**SUPPLEMENTAL METHODS:**

***Co-immunoprecipitation of cFAS and Apolipoprotein B (ApoB)***

FPLC-derived peak LDL fractions were collected for representative patients with diabetes. 300ul of Protein A Sepharose Beads (Millipore, Burlington, MA) were prepared by 3 washes in 1000ul of 0.1% PBST and centrifugation at 5000g at 4°C for 30 seconds. 150uL of the bead/PBST mixture was then added directly to the serum LDL isolate collected from FPLC. The sample/bead mixture was pre-cleared for 2 hours at 4°C with gentle rocking, and then centrifugation at 5000g at 4°C for 30 seconds. Beads were then collected and incubated with either FAS antibody (Abcam, Cambridge, MA) or ApoB antibody (ThermoFisher Scientific, Waltham, MA) at 1:1000 concentration and incubated overnight at 4°C with gentle rocking. Protein A magnetic beads (Bio-Rad Laboratories, Inc., Hercules, CA) were washed in the same manner as the Protein A Sepharose Beads. 150uL of magnetic beads are then incubated with the sample/antibody solution for 4 hours at 4°C with gentle rocking. The beads were then isolated using a magnetic rack and the supernatant was removed. The isolated magnetic beads were then washed twice with 1000uL of 0.1% PBST, and the supernatant of each wash was collected as a washing control for subsequent Western blot analysis. The residual beads/antibody/protein complex was then dissociated by incubation with 30ul of a 2x Laemmeli Buffer (Bio-Rad Laboratories, Inc., Hercules, CA) at 72°C for 10 minutes. The resultant sample was collected for Western blotting analysis.

Equal volumes of 35uL of FPLC cholesterol fraction, immunoprecipitation washes, the final immunoprecipitation product, as well as a positive control (mouse liver homogenate for FAS protein and human serum for ApoB) were resolved on a 7% SDS-TrisAcetate-polyacrylamide gel (ThermoFisher Scientific, Waltham, MA) and electrotransferred onto PVDF membranes (GE Healthcare Bio-Sciences, Pittsburgh, PA). Membranes were then probed with an FAS antibody and ApoB antibody**.** Western blots were resolved using chemiluminescence (ECL Kit, Bio-Rad, Hercules, CA) and imaged using an Odyseey Fc imaging system (LI-COR, Lincoln, NE).

***Fatty acid mass spectrometry***

Modified Bligh-Dyer method was performed to extract saturated fatty acids (SFAs) and unsaturated fatty acids (USFAs) from 50 μL of lysates of Max diseased carotid plaque segments.[1] d4-fatty acid (16:0) was used as an internal standard for other free fatty acids. The internal standard was added to the samples before extraction. The extracted free fatty acids were further derivatized by amino methyl phenyl pyridium (AMPP) into FA-AMPP derivatives in order to obtain high sensitivity in mass spectrometry. Measurement of the FA-AMPP derivatives were resolved from other lipids (phospholipids, ceramides, and sphingomyelin) was performed with a Shimadzu 20A HPLC system and a Shimadzu SIL-20AC HT auto-sampler coupled to a QExactive mass spectrometer operated in full mass mode under ESI(+). Data processing was conducted with Xcalibur (Thermo). Four blank samples were evaluated along with the experimental samples. The average signal of the blank samples was subtracted from the actual signal in the experimental samples to eliminate any interference introduced by regents and/or glassware. All samples were normalized to sample protein concentrations, and the relative concentrations of SFAs and USFAs were then evaluated as previously described.[2]

**References:**

1. Zayed, M.A., et al., *Diabetes adversely affects phospholipid profiles in human carotid artery endarterectomy plaques.* J Lipid Res, 2018. **59**(4): p. 730-738.

2. Chakravarthy, M.V., et al., *Identification of a physiologically relevant endogenous ligand for PPARalpha in liver.* Cell, 2009. **138**(3): p. 476-88.