Identifying Genetic Risk Factors for Vascular Calcification

Vascular calcification (VC), the abnormal accumulation of calcium deposits in the arterial wall, stiffens arteries and increases cardiovascular risk. Genome-wide association studies (GWAS) have consistently reported non-coding variants—single nucleotide polymorphisms (SNPs) at the LPA, CDKN, and HDAC9 loci to be associated with different VC pathologies. However, how the SNPs at these loci contribute to arterial disease remains poorly understood. In our study, we aim to identify their regulatory function in the genome.

We selected 11 GWAS lead SNPs at the LPA, CDKN, and HDAC9 loci and expanded them into a pool of 79 SNPs ($r^2 \geq 0.8$). The candidate pool was analyzed in RegulomeDB, an *in silico* tool that ranks non-coding variants by their likelihood of disrupting regulatory elements. The resulting SNPs were then analyzed in 3DSNP, which uses chromatin interaction data (e.g., Hi-C) to link SNPs in regulatory regions to their distal target genes and score them, identifying 16 high-scoring SNPs that potentially alter enhancers that regulate target genes critical to vascular health.

Toconfirm these predictions experimentally, we are using in vitro luciferase reporter assays in human arterial cells to compare enhancer activity between the reference and alternate alleles of each SNP. By identifying functional variants, this work contributes to the discovery of potential predictive biomarkers for VC.