**246c Metabolic Profiling and Flux Analysis of in Vitro Adipogenesis**

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Obesity is rapidly becoming a leading health problem in developed countries. Solid epidemiological data support the pivotal role of body fat (white adipose tissue, WAT) mass in the development of obesity and associated health risks. Expansion of adipose cell mass involves both increases in fat cell size (hypertrophy) and cell number (hyperplasia). The latter occurs through recruitment and differentiation of precursor cells (adipogenesis). White adipocytes, the main cellular component of WAT, secrete a host of factors that affect both whole body and WAT-specific metabolism.

To characterize the metabolic profiles and quantify the metabolic fluxes during *in vitro* adipogenesis, an optimization-based metabolic flux analysis (MFA) method recently developed in our laboratory was applied to 3T3-L1 preadipocyte differentiation. The optimization-based method afford resolution of several key cyclic pathways that constitute adipocyte lipid metabolism. Results show that our *in vitro* model captures key differences between preadipocytes and adipocytes. Adipogenesis brought about significant flux increases of multiple pathways, including glycolysis, TCA cycle, triglyceride synthesis and degradation, and ketogenic amino acid degradation. Importantly, our predicted carbon distribution agrees well with $^{14}$C-labeled glucose tracer studies previously published by other groups.

K-means clustering revealed distinct groups of reactions in preadipocyte and adipocytes that exhibit varying activity time profiles. These data showed that significant changes in global cellular metabolic regulation underlie the transition of preadipocytes into mature, lipid-filled adipocytes. In particular, MANOVA of metabolite concentration and derived flux data pointed to intracellular free fatty acid (FFA) concentration as the key marker of adipogenesis. This finding sets the stage for on-going and future work to control FFA levels through ectopic metabolic enzyme gene expression, and thereby modulate adipogenic fat mass increase.