Coding Variation in Subject Z

Gerstein Lab

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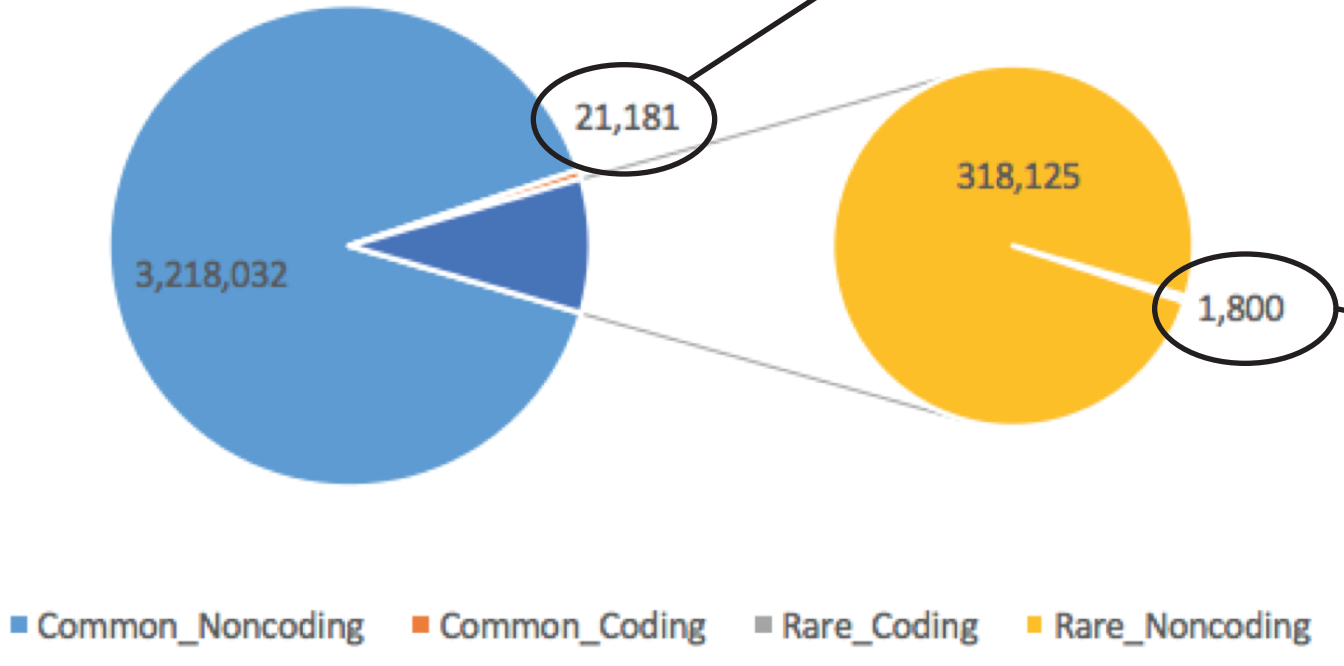
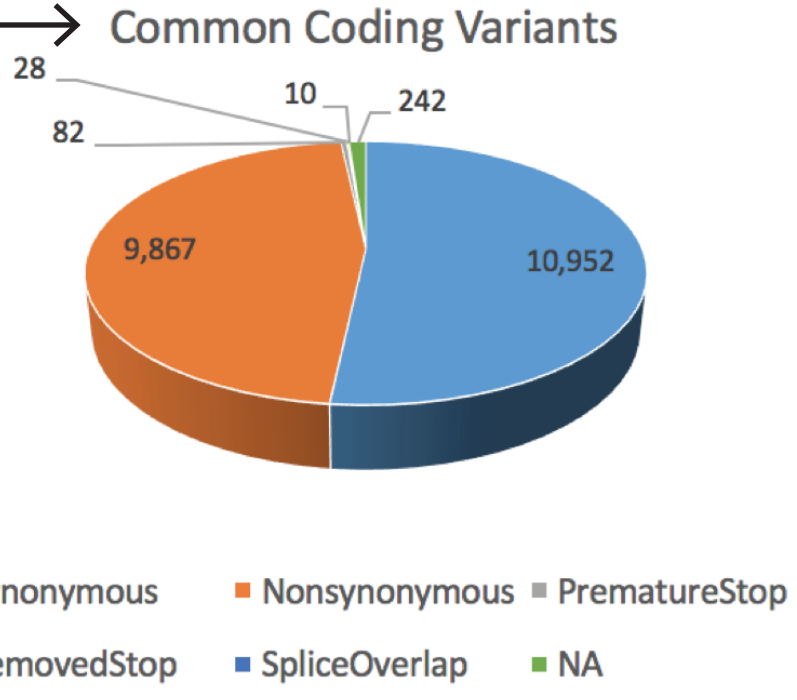
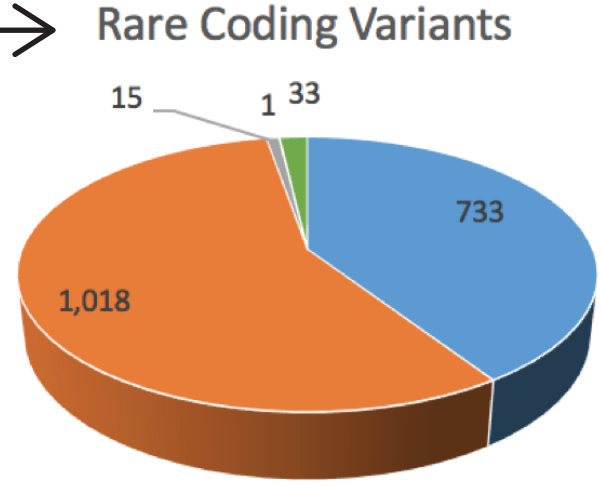
Overview & Coding Variants







