

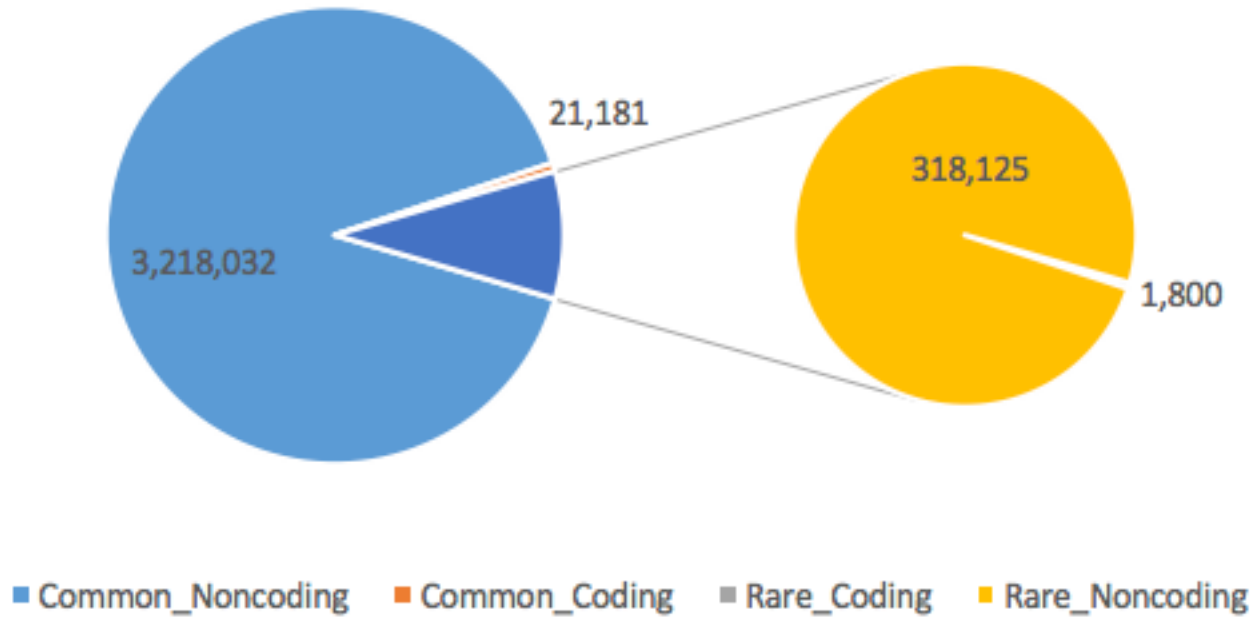
# Coding Variation in Subject Z

With applications using tools developed in the lab:  
STRESS, ALOFT

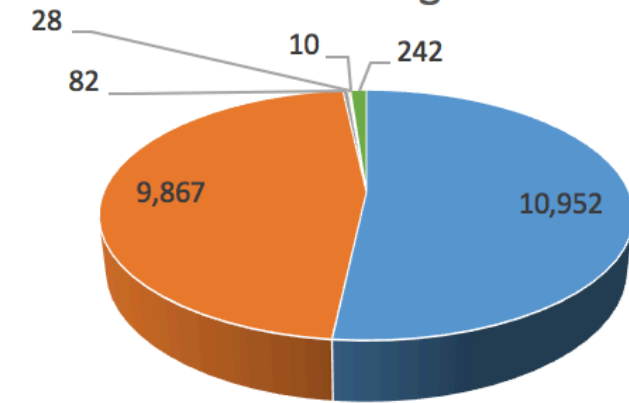
March 1, 2016

# Overview & Coding Variants

## SNVs of Individual Z

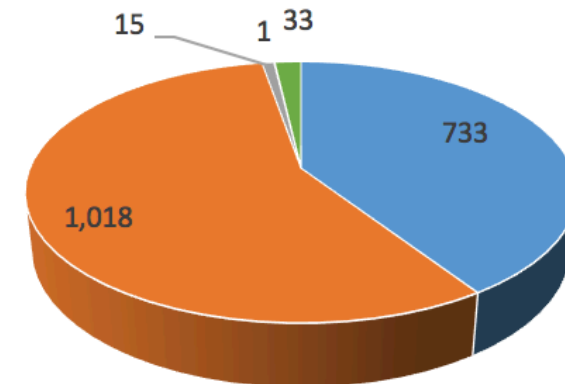


## Common Coding Variants



- Synonymous
- Nonsynonymous
- PrematureStop
- RemovedStop
- SpliceOverlap
- NA

## Rare Coding Variants

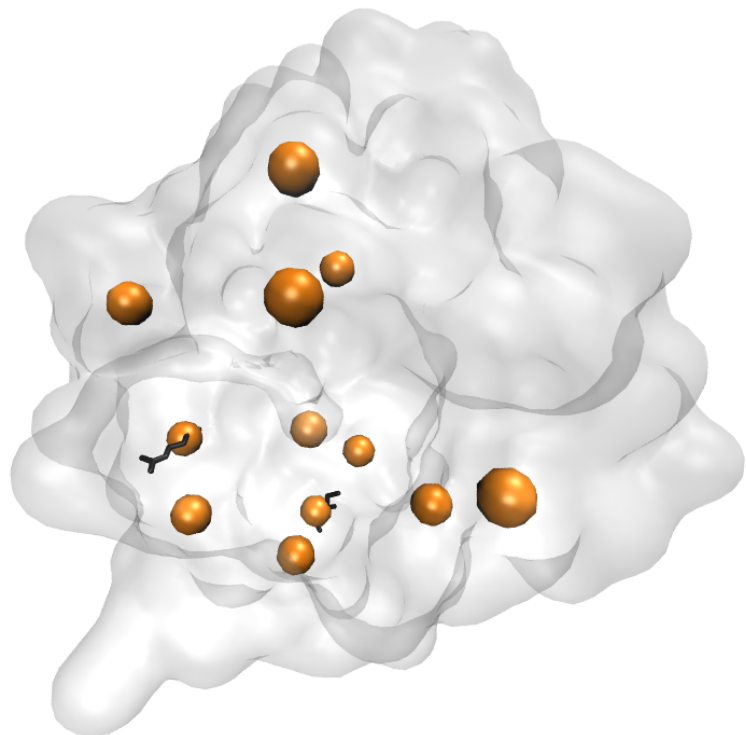


