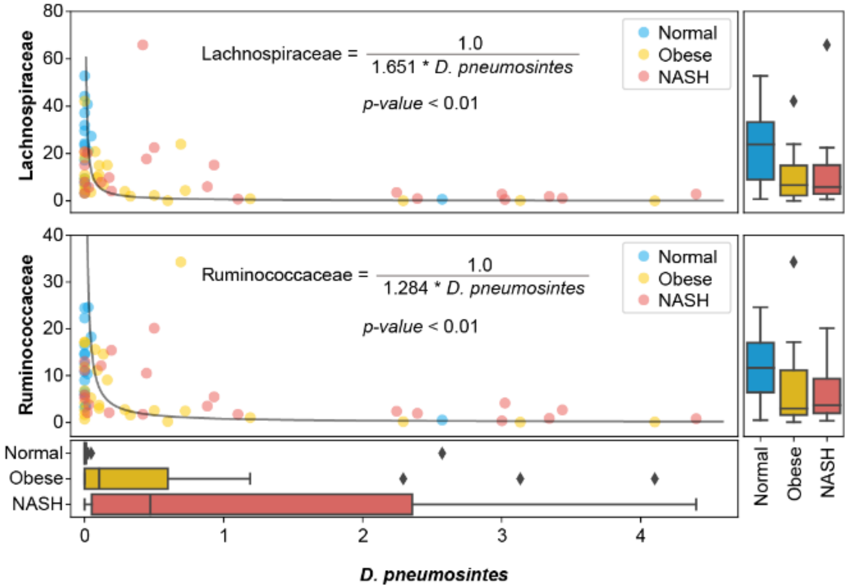
Keystone species of NASH drive the changes of the diseased gut microbiome toward a normal microbiome.



Results

Potential mechanisms for the keystone species to impact the NASH microbiome.





Summary

- The dysbiosis of butyrate-producing bacteria is a critical factor contributing to the development of NAFLD.

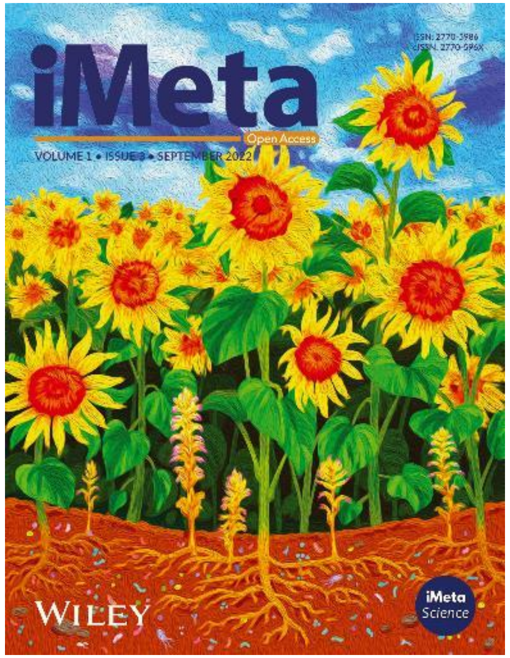
- Causal algorithm intergraded with ecological theory and dynamic intervention simulation could mine microbial keystone species from metagenomic data.

- Keystone species of NASH, such as *P. loveana, A. indistinctus and D. pneumosintes*, provided potential precise intervention strategies for NAFLD treatment.

Wu, Dingfeng, Lei Liu, Na Jiao, Yida Zhang, Li Yang, Chuan Tian, Ping Lan, Lixin Zhu, Rohit Loomba, Ruixin Zhu. 2022. Targeting keystone species helps restore the dysbiosis of butyrate-producing bacteria in non-alcoholic fatty liver disease. ***iMeta***. e61. https://doi.org/10.1002/imt2.61

iMeta: 整合宏组学重新认识生命和环境科学

iMeta Open Access WILEY



"*iMeta*" 是由威立、肠菌分会和本领域数百位华人科学家合作出版的开放获取期刊，主编由中科院微生物所刘双江研究员和荷兰格罗宁根大学傅静远教授共同担任。目的是发表原创研究、方法和综述以促进宏基因组学、微生物组和生物信息学发展。目标是发表前10%(IF ＞ 15)的高影响力论文。期刊特色包括视频投稿、可重复分析、图片打磨、青年编委、前3年免出版费、50万用户的社交媒体宣传等。2022年的三月、六月和九月期已正式在线出版发行!

主页: http://www.imeta.science
出版社: https://wileyonlinelibrary.com/journal/imeta
投稿: https://mc.manuscriptcentral.com/imeta

office@imeta.science

iMeta 宣传片