

ESM Methods

Specific Laboratory Methodology

Total cholesterol, triacylglycerol and HDL cholesterol levels were measured using enzymatic assays on the (AEROSET) system and Abbot autoanalyzers. LDL was calculated using the *Friedewald equation* or measured directly if triacylglycerol levels were more than 3.95 mmol/l. Serum insulin and C-peptide were measured using solid-phase two-site chemiluminescent immunometric assays on the Immulite 2000 analyzer. Interleukin-6 (IL-6), vascular adhesion molecule- 1 (VCAM-1) and adiponectin were measured in duplicate using ELISA kits (R&D Systems, Minneapolis, MN). High sensitivity C-reactive protein (CRP) concentrations were measured using an immunometric assay (DPC Immulite, Los Angeles, CA) that compares well with the Dade Behring CRP assay [25]. All assays have CVs of less than 12% for both within- and between-run precision. Plasma salsalate levels were measured by the clinical laboratory at the Phoenix VA Medical Center, with a lower limit of sensitivity of <5 mg/dl.

Subcutaneous adipose tissue biopsies were performed through an approximately 2 cm open incision on an unselected subset of participants. Immediately after biopsy, fat tissue was rid of connective tissue and blood vessels and subsequently frozen at -80C. Approximately 0.2-0.25g of frozen tissue was homogenized using a PowerGen 700 homogenizer (Fisher Scientific) in 250-300ul complete lysis buffer as specified in the Nuclear Extract Kit (Active Motif, Carlsbad, CA). Aliquots of the tissue lysate were assayed for protein concentration and DNA binding activity of NF- κ were assessed in 20ug of tissue lysate (in duplicate) with ELISA kits (Active Motif, Carlsbad, CA) using a VersaMax plate reader (Molecular Dynamics, Sunnyvale, CA).

Specific Endothelial Function Methodology

Before initiating the clamp or OGTT, endothelial function was assessed at baseline, and after 8 and 12 weeks of intervention. Subjects were instructed to refrain from smoking, ingesting alcohol or caffeine or take

any vasoactive medications on the day of testing. Coefficient of variation for 3 repeated measurements within the same individual on the same day is $< 5\%$ in our laboratory.