# Rare Non-synonymous Coding Variants

- 1018 SNVs -> **824** target genes

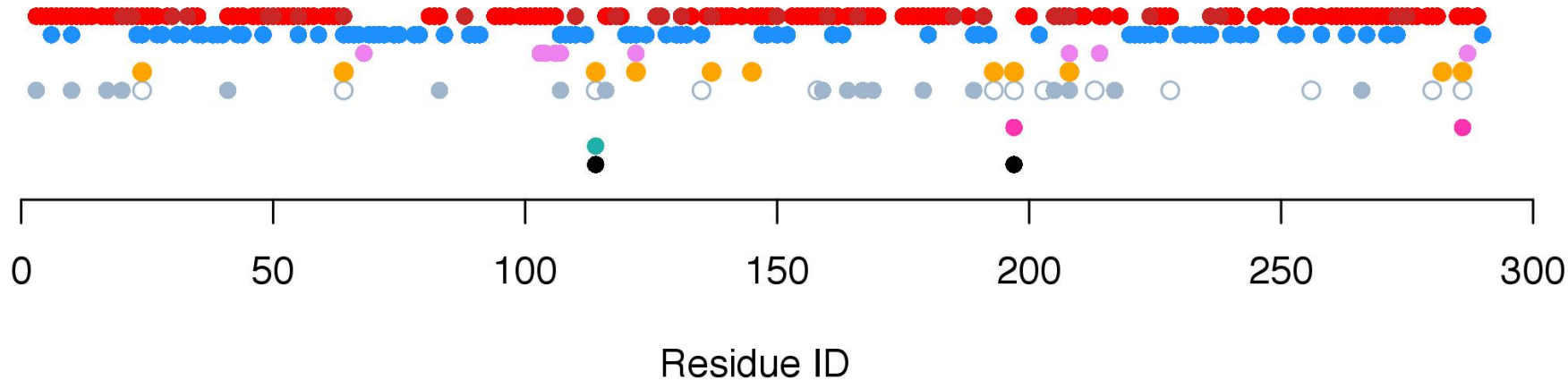
Gene Annotation	Gene Name
Cancer-related	NOTCH2; PDE4DIP; TPR; CRTC3; CDH11; MLLT6; ASXL1; HMGA1; KDM6A
DNA repair	RECQL; RAD51; PPM1D; XRCC1; AP1B1; FANCI; PTPRH; RBBP7; SLX4; POLR2A; DCLRE1C; ANKLE1
Cancer & DNA repair	<b>ATM; PMS2; ERCC5</b>
Actionable Gene	<b>ATM; KDM6A; INSR; FOXP4</b>