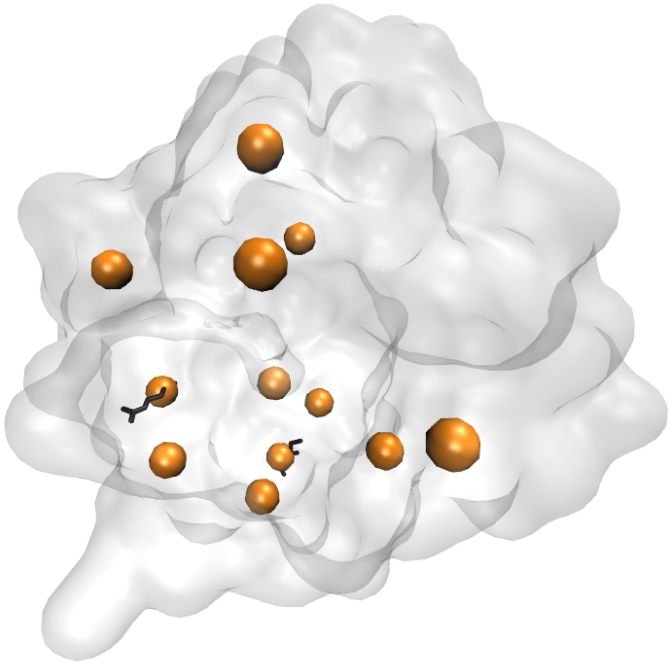
Rare Non-synonymous Coding Variants

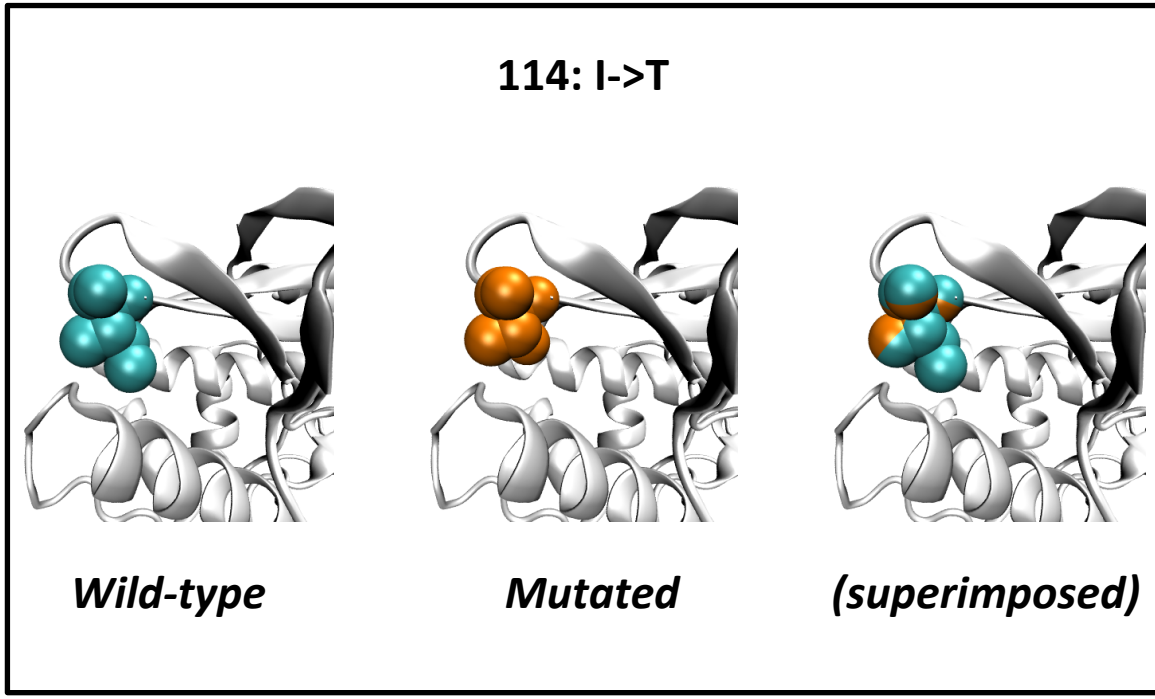
- 1018 SNVs -> 824 target genes

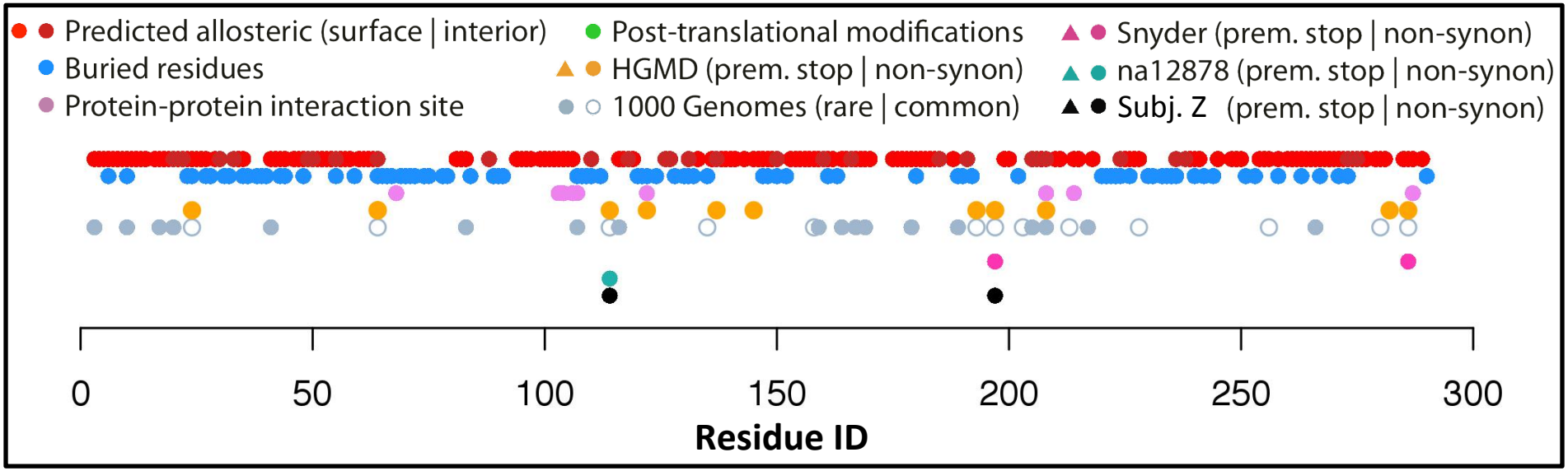
Gene Annotation	Gene Name
Cancer-related	NOTCH2; PDE4DIP; TPR; CRTC3; CDH11; MLLT6; ASXL1; HMGA1; KDM6A
DNA repair	RECQL; RAD51; PPM1D; XRCC1; AP1B1; FANCI; PTPRH; RBBP7; SLX4; POLR2A; DCLRE1C; ANKLE1
Cancer & DNA repair	ATM; PMS2; ERCC5
Actionable Gene	ATM; KDM6A; INSR; FOXP4

