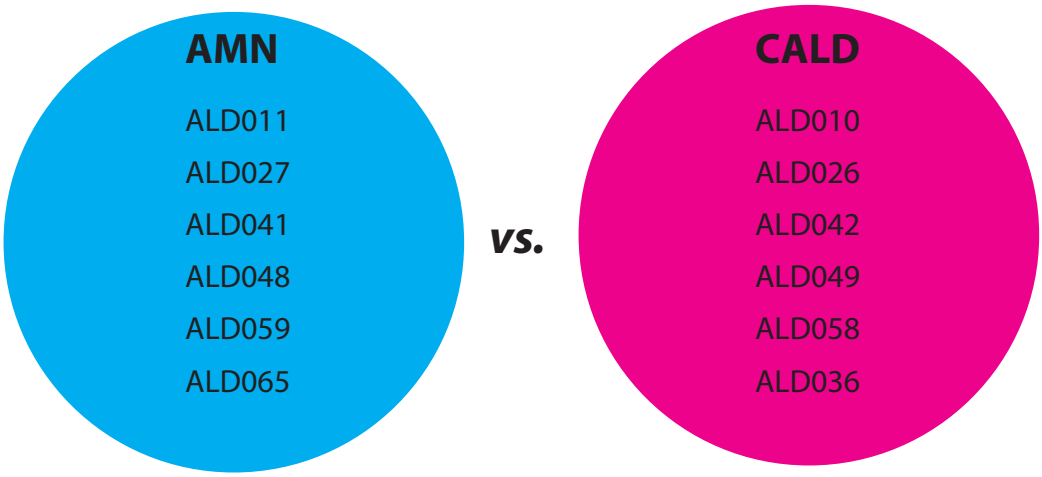
First Approach

Find variants in all CALD, absent from all AMN, and vice versa

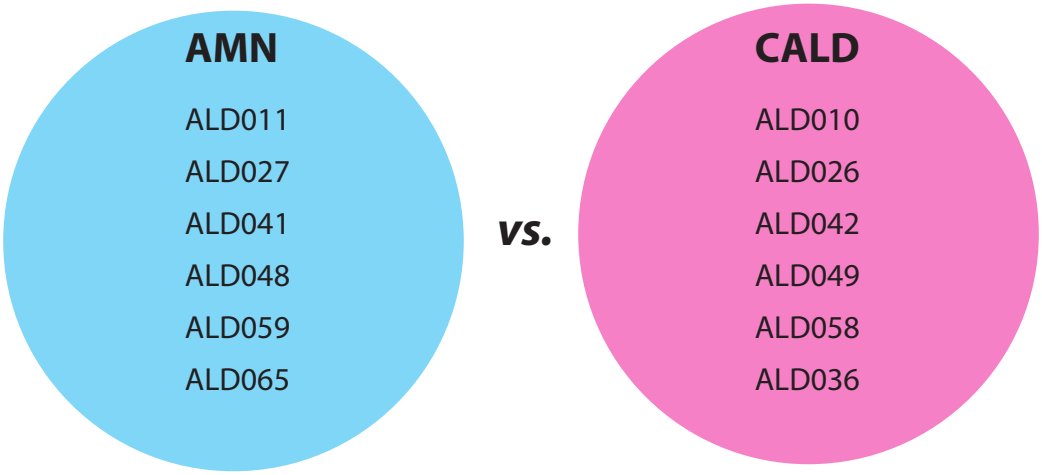


Variants can be:
Het/HomoAlt in one group, and HomoRef in the other
HomoAlt in one group, and Het/HomoRef in the other

Result: Too strict. Issues with genotyping and lack of consensus hurts this approach

Second Approach

Find variants in some (4/6 or 5/6) CALD, absent from most (4/6 or 5/6)AMN, and vice versa



Result: Too loose at 4/6, and assumptions for shared SAME VARIANT modifiers across cohort hurts this approach.

