



Universiteit  
Leiden  
The Netherlands

## Exploration of the endocannabinoid system using metabolomics

Di, X.

### Citation

Di, X. (2023, February 7). *Exploration of the endocannabinoid system using metabolomics*. Retrieved from <https://hdl.handle.net/1887/3515754>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3515754>

**Note:** To cite this publication please use the final published version (if applicable).

## **Curriculum vitae**

Xinyu Di was born on Nov 14th, 1992 in the town of Changjiang, Rugao, China. After graduating from Rugao Senior High School in 2010, he got admitted to the major of Pharmacy at China Pharmaceutical University (CPU) in Nanjing. In 2014, he obtained his bachelor's degree and continued in the same university his master's study in pharmacokinetics. During his master's study, he focused on preclinical pharmacokinetic studies of several small molecules. In October 2017, he started his PhD project under the supervision of Prof. Dr. Thomas Hankemeier, Dr. Isabelle Kohler and Dr. Elke H.J. Krekels at Leiden Academic Centre for Drug Research (LACDR). Between 2017 and 2022, he developed metabolomics platforms for the endocannabinoid system (ECS). With these platforms, he looked into the role of ECS in exercise and cardiometabolic health, explored the role of several enzymes in the ECS and evaluated drugs targeting these enzymes. Since February 2022, he has been working as a postdoc in the group of molecular physiology, led by Prof. Dr. Mario van der Stelt. During his postdoc, supported by the Metabolomics and Analytics Centre, he has been using metabolomics-based tools to look into the pathology of multiple sclerosis.

## List of publications

### Part of this thesis:

1. **Di X**, Driever WPF, van der Plas C, Harms A, Krekels EHJ, van der Stelt M, Isabelle Kohler, Hankemeier T. A platform for the analysis of metabolites in endocannabinoids - related pathways.

In preparation

2. He B\*, **Di X**\*, Guled F, et al. Quantification of endocannabinoids in human cerebrospinal fluid using a novel micro-flow liquid chromatography-mass spectrometry method. *Anal Chim Acta*. 2022;1210.

3. **Di X**\*, Martinez-Tellez B\*, Krekels EHJ, Jurado-Fasoli L, Osuna-Prieto FJ, Sanchez-Delgado G, Garcia-Lario JV, Hankemeier T, Rensen PCN, Ruiz JR<sup>§</sup>, Kohler I<sup>§</sup>. Plasma levels of endocannabinoids and their analogues as potential markers of cardiometabolic risk in young adults.

Submitted

4. Jurado-Fasoli L\*, **Di X**\*, Kohler I\*, et al. Omega-6 and omega-3 oxylipins as potential markers of cardiometabolic risk in young adults. *Obesity (Silver Spring)*. 2022;30(1):50-61.

5. Jurado-Fasoli L\*, **Di X**\*, Sanchez-Delgado G, et al. Acute and long-term exercise differently modulate plasma levels of oxylipins, endocannabinoids, and their analogues in young sedentary adults: A sub-study and secondary analyses from the ACTIBATE randomized controlled-trial. *EBioMedicine*. 2022;85:104313.

\*<sup>§</sup> Authors contributed equally

### Not Part of this thesis:

1. van Esbroeck ACM, Kantae V, **Di X**, et al. Identification of  $\alpha,\beta$ -hydrolase domain containing protein 6 as a diacylglycerol lipase in Neuro-2a cells. *Front Mol Neurosci*. 2019;12(November):286.

2. Osuna-Prieto FJ, Rubio-Lopez J, **Di X**, et al. Plasma Levels of Bile Acids Are Related to Cardiometabolic Risk Factors in Young Adults. *J Clin Endocrinol Metab*. 2022;107(3):715-723.

3. van Esbroeck ACM, Varga Z v., **Di X**, et al. Activity-based protein profiling of the human failing ischemic heart reveals alterations in hydrolase activities involving the endocannabinoid system. *Pharmacol Res*. 2020;151.

4. Ortiz-Alvarez L, Xu H, **Di X**, et al. Plasma Levels of Endocannabinoids and Their Analogues Are Related to Specific Fecal Bacterial Genera in Young Adults: Role in Gut Barrier Integrity. *Nutrients*. 2022;14(10).

5. Mock ED, Mustafa M, Gunduz-Cinar O, Cinar R, Petrie GN, Kantae V, **Di X**, et al. Discovery of a NAPE-PLD inhibitor that modulates emotional behavior in mice. *Nat Chem Biol*. 2020;16(6):667-675.