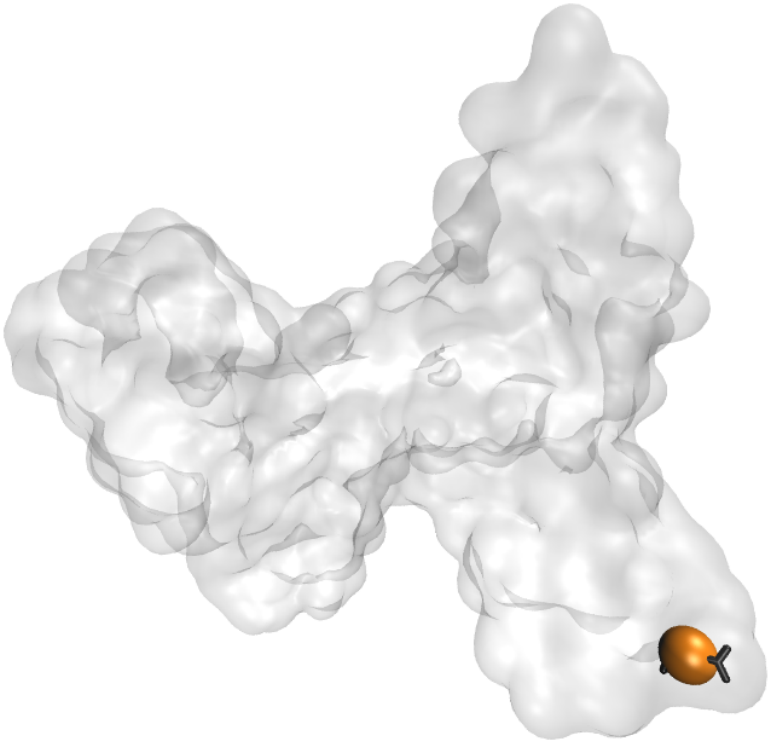
- ATM: Serine/Threonine Kinase; Regulator of p53 and BRCA1; leukemia; ataxia-telangiectasia; breast cancer
- PMS2: Direct p53 effectors; mismatch repair cancer syndrome; colorectal cancer; hereditary nonpolyposis
- ERCC5: Chks in Checkpoint Regulation; DNA Repair; xeroderma pigmentosum
- KDM6A: Transcriptional misregulation in cancer
- INSR: Insulin Receptor; PI3K-Akt signaling pathway; GPCR Pathway; Diabetes mellitus
- FOXP4: Transcriptional repressor that represses lung-specific expression

Arylamine N-acetyltransferase (PDB: 2PFR_A ; gene: NAT2)



