Vascular calcification (VC) is a pathological deposition of calcium minerals in arterial walls, leading to vessel rigidity and significant cardiovascular risk. While genome-wide association studies (GWAS) have identified numerous loci linked to VC, the causal single nucleotide polymorphisms (SNPs) often remain obscured by linkage disequilibrium (LD). Given that the majority of SNPs reside in non-coding regions, we hypothesize that these variants disrupt distal regulatory elements, such as enhancers, to alter target gene expression.

In this study, we expanded 140 GWAS lead SNPs into a candidate pool of ~5000 variants based on strong LD ($r^2 \geq 0.8$). Using the novel E-P-INAnalyzer platform, we integrated cell-specific multiomics datasets - including RNA-seq, H3K27ac ChIP-seq, ATAC-seq, and Hi-C - from primary human coronary artery endothelial cells (HCAECs) and smooth muscle cells (HCASMCs). Our computational pipeline identified 31 high-priority SNPs predicted to alter the function of enhancers regulating target genes critical to vascular health.

To validate these findings, we are performing in vitro luciferase reporter assays to characterize the allele-specific effects of these SNPs on enhancer activity. By mapping these functional variants and their target genes, this work identifies potential predictive biomarkers and provides mechanistic insights into the genetic architecture of vascular calcification, paving the way for earlier clinical intervention.