- **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

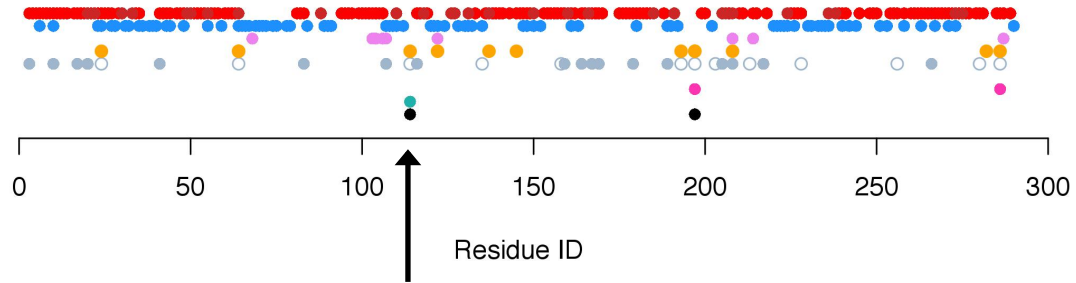


- Predicted allosteric (surface | interior)
- Buried residues
- Protein-protein interaction site
- Post-translational modifications
- ▲ ● HGMD (prem. stop | non-synon)
- ○ 1000 Genomes (rare | common)
- ▲ ● Snyder (prem. stop | non-synon)
- ▲ ● na12878 (prem. stop | non-synon)
- ▲ ● Subj. Z (prem. stop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

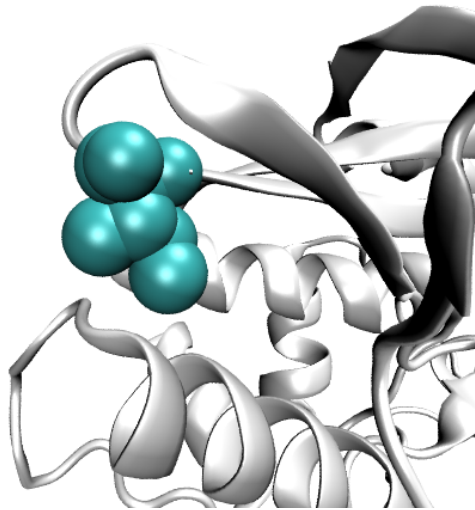
### Arylamine N-acetyltransferase 2 (2PFR\_A: gene = NAT2)



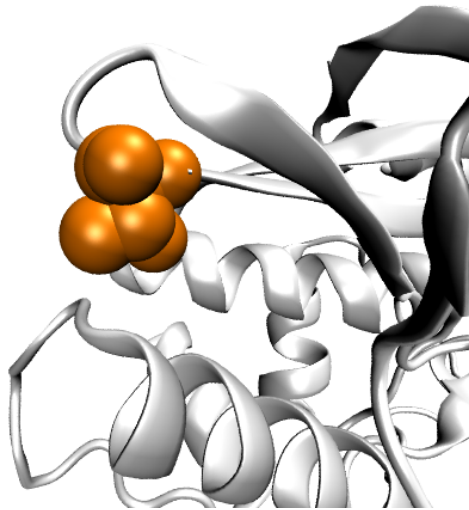
# Arylamine N-acetyltransferase 2 (2PFR\_A: gene = NAT2)