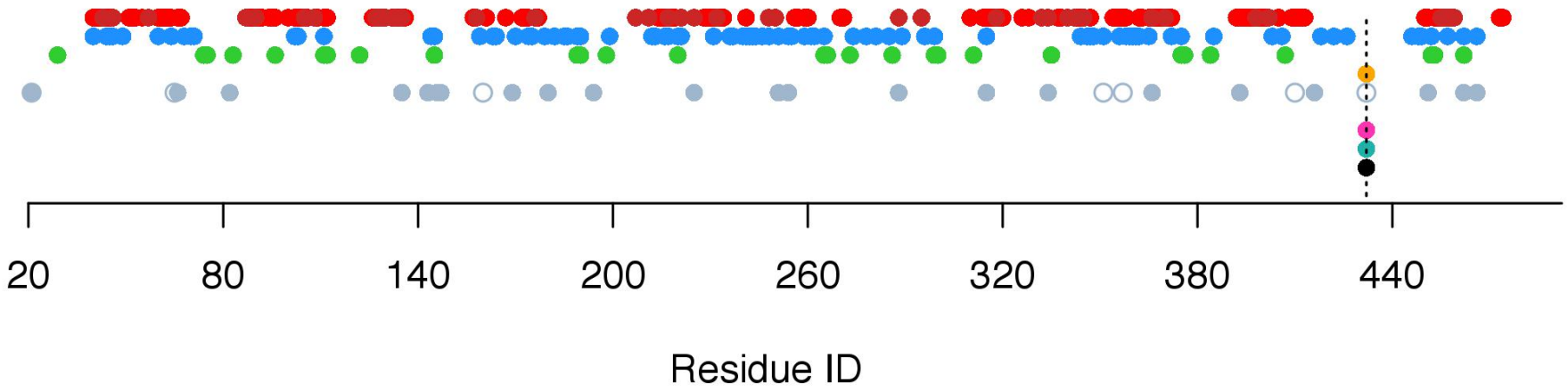




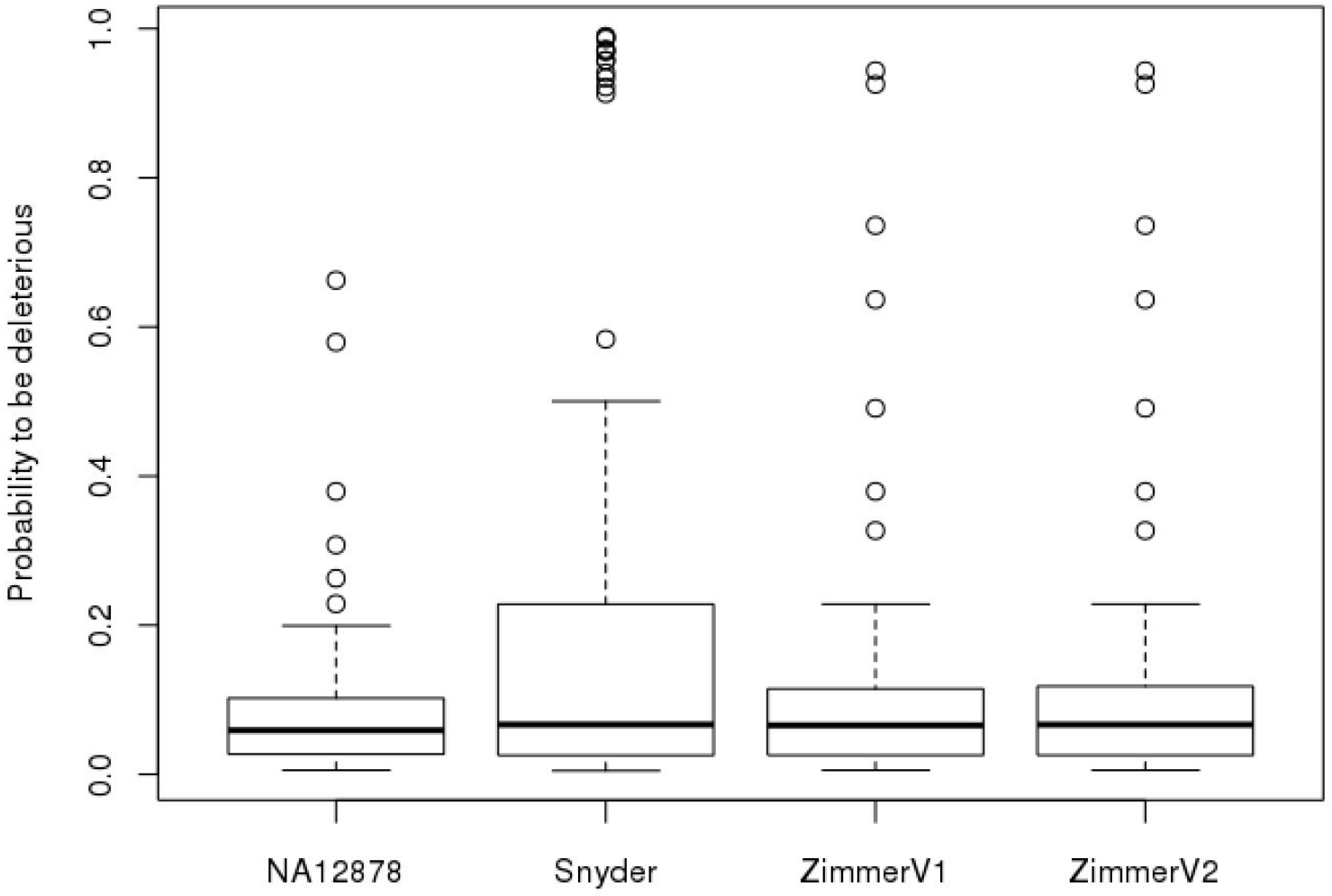


Predicted allosteric (surface | interior)
Buried residues
Protein-protein interaction site
Post-translational modifications
HGMD (prem. stop | non-synon)
1000 Genomes (rare | common)
Snyder (prem. stop | non-synon)
na12878 (prem. stop | non-synon)
Subj. Z (prem. stop | non-synon)