Third Approach

Find family-wise discriminating variants (HIGH/MED impact)

AMN		CALD
ALD011	vs.	ALD010
ALD027	vs.	ALD026
ALD041	vs.	ALD042
ALD048	vs.	ALD049
ALD059	vs.	ALD058
ALD065	vs.	ALD036

Variants can be:
Het/HomoAlt in one group, and HomoRef in the other
HomoAlt in one group, and Het/HomoRef in the other

Results:
For each family 1-6, about 4000-5500 variants in the Het/HomoAlt vs. HomoRef,
And 1500-1900 variants in the HomoAlt vs. Het/HomoRef. Roughly same number of genes affected (~500-1000 less)

A 4000-5500
AMN Het/HomoAlt
CALD HomoRef

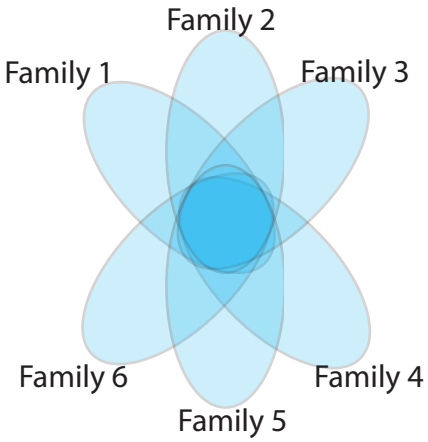
C 4000-5500
CALD Het/HomoAlt
AMN HomoRef

B 1500-1900
AMN HomoAlt
CALD Het/HomoRef

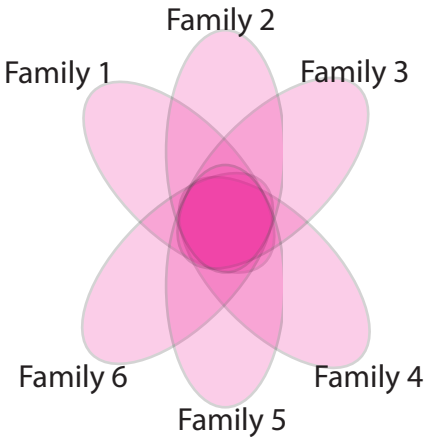
D 1500-1900
CALD HomoAlt
AMN Het/HomoRef

Assume A/B protecting variants
C/D further damaging variants

Ideas now: Look for overlap gene-wise for these sets across each family (A, B, C, D) A and C Shown below:



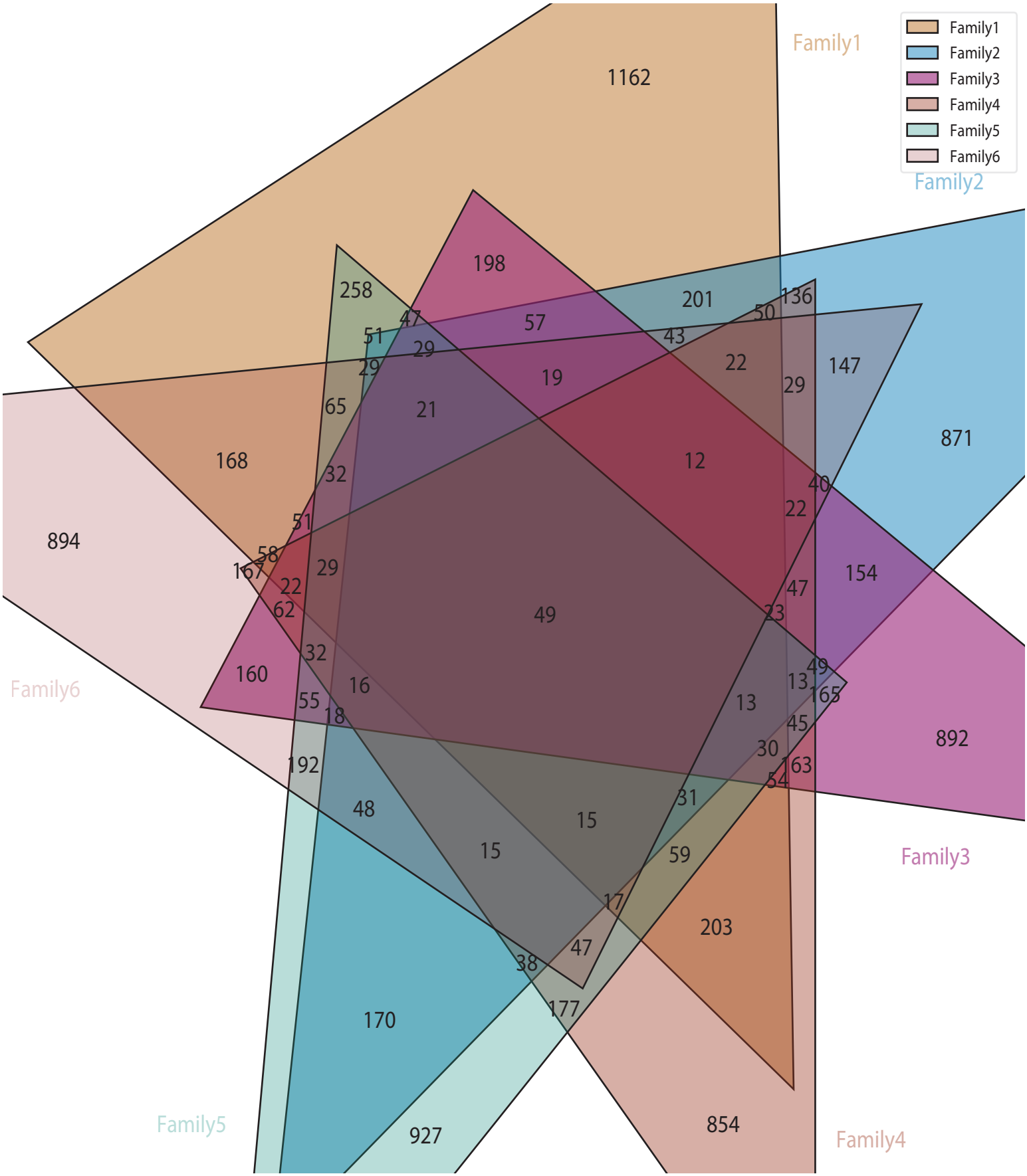
Intersect A



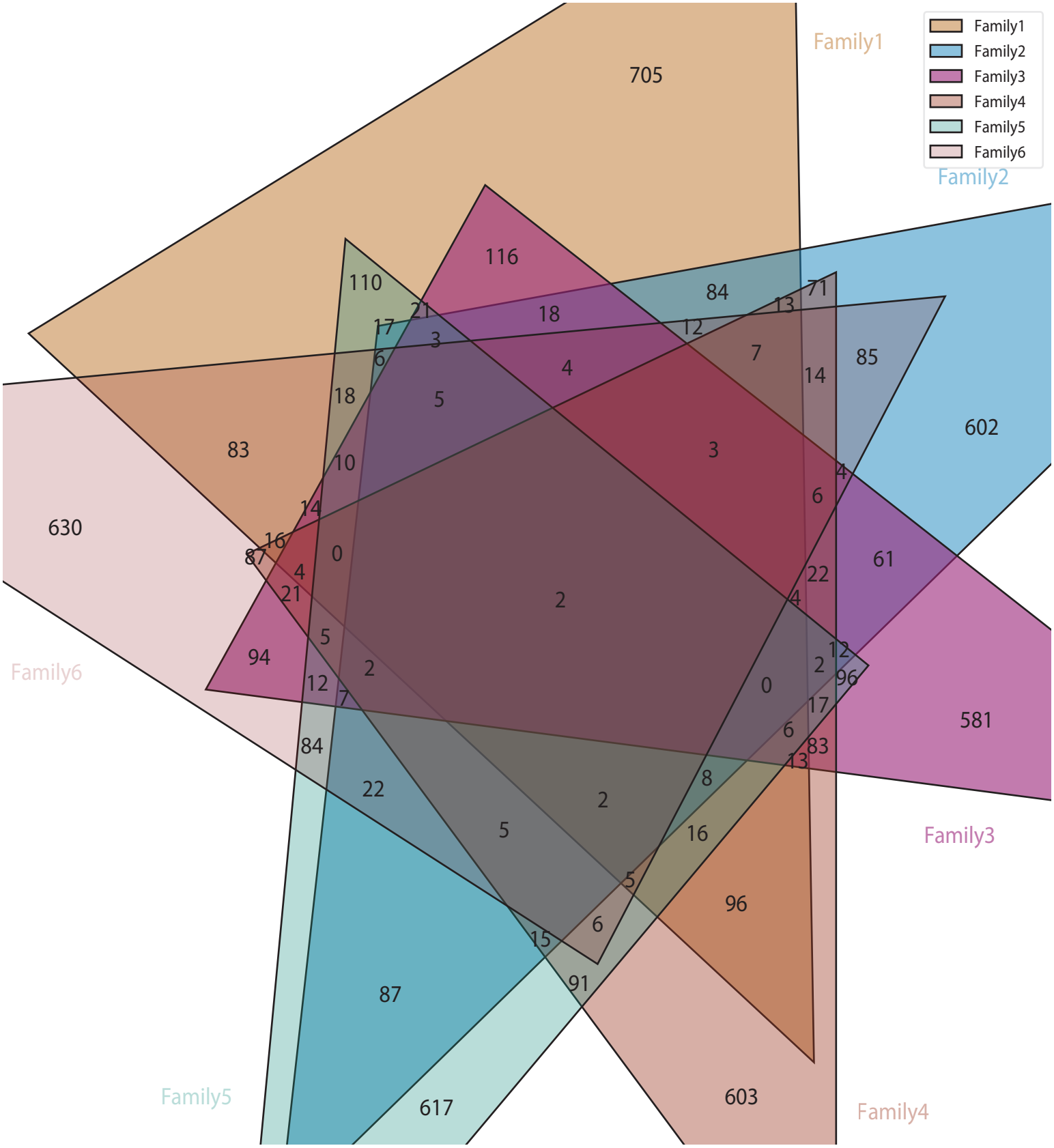
Intersect C

Working on getting Gene lists and