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Title of project: LOXIN variants and sLOX-1 measurements as biomarkers for cardiovascular risk

ABSTRACT

Lectin-like oxidized low-density lipoprotein receptor (LOX-1), a type II transmembrane protein, is a scavenger receptor up regulated during vascular inflammation. LOX-1 is expressed in various cell types including macrophages, endothelial and vascular smooth muscle cells. LOX-1 binds several ligands including oxidized LDL promoting lipid accumulation, foam cell formation, production of reactive oxygen species, and endothelial cell functional abnormalities. A soluble form of LOX-1 (sLox-1) results from proteolytic cleavage by ADAM10 and ADAM17 proteases of its extracellular domain that reflects total LOX-1 levels and represents a potential biomarker for cardiovascular risk. Human polymorphisms in the gene encoding LOX-1 (OLR1) result in splice variants called LOXIN mutations resulting in the loss of the ligand binding domain and functions as a dominant negative (J Am Coll Cardiol. 2017 Jun 6;69(22):2759-2768; J Med Genet 2003;40:933–936). It has been indicated that human carriers of the LOXIN mutation show a reduced propensity for myocardial infarction, but this needs to be substantiated. Our hypothesis is that subjects with high sLox-1 levels will show a propensity for increased CVD whereas LOXIN mutations will confer reduced CVD risk. To date, association studies using either sLox-1 or LOXIN have not been conducted in large population cohorts.