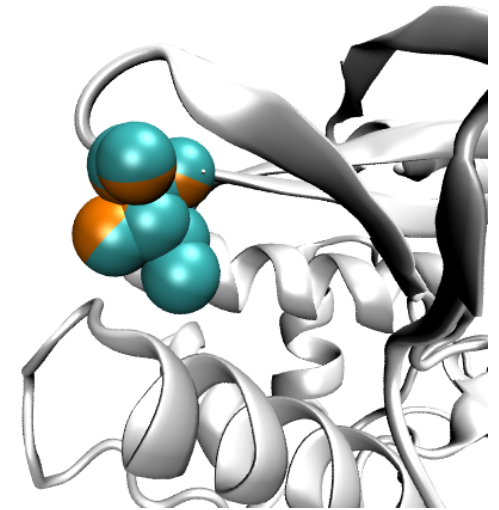
**114: I->T**



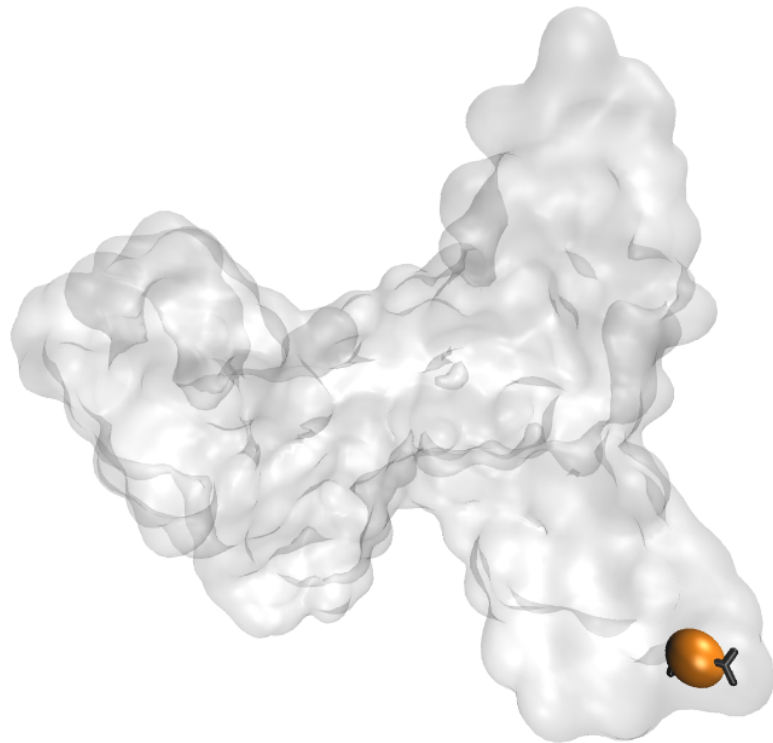
**Wild-type**



**Mutated**

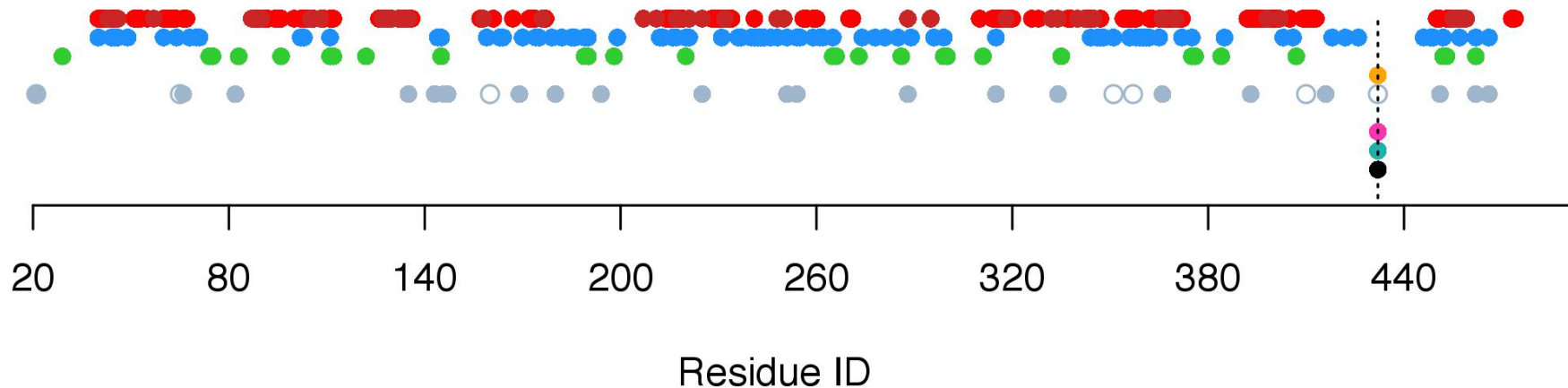


**(superimposed)**

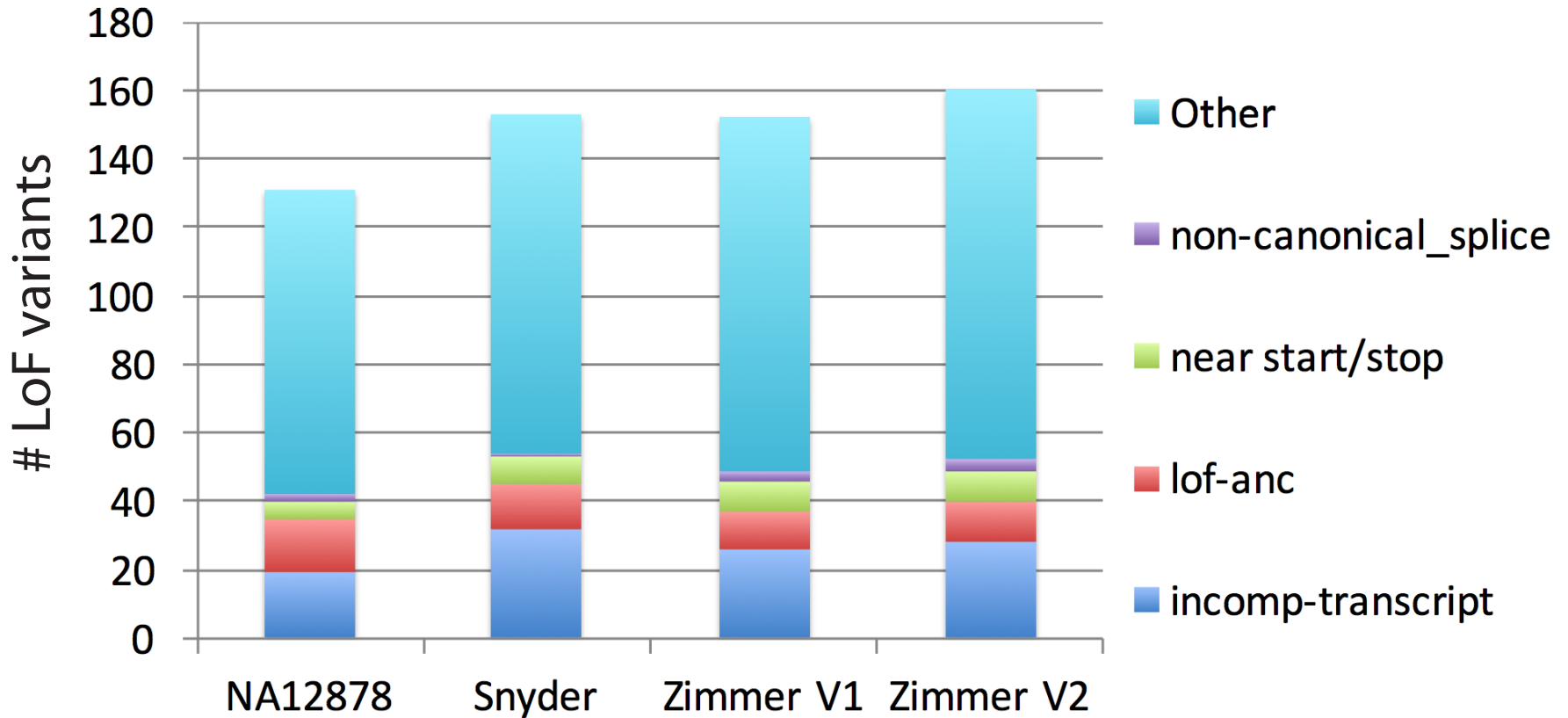


- ● Predicted allosteric (surface | interior)
- Buried residues
- Protein-protein interaction site
- Post-translational modifications
- ▲ ● HGMD (prem. stop | non-synon)
- ○ 1000 Genomes (rare | common)
- ▲ ● Snyder (prem. stop | non-synon)
- ▲ ● na12878 (prem. stop | non-synon)
- ▲ ● Subj. Z (prem.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

