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RESEARCH TOPIC:

Genome-Wide Association study of Subclinical Atherosclerosis in Sub-Saharan African, The role of oxidative stress in the pathogenesis.

RESEARCH PROPOSAL ABSTRACT

Atherosclerosis, a chronic inflammatory disease of the arterial wall, is the major cause of morbidity and mortality from CVD (Cardiovascular Disease) in the world's. The disease involves the formation of plaques in arterial walls and thickening that narrow the arterial passage, restricting blood flow and increasing the risk of stroke and myocardial infarction. There is now a consensus that atherosclerosis represents a state of heightened oxidative stress characterized by lipid and protein oxidation in the vascular wall. Understanding the genetic basis and functional significance of the oxidative modifications of LDL may enhances our knowledge about the biological pathogenesis of atherosclerosis. The influence of genetic variants on the imbalances of antioxidants enzymes have been reported and found related to atherosclerosis. In previous population (Japanese) oxidative stress genes polymorphisms have been found associated with an increased carotid Intima Media Thickness (cIMT), a sub-clinical atherosclerosis marker. Moreover, overexpression of CAT and SOD have been found to lead to a retardation of atherosclerosis in animal models. Nevertheless, controversy still on the role of oxidative stress as cause or consequence.

The overall aim of this study is to investigate the genetic driven susceptibility of sub-Saharan African to atherosclerosis and the role of oxidative stress in the pathogenesis. Specifically, we intend to use two approach to achieve this purpose. The first is the GWAS of atherosclerosis (non-hypothesis driven), and the second is a Mendelian Randomisation (Hypothesis driven) to investigate the causative effect of oxidative stress on atherosclerosis using lipid oxidation as intermediate phenotype.

Within the framework of the AWI-Gen study, 12 000 individuals have been screened for phenotypes and genotypes to investigate the "Genomic and environmental risk factors for cardiometabolic diseases in sub-Saharan Africans". From six sites (Eastern, western and southern Africa), people aged from 40-60 have been recruited for GWAS purpose. Genotyping will be performed on the Africa Array (2.5 M SNPs in development) and by PCR for selected functional SNPs.

It is expected that the GWAS of atherosclerosis in Sub-Saharan African populations could contribute to understanding of the pathophysiology of atherosclerosis.This study will be the first GWAS of attherosclerosis in Su-Saharan african. Characterization of the oxidative stress genes variants could be beneficial for the identification of new prevention and treatment strategy of management of the disease and its derived metabolic complications.