Lipid signaling and inflammation: metabolomics for better diagnosis and treatment strategy

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Stellingen (Propositions)

Behorende bij het proefschrift

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1. The development of an analytical method that possesses both extensive coverage and high sensitivity for signaling lipid profiling is of paramount significance. Such a method would cater to the requirements of analyzing signaling lipids in diverse biological matrices, including blood, cells, cerebrospinal fluid, and tissues. (this thesis)
2. Proper sample handling is the prerequisite to achieve high sensitivity, less matrix effect and to reduce artificial introduction of metabolites in signaling lipid profiling. (this thesis)
3. Signaling lipids are a class of diverse and highly interconnected bioactive lipids. It is essential to study not only individual compounds but also compound ratios as well as compound groups clustered by lipid precursor or enzymatic pathways to decipher “micro” and “macro” regulation of these molecules in pathophysiology. (this thesis)
4. Lipid mediators are potential regulators of the immune and inflammatory orchestra in response to exercise. Exercise metabolomics targeting lipid mediators can provide insights into molecular mechanisms underlying exercise, potentially leading to the development of novel therapeutic interventions for improving health and fitness. (this thesis)
5. The route of translating metabolomics research into clinical practice is still challenging. This requires standardization for sample preparation, data analysis, metabolite quantitation and data interpretation as well as large-scale validation and continuous multidisciplinary teamwork. (this thesis)
6. Expanding our knowledge about lipid dynamic behavior is fueling the hope that mapping their regulatory biochemical pathways on a systems level will revolutionize our ability to prevent, diagnose, and stratify major human diseases. (O'Donnell et al., WIREs: systems biology and medicine 12.1 (2020): e1466.) Such systems-level research should be prioritized to explore the complex interactions between lipids and related enzymes and binding receptors. This could include animal models and cell models that enable the modulation of pathways and components of interest.
7. Lipids act as extracellular and intracellular messengers to control cell fate in normal physiology and disease. When deregulated, lipid signaling contributes to inflammation and cancer, metabolic, cardiovascular and degenerative disease. (Wymann et al., Nature reviews Molecular cell biology 9.2 (2008): 162-176.) This highlights the multifaceted role of lipid signaling and underscores the potential to target signaling lipid pathways in diverse biological contexts, as focused on in this thesis.

8. Interlaboratory comparisons are of importance to discover current gaps, establish references for quality control and quality assessment toward harmonized lipidomics. (Long et al., Metabolites 10.2 (2020): 51.) This is imperative and can be achieved by working on reference material across different laboratories so that standardized workflow can be built for lipidomics researchers to compare and align. Even better is to report absolute concentrations of the individual compounds, but that comes with various challenges, including the purity and stability of the reference compounds.
9. Combining omics data from multiple biological domains (e.g. levels of transcripts, proteins, or metabolites) in multi-omics studies is a promising approach towards a more detailed molecular understanding of health and disease, as well as the chain of cause and effect, which is an essential requirement for guiding novel therapies. (Wörheide et al., Analytica chimica acta 1141 (2021): 144-162.) This can be further improved by new approaches for modeling complex biological systems to identify meaningful patterns and relationships from integrated omics datasets. For example, using tracer based metabolomics for measuring changes in metabolic fluxes will provide information about rates of substrate utilization and enzymatic activities in biological systems. This will help to understand conversion of lipids in different conditions.
10. There is only one good, knowledge, and one evil, ignorance. (Socrates)
11. Today is the oldest you've ever been, and the youngest you'll ever be again. (Eleanor Roosevelt)
12. It's the choices that make us who we are, and we can always choose to do what's right. (Spider-Man)

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Leiden, 24th May 2023