intersecting now. Can build UpSet plots for these lists

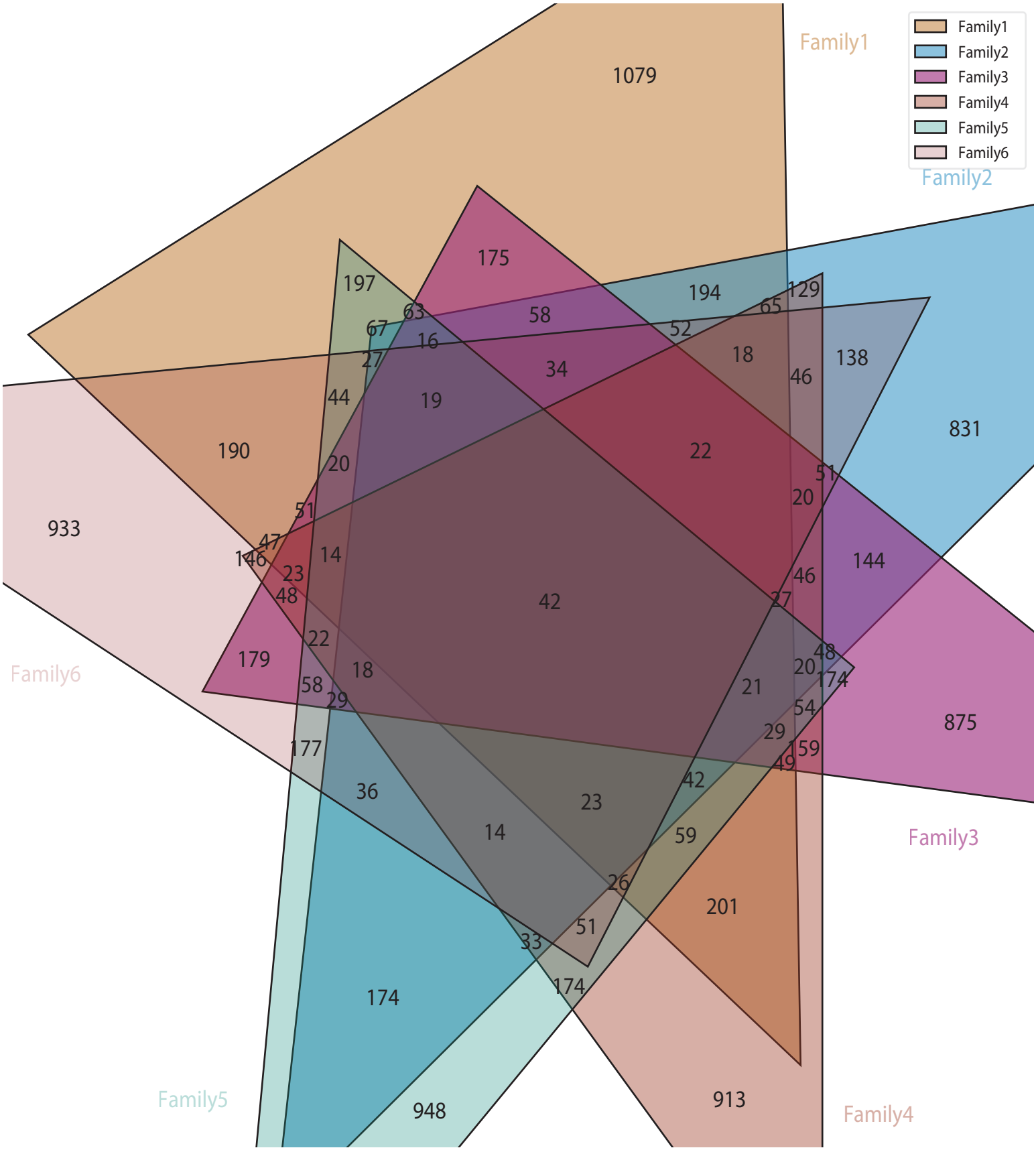
Damaging Het/Homo
(CALD Het || Homo-Alt , AMN Homo-Ref)



