

Input
VCF file

Annotate pLoF variants with variant and transcript specific features

Mismapping

Segmental duplication;
pseudogene; paralog

Functional

NMD prediction; Loss of functional, structural domains, disordered regions, post translational modification sites; gene expression in GTex...

Annotation Issue

Non-canonical splice site;
LoF position...

Conservation

GERP score; dN/dS; 1000G, ESP6500 allele frequency; heterozygosity of genes...

Network

Shortest path to disease genes; network centralities...

Pathogenicity prediction

Prediction model

trained on benign, dominant and recessive disease-causing premature stop mutations

Output

Annotated features for pLoFs

3 pathogenicity scores for premature stop and frameshift variants

e.g.	chr	pos	ref	alt	effect	gene	dominant	recessive	benign	prediction
	1	866453	C	T	prematureStop	SAMD11	0.02	0.92	0.06	Recessive