

## Exploration of the endocannabinoid system using metabolomics $\operatorname{Di},\operatorname{X}.$

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## **Stellingen (Propositions)**

behorende bij het proefschrift

## Exploration of the endocannabinoid system using metabolomics

- 1. Coverage of both upstream and downstream metabolites is essential when studying the role of metabolic enzymes and assessing the pharmacological roles of inhibitors targeting metabolic enzymes. (this thesis)
- 2. Pre-analytical conditions play a crucial role to ensure high-quality metabolomics data, results will be inconclusive with inadequate conditions. (this thesis)
- 3. Combining micro-LC with mass spectrometry allows us to further push the boundaries of sensitivity in metabolomics measurements. (this thesis)
- 4. Using a set of biomarkers that are connected in regulatory networks has more advantages in predictability of diseases compared with a single biomarker candidates. (this thesis)
- 5. More light need to be shed on endocannabinoids and their related metabolites for their potential role as mediators of the inflammatory and immune responses to exercise. (this thesis)
- 6. Metabolomics has started to evolve towards a useful and effective tool for establishing useful physiological response and target engagement markers, as well as for the elucidation of mode of action. (Alarcon Barrera, J.C. et al., Drug Discov. Today, 2022). To increase the use of this tool in drug discovery and development, standardization and automation of metabolomics workflows are required to be able to increase the throughput and integrate results of different studies.
- 7. Multi-omics offers the opportunity to understand the flow of information that underlies disease, omics technologies are now often incorporated into the everyday methodology of biological researchers (Hasin, Y. et al., Genome Biol., 2017). However, limited amount of samples can limit the application of multi-omics technologies. Thus, the development of "one-for-all" sample preparation techniques is necessary.
- 8. Research into targeting the expanded endocannabinoid system (ECS) is in its infancy (Cristino, L. et al., Nat. Rev. Neurol., 2020). The maturation of this field can be accelerated by applying the concepts of pharmacometabolomics.
- 9. Studies on endocannabinoids and the collective ECS will be a path of research to elucidate mechanisms, both molecular and genetic, to explain the benefits of exercise. (Watkins, B.A., Mol. Aspects Med., 2018). This is actually overlooked by most researchers focusing only on endocannabinoids, but not the collective metabolic pathways that are interconnected with ECS.
- 10. Regular exercise, exposure to artificial sunlight and vitamin D help PhD students to survive the winter in the Netherlands.
- 11. Fish is what I desire, and so are bear's paws. (Woziji Shuode)