

## **A metabolomics-based approach to understanding metabolic disease caused by overnutrition in monogastric and ruminant animals**

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Chronic overnutrition causes excessive lipid accumulation, inflammation, and insulin resistance in adipose tissue, events caused by a dysregulation in mitochondrial function and fatty acid metabolism. This metabolic imbalance promotes systemic hyperlipidemia that results in ectopic lipid deposition and whole-body insulin resistance. These metabolic perturbations are present in overconditioned monogastrics (i.e. humans, rodents, and companion animals) and ruminants (i.e. sheep and dairy cows); however, the mechanisms responsible are undefined. Therefore, our aim is to delineate the relationship between fatty acid metabolism, inflammation, and insulin sensitivity in overconditioned monogastrics and ruminants experiencing metabolic disease. To achieve this aim, we utilize novel pharmacological compounds to modify fatty acid metabolism and a mass spectrometry-based metabolomics approach to comprehensively profile the rodent, feline, and bovine metabolome prior and post weight gain. Using GC/MS/MS and Q-TOF LC/MS platforms, we are able to detect, via targeted and untargeted methodologies, approximately two-hundred metabolites including ceramides, fatty acylglycerols, fatty acylcarnitines, cholesterol esters, free fatty acids, phospholipids, TCA cycle intermediates, amino acids, and adenine and pyridine nucleotides. Metabolite profiles are compared to physiological maladaptations caused by nutrient excess. In the presence of excess fatty acids, we are able to demonstrate, in adipose tissue and cultured hypothalamic neurons, a shift in fatty acid flux away from catabolism and towards the production of ceramides, lipid signaling molecules associated with observed inflammation and insulin resistance; responses prevented by increasing fatty acid oxidation. Characterizing the metabolome of overconditioned animals will allow us to develop pharmacological and nutritional strategies to prevent and treat metabolic disease.

### **Biography**

Joseph W. McFadden completed a B.S. in animal science with distinction in research from Cornell University. He then received a M.S. in animal science from the University of Illinois followed by a Ph.D. in dairy science from Virginia Tech. He then completed a postdoctoral fellowship in the Center for Metabolism and Obesity Research and Department of Neuroscience at Johns Hopkins University School of Medicine. Currently, he is an Assistant Professor of biochemistry at West Virginia University and a visiting scientist at Johns Hopkins University. His research focuses on defining the metabolome of overconditioned monogastrics and ruminants to understand metabolic disease.

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