# Role of gut-liver axis in circadian exercise and dietary interventions to improve metabolic health

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# List of Publications

- Kovynev A, Schoonakker MP, van den Burg EL, van Peet P, Schönke M, Pijl H, Rensen PCN, Zeller G and Ducarmon QR. A fast(ing) way to cardiometabolic health: investigating the effects of a year-long cyclic fasting-mimicking diet on gut microbiome in patients with type 2 diabetes. *In preparation.*

- Martinez-Tellez B, Schönke M, Kovynev A, Dominguez E, Alvarez L, Verhoeven A, Gacesa R, Vich A, Ducarmon QR, Pavon D, Cabrera M, Weersma E, Smits W, Giera M, Ruiz J, Rensen PCN. Identification of a human anaerobic gut bacterium that increases muscular strength in the absence of exercise training. *In preparation.*

- Kovynev A, Marwijk C, Rensen PCN, Schönke M. The time-of-day-dependent effect of exercise on immune modulation in health and inflammatory metabolic disease. *Submitted.*

- Chiara V, Vukic M, Chouaref J, Garcia-Perez L, Naber G, Vonk K, Leemans C, Kovynev A, Breukel C, Vloemans S, Cante-Barrett K, Pike-Overzet K, Jacobsen S, Staal F, Daxinger L. The epigenetic reader MORC3 is required for T cell development in the thymus. *Submitted.*

- Kovynev A, Charchuta MM, Begtasevic A, Ducarmon QR, Rensen PCN, Schönke M. Combination of dietary fiber and exercise training improves fat loss in mice, but does not ameliorate MASLD more than exercise alone. **Am J Physiol Gastrointest Liver Physiol** 2025, 328: G399-410. Doi: 10.1152/ajpgi.00317.2024.

- Kovynev A*, Ying Z*, Zhang S, Olgiati E, Lambooij JM, Visentin C, Guigas B, Ducarmon QR, Rensen PCN, Schönke M. Timing matters: Late, but not early, exercise training ameliorates MASLD in part by modulating the gut-liver axis in mice. **J Pineal Res** 2024, 76: e70003. doi: 10.1111/jpi.70003.

- Lian P, Kovynev A, Wang L, Pronk ACM, Verhoeven A, Giera MA, Thijssen S, Martinez-Tellez B, Kooijman S, Rensen PCN, Timmerman H, Wichers HJ, Henricks PAJ, Folkerts G, Schönke M*, Braber S*. Exercise training at different intensities induces heat stress, disrupts the intestinal barrier

function and alters the gut microbiota in mice. **eLife** 2024. doi: 10.7554/eLife.100630.1.

- Groenewegen B, Lingen E, Kovynev A, van den Berg A, Berssenbrugge E, Sanders I, van Prehn J, van Nood E, Goorhuis A, Kuijper E, Smits E, Wiese M, Keller J, Ducarmon QR, Terveer E. The presence of *Clostridioides difficile* in faeces before and after faecal microbiota transplantation and its relation with recurrent *C. difficile* infection and the gut microbiota in a Dutch cohort. **Clin Microbiol Infect** 2024, 31 (4), 568-574. doi: 10.1016/j.cmi.2024.12.003.
- Kovynev A*, Ying Z*, Lambooij JM, van der Zande HJ, Guigas B, Rensen PCN, Schönke M. Early but not late exercise training in mice exacerbates hepatic inflammation in developing nonalcoholic fatty liver disease. **J Clin Transl Hepatol** 2023, 11(5): 1282-1285. doi: 10.14218/JCTH.2023.00094.
- Schönke M, Ying Z, Kovynev A, In het Panhuis W, Binnendijk A, van der Poel S, Pronk ACM, Streefland TCM, Hoekstra M, Kooijman S, Rensen PCN. Time to run: Late rather than early exercise training in mice remodels the gut microbiome and reduces atherosclerosis development. **FASEB J** 2023, 37: e22719. doi: 10.1096/fj.202201304R.

# Curriculum vitae

Artemiy Kovynev was born in 1998 in Moscow, Russia. After finishing an International Baccalaureate High school program at Moscow Gymnasium 45 cum laude in 2016, in the same year he started the Biomedicine track of the Program Liberal Arts and Sciences at Amsterdam University College, and obtained his BSc degree cum laude in 2019. Subsequently, he received a Leiden Excellence scholarship to start his Master's program Biomedical Sciences at Leiden University Medical Center (LUMC) in the same year. During his first Master's internship in the group of Dr. Lucia Clemens-Daxinger, Artemiy discovered his passion for bioinformatics analysis. For his second and final internship, under the supervision of Dr. Maria Wiese and Dr. Quinten Ducarmon, Artemiy combined both bioinformatics and laboratory analyses to investigate the factors that determine the success of fecal microbiota transplantation in the treatment of *Clostridium difficile* infection.