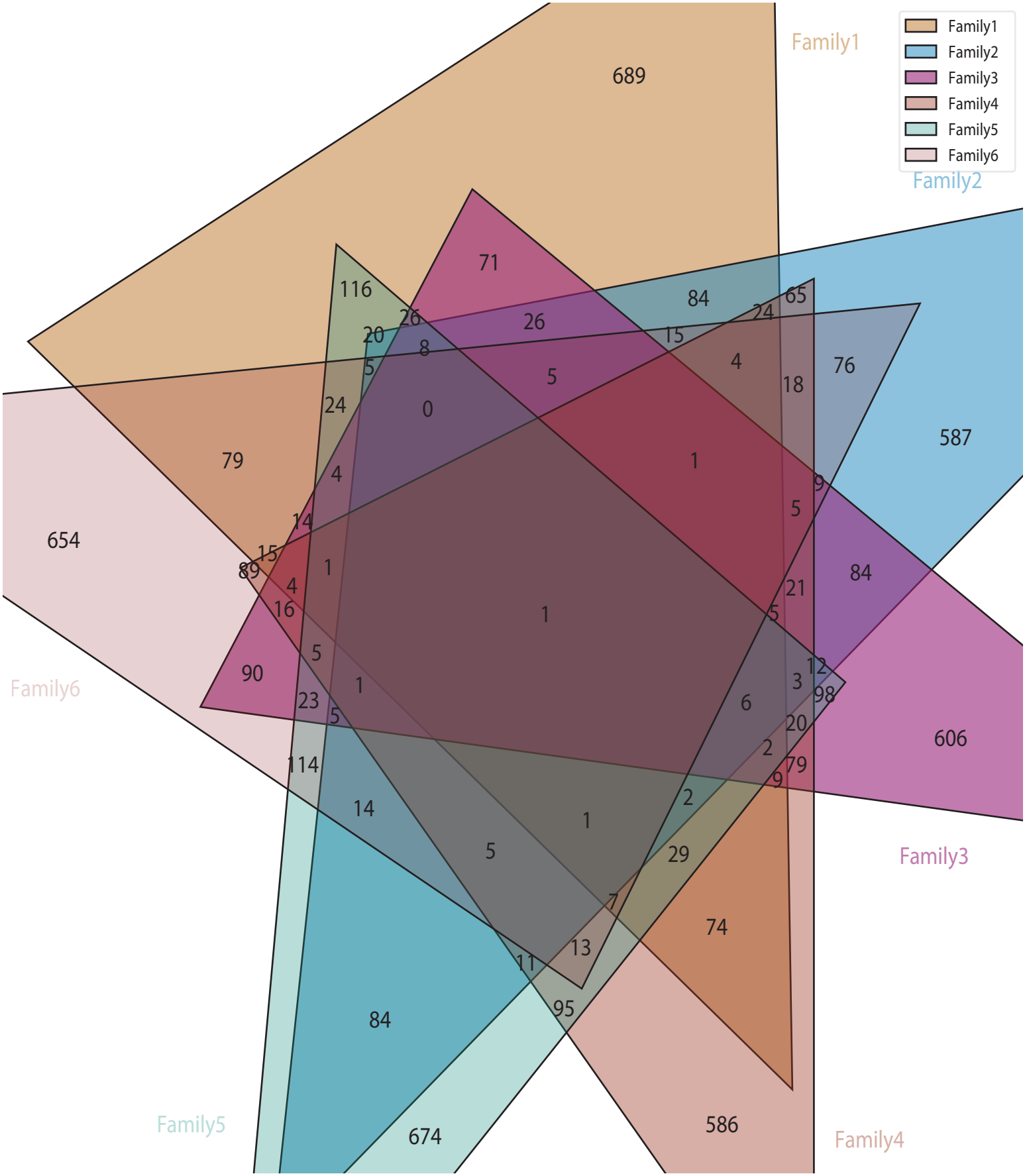
Damaging Homozygous
(CALD Homo-Alt, AMN Het || Homo-Ref)



