# Gene Network Analysis Reveals Association between Somatic Loss of Y and Genes Involved in Hemostasis

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## Background and Hypothesis:

Somatic loss of the Y chromosome (LOY) is associated with diagnoses of various cancers, Alzheimer's disease, and cardiovascular events. In the case of cardiovascular disorders, no mechanistic link to LOY has been elucidated. To explore this relationship, we utilized Weighted Gene Co-Expression Analysis (WGCNA), a powerful technique that can reveal associations between modules of co-expressed genes and clinical traits. We hypothesized WGCNA would reveal a module that illuminates the relationship between LOY and cardiovascular disease.

## Methods:

Information about 403 male participants was obtained from Alzheimer's Disease Neuroimaging Initiative (ADNI), including Genome Wide Association Study (GWAS), microarray, and patient demographic data. GWAS data was obtained from each participant within one year of collecting gene expression data. Using GWAS data for each participant, a median log R ratio was calculated for probes in the male specific region of the Y (MSY), which showed detectable LOY in 16 participants. Microarray data was used for WGCNA. Genes with correlated expression levels were organized into modules which were tested for associations with age, Alzheimer's disease status, APOE-$\varepsilon$4 allele status, and LOY. Ensembl IDs were used to investigate Gene Ontology (GO) enrichment in the GO database.

## Results:

One module was associated with LOY ($p=0.001$). GO enrichment revealed significant representation of 47 GO terms within this module. Highly enriched GO terms included "platelet aggregation" (FDR = $8.05 \times 10^{-6}$), "blood coagulation, fibrin clot formation" (FDR= 0.0328), "regulation of megakaryocyte differentiation" (FDR=$3.01 \times 10^{-5}$), and other terms related to the vascular response to injury.

## Potential Impact:

WGNCA revealed a module associated with LOY that is related to vascular injury response. While LOY is associated with cardiovascular events, more work is needed to explore its association with biomarkers for cardiovascular disease. Our findings warrant more investigation into the relationship between LOY and cardiovascular dysfunction in males.