Dynamic system-wide mass spectrometry based metabolomics approach for a new Era in drug research

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Stellingen

Behorende bij het proefschrift

Dynamic System-Wide Mass Spectrometry based Metabolomics Approach for a New Era in Drug Research

1. The usefulness of MS^E as an untargeted methodology for both quantitation and identification in the same analysis has been clearly demonstrated. (*This thesis*)

2. The use of TAP fragmentation together with ion mobility separation of fragment ions enabled the localization of the fatty acyl positions and double bonds in PCs and LPCs. (*This thesis*)

3. Changes in HDL lipid composition, coupled with increased fecal sterol excretion and increased HDL cholesterol efflux capacity, indicate that anacetrapib is promoting cholesterol excretion in this hamster model, possibly via reverse cholesterol transport. (*This thesis*)

4. Silencing of Slc27a5 in mice significantly altered the conjugation state and concentration of bile acids in the plasma, which resulted in positive effects on lipid and lipoprotein profiles and diet-induced obesity. (*This thesis*)

5. The use of stable isotopically labeled substrates and analysis by mass spectrometry have provided substantial insight into rates of synthesis, disposition, and utilization of lipids in vivo**.** (McLaren, D.G. et.al. *J. Lipid Res.* 2011 52:(6) 1150-1161)

6. Increased serum apolipoprotein (Apo) B and associated LDL levels are well-correlated with an increased risk of coronary disease (Tadin-Strapps, M. et.al. *J. Lipid Res*. 2011 52:(6) 1084-1097)

7. The advantages of using ^2H_2O to quantify cholesterol synthesis include; i) homogeneous precursor labeling, ii) incorporation of ^2H via multiple pathways, and iii) the ability to perform long-term studies in free-living subjects (Previs, S.F et.al. *J. Lipid Res*. 2011 52:(7) 1420-1428)

8. The concept of systems-based strategies in medicine is emerging, with systems pathology guiding an understanding of the multidimensional aspects of disease system fingerprints and systems pharmacology providing insight into dynamic system responses upon (multiple) drug perturbations (van der Greef, J. *Syst Biol (Stevenage)* 2005, 152, 174-178)

9. As we encounter new challenges, the road to success is always under construction

10. The important thing in science is not to obtain new facts but to discover new ways of thinking about them

11. Problems worth of attack prove their very worth by hitting back with perseverance

José M. Castro Pérez, Leiden, October 2011