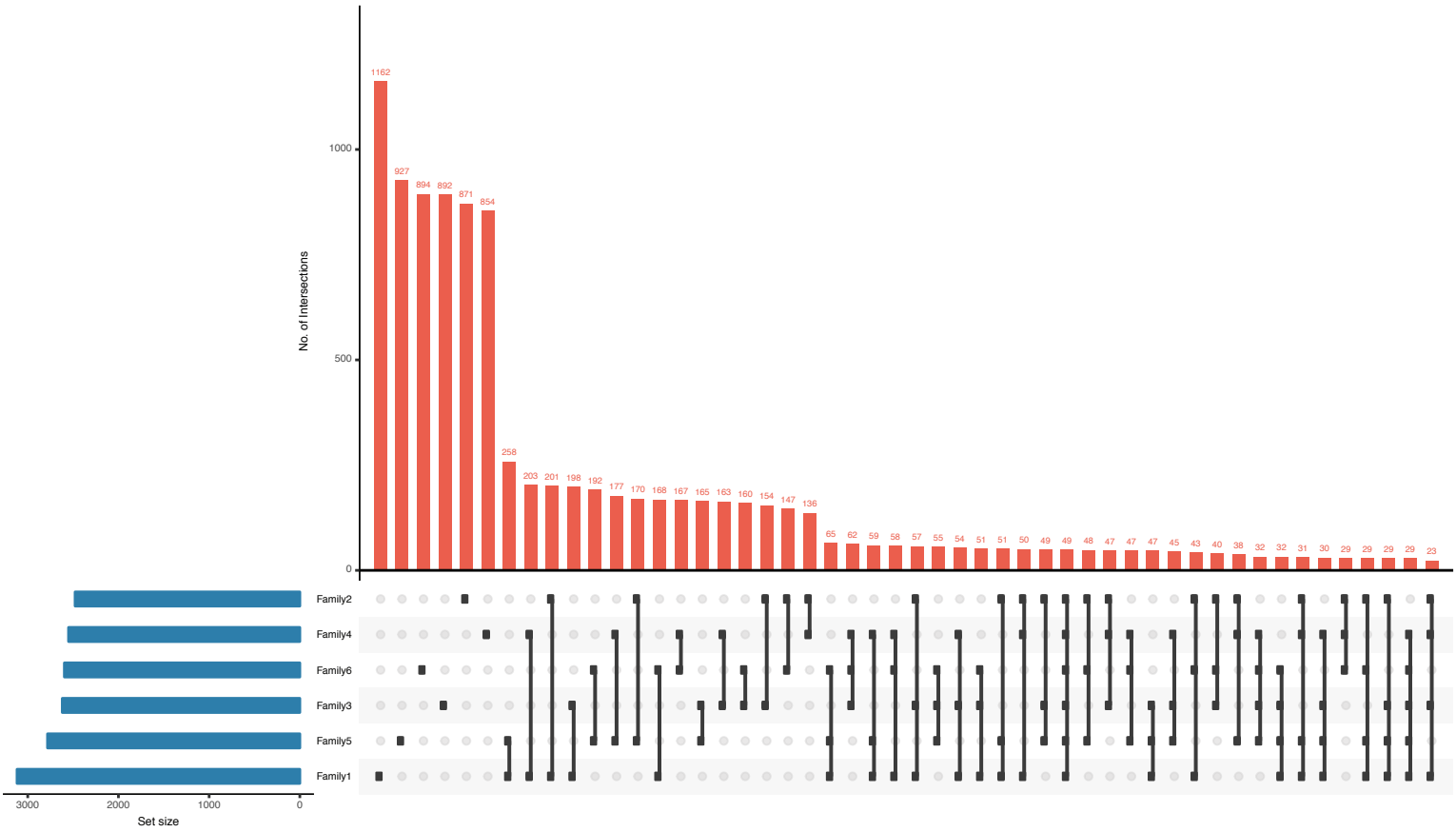
Protective Het/Homo
(AMN Het || Homo-Alt , CALD Homo-Ref)