6. Zhou J, Mock ED, Martella A, Kantae V, **Di X**, et al. Structure-Activity Relationship Studies of  $\alpha$ -Ketoamides as Inhibitors of the Phospholipase A and Acyltransferase Enzyme Family. *J Med Chem.* 2020;63(17):9340-9359.
7. Osuna-Prieto FJ, Martinez-Tellez B, Ortiz-Alvarez L, **Di X**, et al. Elevated plasma succinate levels are linked to higher cardiovascular disease risk factors in young adults. *Cardiovasc Diabetol.* 2021;20(1).
8. Zhou J, Mock ED, Martella A, Kantae V, **Di X**, et al. Activity-Based Protein Profiling Identifies  $\alpha$ -Ketoamides as Inhibitors for Phospholipase A2 Group XVI. *ACS Chem Biol.* 2019;14(2):164-169.
9. Jurado-Fasoli L, Yang W, Kohler I, Dote-Montero M, Osuna-Prieto FJ, **Di X**, et al. Effect of Different Exercise Training Modalities on Fasting Levels of Oxylipins and Endocannabinoids in Middle-Aged Sedentary Adults: A Randomized Controlled Trial. *Int J Sport Nutr Exerc Metab.* 2022;32(4):275-284.
10. Vázquez-Lorente H, Jurado-Fasoli L, Kohler I, **Di X**, et al. Linoleic acid-derived oxylipins and isoprostanes plasma levels are influenced by 1,25-Dihydroxyvitamin D levels in middle-aged sedentary adults: The FIT-AGEING study. *Exp Gerontol.* 2022;169.
11. Xu H, Jurado-Fasoli L, Ortiz-Alvarez L, Kohler I, **Di X**, et al. Plasma Levels of Omega-3 and Omega-6 Derived Oxylipins Are Associated with Fecal Microbiota Composition in Young Adults. *Nutrients.* 2022;14(23):4991.

## Acknowledgements

The work presented in this thesis would not have been possible without the support from many, many people. I would like to express my sincere gratitude to everyone who has contributed to it.

It was wonderful to be able to join our research group. I would like to thank Thomas for giving me this opportunity, the access to the best mass specs, and for all the inspiration from his immense knowledge. I would also like to thank Isabelle and Elke for their encouragement, patience and trust throughout my PhD study. Thank you for helping me structuring the chapters, listening to all my complaints about life and instruments. And again, thank you all for your tremendous help with the writing of this thesis.

I would like to thank all my collaborators, both internal and external, from whom I have learned a lot. I am grateful to my collaborators from University of Granada, Borja and Lucas, who have greatly contributed to parts of this thesis, for conducting interesting research programs together and for the knowledge on clinical studies and data analysis. To Wouter, Elliot, Annelot, Ming, Timo, Tom, and many others from Mario's group, thank you for all the support and knowledge that you shared, your ideas broadened my view a lot. It was really nice to have worked with all of you.

I would like to thank all my colleagues at MAC and BMFL. To Amy, thank you for all the discussions on being a good analyst. To Loes, Cathy, Ina and Ariadne, thank you for helping with all sorts of issues. To Nelus, Wei and Vasu, thank you for helping me start up with my project in this lab. To Bingshu, thank you for saving me from the clogging of micro-LCs. To Faisa, Gerwin and Tim, thank you for your expertise with troubleshooting the mass specs. To Michael and Alida, thank you for the nice tools that you have developed. To Lieke, Jelte, Marielle and Sam, thank you for sharing the experience with the signaling platform. To Tom, Barbara, Vahid, Marielle and Sam, thank you for the snacks and laughs we shared. To Marielle and Hyung, thank you for the nice translation of the Dutch summary for me. To my student Corné, thank you for the work on the NAPes. Specially, I want to thank the engineers Robert, Huub and Jer-gung, for taking care of the instruments and giving me ideas on troubleshooting. To everyone that I have met in the last five years, thank you for the talks and drinks we had together. Lastly, I want to especially thank my Chinese colleagues Wei, Tian, Zhengzheng, Wei, Huaqi, Yupeng, Joyee, Pingping, Bingshu, Congrou, Mengle, Chunyuan, Yu, Lu and Xiaoyue; with you I'm not far away from home.

I would also like to thank all my friends that I met here in the Netherlands and back in China, thank you for your company and encouragements.

Finally, I would also like to thank my family for their long-term support and understanding. And to my grandfather, I know that you are always with me.