After obtaining his MSc degree in 2021, Artemiy started his PhD program under the guidance of Prof. dr. Patrick Rensen, Dr. Milena Schönke and later also Dr. Quinten Ducarmon, at the department of Internal Medicine, division of Endocrinology, LUMC. Artemiy studied the impact of lifestyle interventions, such as timing of exercise training and dietary fiber intake, on amelioration of metabolic dysfunction-associated steatotic liver disease (MASLD), via the modulation of the gut microbiome and the activity of gut-liver axis. Artemiy continued combining bioinformatics approaches with mouse studies and lab work, to showed amongst others that only late exercise training modifies the gut microbiome, which causally attenuates MASLD development. These findings were published in the Journal of Pineal Research, and this paper received the awards for best paper of the year by both the Dutch Society for Endocrinology (NVE) and the Netherlands Association for the Study of Obesity (NASO). This and other research on the timing of exercise and dietary interventions are presented in this thesis.

After recently obtaining Dutch citizenship, Artemiy will continue his research into the impact of the gut-liver axis on cardiometabolic and liver health during his postdoctoral position at Amsterdam University Medical Center (AUMC), under the guidance of Prof. dr. Max Nieuwdorp and Prof. dr. Wouter de Jong. Artemiy has also recently joined the early career network board of NASO, working with other

young scientists to improve obesity and metabolic research in the Netherlands further.

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I would like to thank all of my (ex)colleagues at D4 and C7 for making working in LUMC a truly warm and pleasant experience, which made these 4 years really enjoyable. It is crazy to think back to the start of my PhD, and how many nice and fun memories we have formed with so many of you over that time. Dear Cong, thank you for always willing to grab a coffee and listen to what was on my mind in the beginning of my PhD. Dear Zhixiong, thank you for being my first gym buddy and guide, in addition to our very fruitful scientific collaborations. Dear Xiaoke, thank you, among many other things, for nice little treats and always being so positive! Dear Ellen, thank you for becoming a great friend during your stay in Leiden and beyond. Dear Jamie, I have really enjoyed our (sometimes very sarcastic) conversations about the state of academia, and thanks so much for all the positivity in the lab! Dear Amanda and Salwa, thank you for all the help with animal experiments, and fun memories during lab outings and many different games. Dear Beatrice, Maaike, Carlijn, Antonio, Borja, Jing, Jingxi, Kaiming, Mariëtte, Melanie, Mohan, Robin, Sander, Trea, Tim, Reshma, Yandi and Yao, I also want to extend my sincere gratitude to you guys, as well as Annelies, Anne, Chris, Jan, Janneke, Jari, Jennifer, Max, Melissa, Onno, River, Tijmen, as, you all have made working in LUMC pleasant and fun. Dear Diana, Clara, Christiana, Amina, Mieszko, Emanuele and Luna, my students thank you for all the contributions to our research, and I hope you have also learned a lot during your internships. Lastly, Sen, I am very happy that we became great friends since your arrival to the Netherlands, and shared many joyful moments both in academia (with a publication together) and outside of it, and I am so grateful that you will now be my paranymph.

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them, despite 9 hours of time difference. Dear Laurens and Jasmijn, I am so grateful that we do so many fun things together so often, as these times of rest and relaxation are the greatest support I can get. Dear Anne and Romy, from the bottom of my heart, thank you for your love, care and small presents that held my spirits up in the last 4 years. Dear Inge, Steijn, Sebas, Bram, Jasper, Karlijn, Vayar and Rolain, I really cherish our time together.

Лиза, не смотря на тысячи километров между нами, я очень рад что наша дружба и взаимная поддержка становились только крепче за эти годы. Леша и Вика, спасибо за ваши визиты и возможность всегда остановиться в Белграде. Дорогие бабушки, спасибо, что вы всегда интересуетесь моей работой, даже если она не всегда понятна. Максим, я рад, что с тобой мы всегда можем отдохнуть в любой вечер, играя в разные игры, или сходив на футбол или в театр в Лондоне, и это время с тобой крайне важно для меня. Мама и Папа, если бы не ваша помощь и поддержка, меня бы вообще не было в Нидерландах, и вся эта работа была бы невозможна, поэтому вам я благодарен больше всего.

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