Research Summary for Samuel Taylor

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Evaluation of Compounds that Inhibit Fatty Acid Uptake in Mice

Lipotoxicity is characterized by apoptosis due to the toxic spillover of fatty acids from adipocytes into non-adipose tissue. Adipocytes function under high lipid concentrations and serve to regulate triglyceride levels in the body, but their storage capacity is limited, and adipocytes are frequently unable to regulate body triglyceride levels in cases of obesity. In such cases, lipid metabolic products (including ceramides and free fatty acids) become toxic at high concentrations. Lipotoxicity is seen in an array of cell types, including liver, kidney, heart, and pancreatic cells. My research will seek to extend previous work done in identifying and characterizing small molecule fatty acid uptake inhibitors as potential drug therapies. A high-throughput screen was first employed to identify inhibitors of the liver Fatty Acid Transporter, FATP2. Positive results were then evaluated in a cell-based system, and two compounds were selected for continued study. I will be examining the effects of these compounds when delivered orally in mice, with particular attention to assessing the compounds' toxicity, measuring inhibition of ^{13}C-oleate absorption, and quantifying lipids in the liver, bloodstream, and feces.