Lipidomics study in liver metabolic diseases

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Stellingen (Propositions)

Behorende bij het proefschrift

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1. The liver plays a central role in lipid metabolism and transport, and is responsible for maintaining a healthy lipid composition. Liver dysfunction can disrupt lipid metabolic pathways causing dyslipidemia. Therefore, lipidomics becomes important for identifying biomarkers, offering a non-invasive technique in early detection and monitoring the progression of liver metabolic diseases. *(This thesis*)

2. The HILIC-MS/MS lipidomics method developed in this thesis offers broad coverage and superior quantitative capabilities. It can aid in deciphering the complex interactions between the lipidome and diverse components of the biological system. *(This thesis)*

3. Characterizing acyl-CoA intermediates and their behavior in different physiological and pathological conditions can provide deeper insights into mitochondrial metabolic networks. Developing a simpler (bio)-analytical method for comprehensive measurements of these compounds is highly valuable for high-throughput and potential clinical integration. *(This thesis)*

4. Employing multiple study models (such as *in silico*, *in vivo* and *in vitro*) can aid in understanding the systemic changes associated with metabolic disorders, as data from the different models can be cross-validated, thereby enhancing the reliability of preliminary findings. *(This thesis)*

5. "By integrating multi-omics, scientists can filter out novel associations between biomolecules and disease phenotypes, identify relevant signaling pathways, and establish detailed biomarkers of disease *(Chen C et al., MedComm. 2023;4:e315)*." Integrating multiple omics disciplines is challenging due to mismatches in analytical tools and experimental designs. One strategy for smoother integration would be to standardize and normalize data into a uniform scale like min-max scaling, which involves transforming quantitative data such as intensity or concentration from different omics disciplines to a common range.

6. "The aim of clinical routine should be to expand from single lipid analysis to multianalyte lipid panels or lipidomic analysis in order to aim for more specific readouts concerning lipid-associated pathophysiologies with a potential application in personalized and

"precision medicine" *(Zandl-Lang M et al. International Journal of Molecular Sciences. 2023; 24(2):1709)*." However, clinical assays often demand absolute quantitation to facilitate transferability between labs. Despite community-driven efforts, including developing standardized protocols, reference standards and collaboration, achieving absolute quantification in lipidomics remains challenging, and quantitation is not addressed in many lipidomics research papers.

7. "Given acylcarnitines are often the carriers of the acyl moiety, acylcarnitine metabolite levels are thought to correlate with the levels of the corresponding acyl-CoA metabolite. *(Liu X et al., Mol Cell Proteomics. 2015 Jun;14(6):1489-500)*." This is true in most cases, however, in attaining a comprehensive understanding of metabolic pathways and associated disorders, profiling both acyl-CoA and acylcarnitine, and interpreting their correlations holds paramount significance.

8. "The discovery of several diagnostic biomarkers through omics study of blood and tissue samples using MS (mass spectrometry) technology has opened up a new avenue in clinical diagnosis (*Banerjee S. ACS Omega. 2020 Jan 30;5(5):2041-2048)*." Transitioning mass spectrometers from lab to bedside is vital for unlocking the diagnostic potential of biomarkers in patient care where immediate decision support is required. Developing affordable, miniaturized mass spectrometers for point-of-care use and simplifying data interpretation are essential steps toward this goal.

9. "If we knew what we were doing it wouldn't be research." – Albert Einstein

10. In research, setbacks are not regarded as failures, rather as valuable opportunities for learning and progressing towards our intended objectives.

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