

## **Mass spectrometry-based lipidomics to explore the biochemical effects of naphthalene toxicity or tolerance in a mouse model**

### **ABSTRACT**

Naphthalene causes mouse airway epithelial injury. However, repeated exposures of naphthalene result in mouse airway tolerance. Previous results showed that toxicity or tolerance was correlated with changes of phosphorylcholine-containing lipids. In this study, a mass spectrometry-based lipidomic approach was applied to examine the effects of naphthalene-induced injury or tolerance in the male ICR mice. The injury model was vehicle x 7 plus 300 mg/kg naphthalene while the tolerant one was 200 mg/kg daily x 7 followed by 300 mg/kg naphthalene on day 8. The lung, liver, kidney, and serum samples were collected for profiles of phosphorylcholine-containing lipids including phosphatidylcholines (PCs) and sphingomyelins (SMs). A partial least-square-discriminate analysis model showed different lung phosphorylcholine-containing lipid profiles from the injured, tolerant, and control groups. Perturbation of diacyl-PCs and plasmalogen phospholipids may be associated with enhanced membrane flexibility and anti-oxidative mechanisms in the lungs of tolerant mice. Additionally, alterations of lyso-PCs and SMs may be responsible for pulmonary dysfunction and inflammation in the lungs of injured mice. Moreover, serum PC(16:0/18:1) has potential to reflect naphthalene-induced airway injuries. Few phosphorylcholine-containing lipid alterations were found in the mouse livers and kidneys across different treatments. This study revealed the changes in lipid profiles associated with the perturbations caused by naphthalene tolerance and toxicity; examination of lipids in serum may assist biomarker development with the potential for application in the human population.