Genetic architecture of late onset common disease

- Non-ancestral regulatory variant
- Ancestral regulatory variant
- Ancestral coding variant
- Non-ancestral coding variant

Nonsyndromic protective variants

- Syndromic protective variant

High penetrance of single gene mutation (Mendelian Phenocopy)

Environment

Sporadic late onset disease

Early-onset

Late-onset

Age
Genetic architecture of early onset common disease

Increased number of protective variants enriched by natural selection

Sporadic early onset disease

Single gene mutation

Variable/low penetrance of single gene mutation

Early-onset

Late-onset

Age