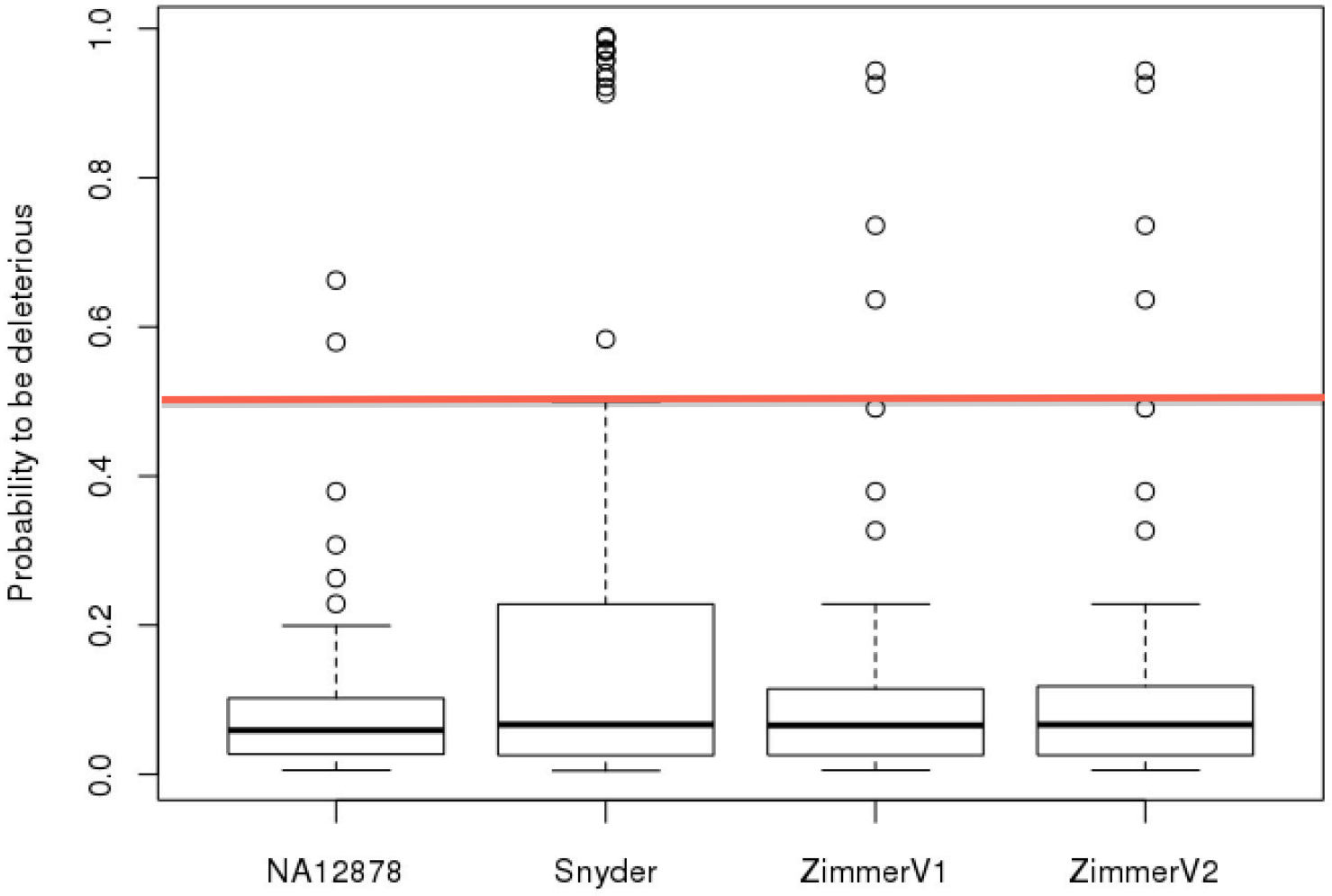
Vitamin D-binding protein (1KW2_A: gene = GC)



LOF variants



LOF variants



LoF variants that are predicted to be the most deleterious (along with their associated genes)

Subject Z

No disease associations in OMIM (but CCDC47 is associated with Schizophrenia)

chr	pos	ref	alt	gene	Score	genotype	Gene function
6	17606162	C	T	FAM8A1	0.94365	0/1	Unknown, Autism related ? Pubmed: 22495306
6	155577717	T	A	TIAM2	0.63655	0/1	Cell migration
17	61829719	A	C	CCDC47	0.92540	0/1	unknown
19	759925	C	A	MISP	0.73605	0/1	Mitotic spindle positioning

Snyder

chr	pos	ref	alt	gene	Score	genotype	OMIM
2	44079970	C	A	ABCG8	0.92190	0/1	Sitosterolemia
2	215854316	T	A	ABCA12	0.97240	0/1	Ichthyosis
2	216240022	G	T	FN1	0.98975	0/1	fibronectin deficiency
9	111718091	G	T	CTNNAL1	0.98845	0/1	
9	130635074	G	T	AK1	0.96915	0/1	Hemolytic anemia
10	29581479	C	A	LYZL1	0.58365	0/1	
11	64056777	C	A	GPR137	0.94075	0/1	
12	18800840	G	T	PIK3C2G	0.95735	0/1	
12	122400030	C	A	WDR66	0.93380	0/1	
14	71570264	C	A	PCNX	0.98635	0/1	
15	68504073	G	T	CLN6	0.97080	0/1	Ceroid lipofuscinosiss
15	93007504	C	A	ST8SIA2	0.91290	0/1	
20	5157344	C	A	CDS2	0.95755	0/1	

Enrichment of genes affected by LoF SNVs in SubjectZ

Significant representation in **olfactory genes**!