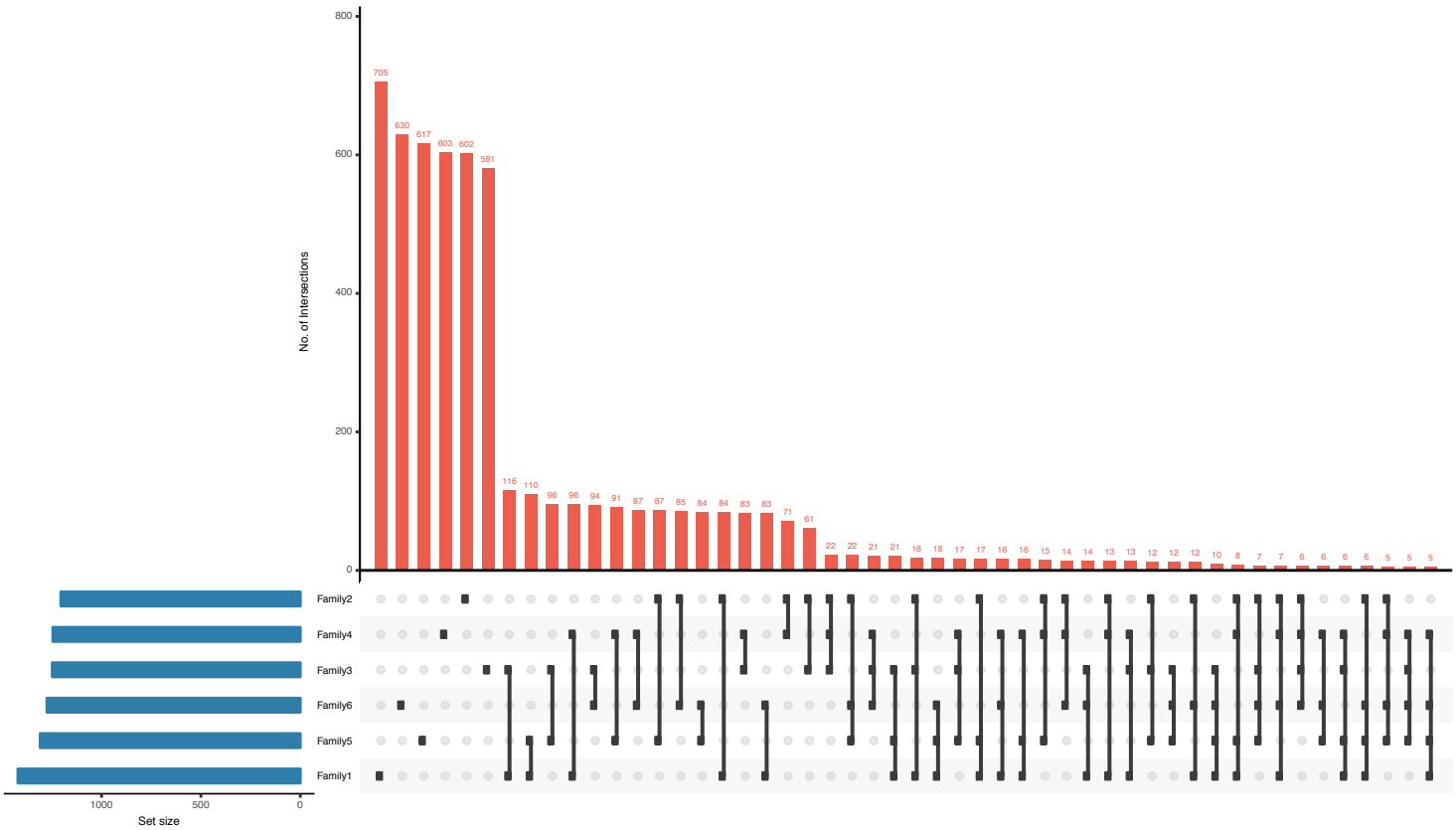
Protective Homo
(AMN Homo-Alt , CALD Het || Homo-Ref)



