

Targeting inter-organ cross-talk in cardiometabolic diseases

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LIST OF PUBLICATIONS

- Liu C, Zwaan M, Verhoeven A, Schinkelshoek MS, Fronczek R, Lammers GJ, Wang Y, Giera M, Boon MR, Rensen PCN, Schönke M. γ-hydroxybutyric acid attenuates diet-induced metabolic dysfunction in developing and existing obesity. *In preparation*.
- Zhou E, Nakashima Hiroyuki, Li R, van der Zande HJP, Liu C, Li Z, Müller C, Bracher F, Mohammed Y, de Boer JF, Kuipers F, Guigas B, Rensen PCN, Giera M, Wang Y. Inhibition of Δ24dehydrocholesterol reductase ameliorates diet-induced hepatic steatosis and inflammation through liver X receptor α without inducing hyperlipidemia. *Revision submitted*.
- Liu C, Song Z, Li Z, Boon MR, Schönke M, Rensen PCN, Wang Y. Dietary choline increases markers of brown fat activation and improves cholesterol metabolism in *APOE*3-Leiden.CETP* female mice. Int J Obes 2023; *in press.*
- 4. Li Z, Zhou E, Liu C, Wicks H, Yildiz S, Razack F, Ying Z, Kooijman S, Koonen DPY, Heijink M, Kostidis S, Giera M, Kuijper EJ, Smits WK, van Dijk KW, Rensen PCN, Wang Y. Dietary butyrate ameliorates metabolic health dependent on gut microbiota and associated with selective proliferation of *Lachnospiraceae bacterium 28-4*. JCI Insight 2023; 8: e166655.
- 5. Liu C, Schönke M, Spoorenberg B, Lambooij JM, van der Zande HJP, Zhou E, Tushuizen ME, Andréasson AC, Park A, Oldham S, Uhrbom M, Ahlstedt I, Ikeda Y, Wallenius K, Peng XR, Guigas B, Boon MR, Wang Y, Rensen PCN. FGF21 protects against hepatic lipotoxicity and macrophage activation to attenuate fibrogenesis in nonalcoholic steatohepatitis. eLife 2023; 12: e83075.
- Liu C, Li Z, Song Z, Fan X, Shao H, Boon MR, Schönke M, Rensen PCN, Wang Y. Choline and butyrate beneficially modulate the gut microbiome without affecting atherosclerosis in *APOE*3-Leiden.CETP* mice. Atherosclerosis 2022; 362: 47-55.
- Liu C, Schönke M, Zhou E, Li Z, Kooijman S, Boon MR, Larsson M, Wallenius K, Dekker N, Barlind L, Peng XR, Wang Y, Rensen PCN. Pharmacological treatment with FGF21 strongly improves plasma cholesterol metabolism to reduce atherosclerosis. Cardiovasc Res 2022; 118: 489-502.
- Liu C, Huang S, Wu Z, Li T, Li N, Zhang B, Han D, Wang S, Zhao J, Wang J. Cohousing-mediated microbiota transfer from milk bioactive components-dosed mice ameliorate colitis by remodeling colonic mucus barrier and lamina propria macrophages. Gut Microbes 2021; 13: 1-23.
- 9. Zhou E, Li Z, Nakashima H, Liu C, Ying Z, Foks AC, Berbée JFP, van Dijk KW, Rensen PCN, Wang Y. Hepatic scavenger receptor class B type 1 knockdown reduces atherosclerosis and enhances the antiatherosclerotic effect of brown fat activation in *APOE*3-Leiden.CETP* mice. Arterioscler Thromb Vasc Biol 2021; 41: 1474-1486.
- 10. Huang S, Wu Z, Li T, Liu C, Han D, Tao S, Pi Y, Li N, Wang J. Perturbation of the lipid metabolism and intestinal inflammation in growing pigs with low birth weight is associated with the alterations of gut microbiota. Sci Total Environ 2020; 719: 137382.
- Huang S, Liu C, Li N, Wu Z, Li T, Han D, Li Z, Zhao J, Wang J. Membrane proteomic analysis reveals the intestinal development is deteriorated by intrauterine growth restriction in piglets. Funct Integr Genomics 2020; 20: 277-291.
- 12. Huang S, Li N, Liu C, Li T, Wang W, Jiang L, Li Z, Han D, Tao S, Wang J. Characteristics of the gut microbiota colonization, inflammatory profile, and plasma metabolome in intrauterine growth restricted piglets during the first 12 hours after birth. J Microbiol 2019; 57: 748-758.

- 13. Hamid H, Zhang J, Li W, Liu C, Li M, Zhao L, Ji C, Ma Q. Interactions between the cecal microbiota and non-alcoholic steatohepatitis using laying hens as the model. **Poult Sci 2019**; 98: 2509-2521.
- 14. Huang S, Wu Z, **Liu C**, Han D, Feng C, Wang S, Wang J. Milk fat globule membrane supplementation promotes neonatal growth and alleviates inflammation in low-birth-weight mice treated with lipopolysaccharide. **Biomed Res Int 2019**; 2019: 4876078.
- 15. Liu C, Zhang J, Li M, Zhao L, Ji C, Ma Q. Alterations and structural resilience of the gut microbiota under dietary fat perturbations. J Nutr Biochem 2018; 61: 91-100.

CURRICULUM VITAE

Cong Liu was born on August 5, 1993 in Linyi, Shandong province, China. In June 2012, she graduated from the First High School in Linyi. In September 2012, she entered the bachelor program 'Animal Science' at Shandong Agricultural University, Tai'an, China, and obtained her BSc degree in June 2016.

In September 2016, she started her 2-year master program 'Animal Nutrition & Feed Science' at China Agricultural University, Beijing, China. She worked on a research project entitled 'Alterations and structural resilience of the gut microbiota under dietary fat perturbations' under supervision of Prof. dr. Jianyun Zhang and Prof. dr. Qiugang Ma, at the State Key Laboratory of Animal Nutrition, China Agricultural University. She obtained her MSc degree in June 2018. Based on increased interest in inflammatory bowel diseases in relation to the gut microbiota, she next performed a 4-month internship at the Academy of National Food and Strategic Reserves Administration, Beijing, China, under supervision of Prof. dr. Junjun Wang. During this internship she participated in five projects and was responsible for the research project entitled 'Effects of human milk bioactive components on the gut microbiome and inflammatory bowel diseases (IBD)'.

In October 2018, based on sparkled interest in cardiometabolic diseases, she joined the research group of Prof. dr. Patrick Rensen within the Department of Internal Medicine, Division of Endocrinology, of Leiden University Medical Center initially as a research assistant. By using *APOE*3-Leiden.CETP* mice, a well-established mouse model with human-like lipoprotein metabolism, she investigated the role of FGF21 in lipid metabolism in relation to atherosclerosis development. In October 2019, she started her PhD training in the same group under the supervision of Prof. dr. Patrick Rensen, Prof. dr. Yanan Wang and Dr. Milena Schönke, focusing on targeting inter-organ cross-talk in cardiometabolic diseases. The results of her research are presented in this thesis. During her PhD training, she was awarded a Young Investigator Fellowship of the 88th and 90th European Atherosclerosis Society congress in 2020 and 2022, respectively, and a Young Investigator Travel Award of the Keystone Symposium 'Inter Organ Crosstalk in Non-Alcoholic Steatohepatitis' in 2022.

In 2023, Cong will join the research group of Dr. Daniel Puleston at Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai in New York City as a postdoctoral researcher to expand her knowledge on the interplay between immunology and metabolism within cardiometabolic diseases and in tumor development.

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