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The prevalence of obesity has increased drastically over the past decade, and already a decade ago, the CDC estimated that the medical costs of obesity will reach $150 plus billion dollars per year. Obesity is associated with chronic lowgrade inflammation, and obesity and chronic inflammation are risk factors for many chronic diseases, such as cardiovascular diseases and type 2 diabetes. Thus, understanding the altered biochemical pathways associated with obesity may help to develop and advance disease management and intervention strategies.

In this context, we will discuss workflows of LC-MS metabolomics to detect and identify metabolites in complex samples with the goal to study biochemical pathways associated with lipid metabolism. We will review the advantages of detecting metabolome and lipidome differences by utilizing advanced mass spectrometry techniques. MS-driven studies provide researchers with the ability to profile hundreds of metabolites and lipids in a single sample. The metabolites detected by mass spectrometric analyses are then subjected to statistical evaluations that result in metabolites and lipid species most significantly associated with pathways altered during adipocyte differentiation. We will briefly review how stable isotope tracer metabolomics can help to decipher which pathways are associated with adipocyte maturation. We will then change gears to learn how hydrogen deuterium exchange mass spectrometry can be utilized for studying FXR, the key regulator of bile acid, glucose and lipid homeostasis, with the goal to identify small molecule binders to FXR that have the potential to modulate directly or indirectly bile acid metabolism and hypertriglyceridemia. We close with a perspective that polyphenols have the potential to modulate bile acid homeostasis and gut microbiota to counteract obesity.

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