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**Project title**: Targeting TSP-1 in atherosclerotic complications associated with metabolic syndrome

**ABSTRACT**:  
Metabolic syndrome refers to a cluster of metabolic risk factors including insulin resistance, hyperglycemia, obesity and hyperleptinemia. This is a serious health condition which significantly augments risks of cardiovascular complications including atherosclerosis, coronary heart disease and myocardial infarction. Prevalence of atherosclerotic complications increase two-to-four-fold in individuals with metabolic syndrome, accounting for increased morbidity and mortality in these patients. However, mechanisms responsible for accelerated atherosclerosis in metabolic syndrome remain poorly understood. We and others have reported that hyperleptinemia and hyperglycemia, characteristic of metabolic syndrome, upregulate a proatherogenic matricellular protein, thrombospondin-1 (TSP-1), expression in human and mouse aortic smooth muscle cells. Multiple reports highlight the importance of TSP-1 in accelerated development of atherosclerosis and restenosis. Growing evidence demonstrate that TSP-1 levels are significantly increased in both diabetic and obese patients and animal models. Despite these associations, contribution of TSP-1 to vascular disease in metabolic syndrome remains unknown. The proposed studies will investigate the role of TSP-1 in development of atherosclerotic disease associated with metabolic syndrome using an in vivo mouse model of combined metabolic syndrome and atherosclerosis.