Non-alcoholic fatty liver disease (NAFLD) is a major clinical problem, often associated with adult onset diabetes. Studies on mice with genetically fatty livers (OB/OB strain) suggested that the glucagon-like peptide (GLP) proteins have a novel direct effect on hepatocytic fat metabolism. Treatment with Exendin-4, a GLP-1 receptor agonist that improves insulin secretion in diabetics, reduced hepatic steatosis and fatty acid synthesis in these mice. Medlab and the TMC GI group studied normal rats given fatty livers by feeding a methionine-choline deficient (MCD) diet for 75 days. This report studies on tissue from normal rats given an MCD diet which emulated NAFLD and then treated with Exendin-4 to see if a similar effect would occur as with the OB/OB mice in the previous cited research.

Hypothesis- Exendin4 will reduce hepatosteatosis in this MCD rat model.

Animals were divided into five groups:
1. Untreated
2. MCD only
3. MCD + exendin
4. MCD + exendin + metformin

This subacute study with the MCD + exendin model is to evaluate: 1) the MCD model treated with Exendin-4 for 75 days, and 2) the OB/OB mouse model. The Exendin-treated group shows: - increased steatosis - lowered circulating GLP-1 - proliferation of pancreatic cells - liver and pancreatic cellular change (pyknotic cells)

Further study is needed (adipocytokines) but compared to the OB/OB mouse model (1) the MCD model treated with exendin 4 does not produce physiological benefit

Limitations
- Animal model does not perfectly replicate nonalcoholic steatosis
- Ongoing studies are using inbred ob/ob mice with the MCD diet to further study the problem
- More in-depth work on the adipocytokines needs to be completed

References