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A Combined Study of Renal Lipidome in db/db Mouse using LC-MS/MS and Imaging Mass Spectrometry

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Objectives : About 529 million people are living with diabetes, with 1 in 3 of them having diabetic nephropathy (DN), which is associated with end-stage kidney disease. Lipid dysmetabolism is a well-known feature of diabetes, causing lipid accumulation in various organs, including the kidney, and can deteriorate diabetic kidney disease (DKD). However, the link between kidney disease and lipid accumulation is unclear, but some studies suggest triglyceride (TG) is a significant lipid species as they shows large variations.
Methods : To investigate the TG differences between healthy and diabetic kidneys, we analyzed db/db mouse kidney with tandem mass spectrometry (LC-MS/MS) and imaging mass spectrometry (IMS). For LC-MS/MS analysis, neutral, positive, and anionic lipids were extracted from three parts of the kidney: the whole kidney, medulla and cortex, and identification and relative quantification was performed. For IMS analysis, the kidney tissues slides were coated with matrix and analyzed.
Results : We identified 51, 62, and 27 TGs in the whole kidney, medulla, and cortex, respectively. Most TG species showed an increasing trend in db/db compared to db/m, with TG 58:11 showing the biggest difference. Also, we could find a pattern: TGs with more double bonds increased more in db/db compared to db/m than TGs with fewer double bonds. Also comparing the LC-MS/MS result with the IMS result, the IMS result was in accordance with the LC-MS/MS result, and found that important TG species can differ from each kidney part.
Conclusions : In summary, our integrated lipid analysis showed that the quantity and quality of lipids in diabetic kidneys are different from those in healthy kidneys, and even the same TG species can vary in amount, depending on the location of the kidney part. Our study can help better understand the lipid differences in diabetic kidneys and therefore unveil the mechanisms between lipid dysmetabolism and DKD.