THE UNIVERSITY OF ARIZONA
COLLEGE OF AGRICULTURE & LIFE SCIENCES
Nutritional Sciences & Wellness

SEMINAR ANNOUNCEMENT

The School of Nutritional Sciences and Wellness presents:

"Computational Approaches to the Effects of LPS-induced Inflammation on Plasma Lipidome in Healthy Males"

By

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https://arizona.zoom.us/j/82678706371

Computational Approaches to the Effects of LPS-induced Inflammation on Plasma Lipidome in Healthy Males

Background: Lipopolysaccharide (LPS) found in the outer membranes of gram-negative bacteria is composed of three primary regions: lipid A, the core, and the O-antigen. It activates acute systemic immune responses and that can lead to fatal septic shock. Key cellular and humoral events associated with LPS activation are understood, however, the lipid related pathways and networks involved in the response are unclear. Untargeted compositional lipidomics can detect the alteration of lipid profiles in response to LPS-induced acute systemic inflammation. Computational approaches such as linear regression models and machine learning methods can track the changes in lipidomes both within and between lipid classes. Connecting known biomarkers with the results from the computational approaches presents a clearer view of the molecular underpinnings of the inflammatory response.

Method: Healthy young males (n=10, age=27 ± 1 yrs) consuming a low-fish diet were recruited and injected with a sterile solution of protein-free endotoxin at a dose 0.6ng/kg body weight. Blood samples were collected at 0 h (baseline), 1 h, 2 h, 3 h, 4 h, 8 h, 24 h, 48 h, 72h and 168 h post LPS injection. IL-6, TNF-a, CRP, sPLA2- IIA were measured at these time point. Plasma lipidomes were measure by UPLC-MS/MS at timepoint: 0h(baseline), 2h, 4h, 8h, 24h, 72h. LipidSearch software was used for annotation and quantification. Data preparation, statistical analysis, and data visualization were performed in R. A linear mixed-effects model was used to compare measurements at different time points. Hierarchical clustering analysis separated lipid species into different groups based on data points having similar characteristics.

Result: IL6 and TNF-α exhibited peaks at 2h and resolved by 8h. CRP increased at 8h, peaked at 24h, and wasn't fully resolved after a week. The sPLA2-IIA increased at 4h and peaked at 8h. There were 1027 lipids detected and 355 lipids in 14 lipid classes showed significant alteration ($p<0.05$), which about 50% were triglycerides. Total lipid content (sum of the 1027 lipids intensities) for each patient started rising at 2h and came back down after 4h. Based on the significantly different lipids, acyl-carnitines, ceramides, cholesterol esters had uniform class patterns, but most of the classes including phospholipids, lysophospholipids, diglycerides, and triglycerides had a major separation at 8h and 24h.

Conclusion: Rapid increase of triglycerides caused the total lipid content in plasma to increase, which suggests that lipolysis in adipose tissue and de novo hepatic fatty acid synthesis quickly released triglycerides in response to LPS injection. Decreased medium chain acyl-carnitines paired with increasing triglycerides suggests suppression of the oxidation of fatty acids in the liver occurred in the first 8 hours. For the dramatic spike in sPLA2-IIA, we were expecting major increases in lysophospholipids especially lysoPEs at 8h, but only a few of the lysoPEs increased. Interestingly, at 8h and 24h, many phospholipids, lysophospholipids, diglycerides, and triglycerides had divided trends, for which the mechanism is still not understood.