Categories Affected by ***Non-Synonymous*** SNVs

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
	SP_PIR_KEYWORDS	polymorphism	RT		556	79.2	5.1E-32	2.5E-29
	SP_PIR_KEYWORDS	alternative splicing	RT		338	48.1	3.8E-8	9.3E-6
	GOTERM_BP_FAT	cellular component morphogenesis	RT		30	4.3	1.7E-4	6.6E-2
	PIR_SUPERFAMILY	PIRSF003152:G protein-coupled olfactory receptor, class II	RT		26	3.7	2.8E-4	3.2E-2
	PIR_SUPERFAMILY	PIRSF800006:rhodopsin-like G protein-coupled receptors	RT		41	5.8	3.1E-4	2.3E-2
	GOTERM_BP_FAT	sensory perception of smell	RT		31	4.4	3.1E-4	9.7E-2
	SP_PIR_KEYWORDS	coiled coil	RT		102	14.5	3.2E-4	1.9E-2
	GOTERM_BP_FAT	cell morphogenesis	RT		27	3.8	3.7E-4	1.0E-1
	GOTERM_BP_FAT	sensory perception of chemical stimulus	RT		33	4.7	4.0E-4	9.3E-2
	SP_PIR_KEYWORDS	olfaction	RT		30	4.3	4.0E-4	2.1E-2
	KEGG_PATHWAY	Olfactory transduction	RT		27	3.8	4.3E-4	2.8E-2
	KEGG_PATHWAY	Antigen processing and presentation	RT		11	1.6	4.7E-4	2.1E-2
	PIR_SUPERFAMILY	PIRSF005491:tumor associated protein MAGE	RT		6	0.9	5.2E-4	2.9E-2

Categories Affected by ***Premature Stop*** SNVs

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
	PIR_SUPERFAMILY	PIRSF800006:rhodopsin-like G protein-coupled receptors	RT		12	14.0	1.3E-5	3.2E-4
	GOTERM_MF_FAT	olfactory receptor activity	RT		10	11.6	4.0E-5	5.3E-3
	GOTERM_BP_FAT	sensory perception of smell	RT		10	11.6	5.4E-5	1.7E-2
	SP_PIR_KEYWORDS	olfaction	RT		10	11.6	7.3E-5	9.2E-3
	GOTERM_BP_FAT	sensory perception of chemical stimulus	RT		10	11.6	1.2E-4	1.9E-2
	INTERPRO	Olfactory receptor	RT		10	11.6	1.4E-4	2.4E-2
	PIR_SUPERFAMILY	PIRSF003152:G protein-coupled olfactory receptor, class II	RT		8	9.3	2.1E-4	2.5E-3
	KEGG_PATHWAY	Olfactory transduction	RT		9	10.5	4.2E-4	1.7E-2
	INTERPRO	GPCR, rhodopsin-like superfamily	RT		12	14.0	4.3E-4	3.7E-2
	INTERPRO	7TM GPCR, rhodopsin-like	RT		12	14.0	4.4E-4	2.5E-2
	SP_PIR_KEYWORDS	g-protein coupled receptor	RT		12	14.0	8.2E-4	5.1E-2
	SP_PIR_KEYWORDS	sensory transduction	RT		10	11.6	1.1E-3	4.7E-2
	GOTERM_BP_FAT	sensory perception	RT		11	12.8	1.4E-3	1.4E-1
	SP_PIR_KEYWORDS	transducer	RT		12	14.0	1.4E-3	4.4E-2
	GOTERM_BP_FAT	G-protein coupled receptor protein signaling pathway	RT		13	15.1	1.6E-3	1.2E-1