Runs of Homozygosity (ROHs) are recognized signature of recessive inheritance. Contributions of ROHs to the genetic architecture of coronary artery disease and regulation of gene expression in cells relevant to atherosclerosis are not known. Our combined analysis of 24,320 individuals from 11 populations of white European ethnicity showed an association between coronary artery disease and both the count and the size of ROHs. Individuals with coronary artery disease had approximately 0.63 (95% CI: 0.4-0.8) excess of ROHs when compared to coronary-artery-disease-free control subjects (p = 1.49 × 10^{-9}). The average total length of ROHs was approximately 1,046.92 (95% CI: 634.4-1,459.5) kb greater in individuals with coronary artery disease than control subjects (p = 6.61 × 10^{-7}). None of the identified individual ROHs was associated with coronary artery disease after correction for multiple testing. However, in aggregate burden...
analysis, ROHs favoring increased risk of coronary artery disease were much more common than those showing the opposite direction of association with coronary artery disease ($p = 2.69 \times 10^{-33}$). Individual ROHs showed significant associations with monocyte and macrophage expression of genes in their close proximity—subjects with several individual ROHs showed significant differences in the expression of 44 mRNAs in monocytes and 17 mRNAs in macrophages when compared to subjects without those ROHs. This study provides evidence for an excess of homozygosity in coronary artery disease in outbred populations and suggest the potential biological relevance of ROHs in cells of importance to the pathogenesis of atherosclerosis.