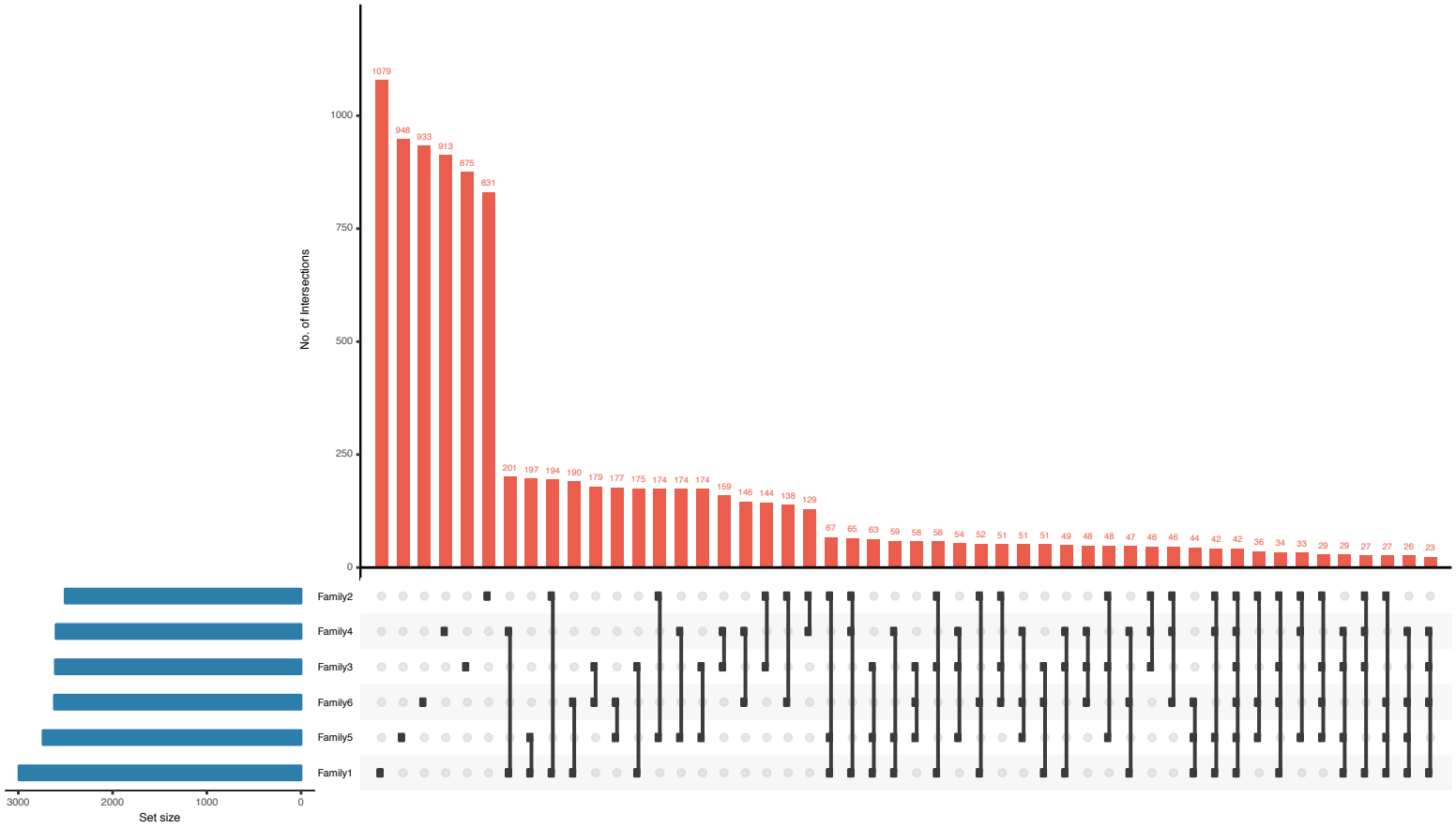
Damaging Het/Homo
(CALD Het || Homo-Alt , AMN Homo-Ref)



Damaging Homozygous
(CALD Homo-Alt, AMN Het || Homo-Ref)



Protective Het/Homo
(AMN Het || Homo-Alt , CALD Homo-Ref)



Protective Homo
(AMN Homo-Alt , CALD Het || Homo-Ref)