### Vitamin D-binding protein (1KW2\_A: gene = GC)

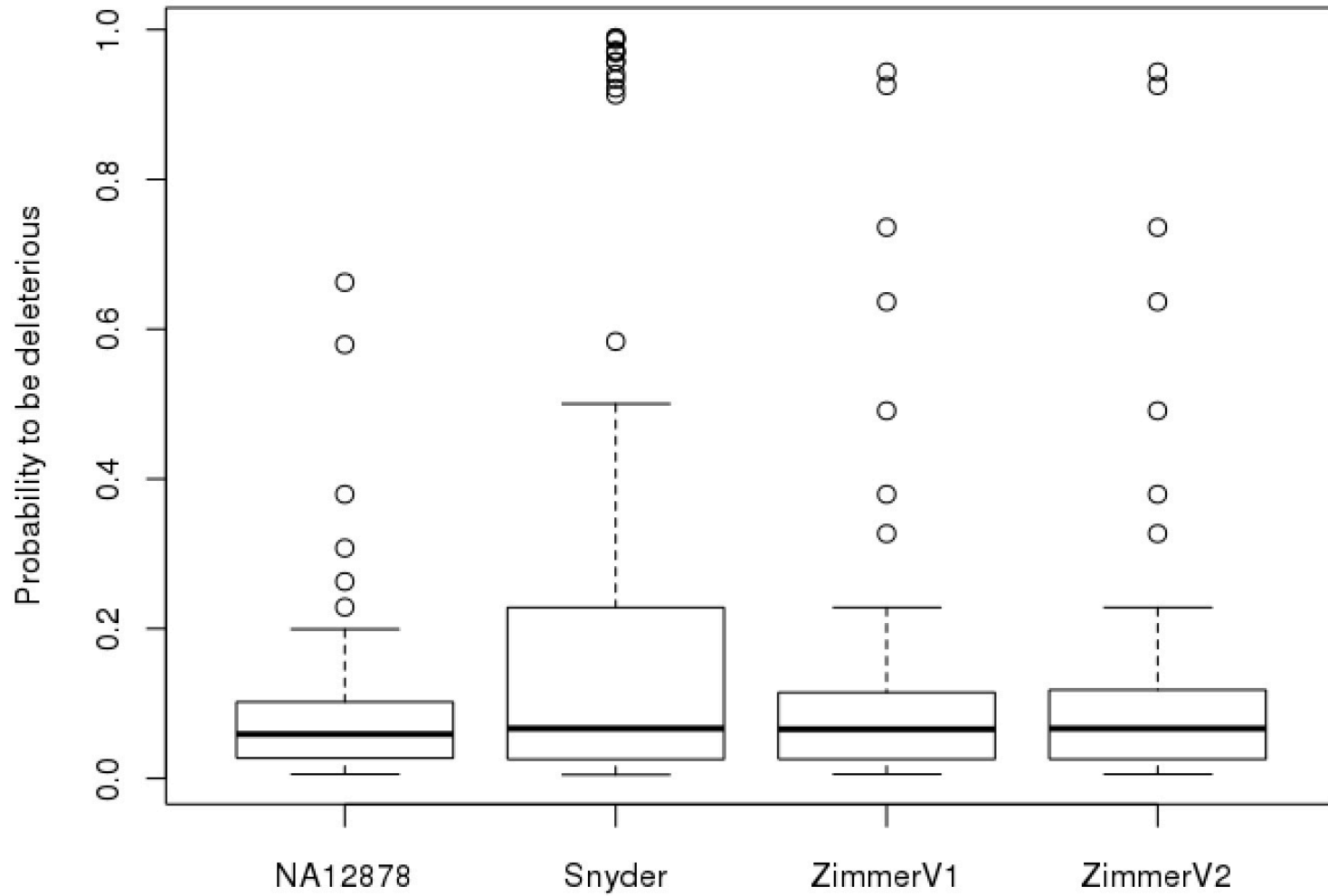


# LoF Variants Across Different Genomes



	Other
NA12878	89 (56 NMD)
Snyder	99 (67 NMD)
Zimmer V1	103 (58 NMD)
Zimmer V2	108 (63 NMD)

# LOF variants





# Potential deleterious variant

## Zimmer

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

No disease associations in OMIM

CCDC47 associated with Schizophrenia

# Potential deleterious variant

**Snyder** .... something is wrong ... (metabolism ???)

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	

**Current Background: Homo sapiens**  
**702 DAVID IDs**

**Options**

Rerun Using Options    Create Sublist

**231 chart records**

[Download File](#)























Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamin
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">polymorphism</a>	RT		556	79.2	5.1E-32	2.5E-29
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">alternative splicing</a>	RT		338	48.1	3.8E-8	9.3E-6
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">glycoprotein</a>	RT		215	30.6	6.7E-8	1.1E-5
<input type="checkbox"/>	INTERPRO	<a href="#">EGF-like region, conserved site</a>	RT		32	4.6	9.6E-8	9.4E-5
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cell adhesion</a>	RT		54	7.7	1.1E-7	2.2E-4
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">biological adhesion</a>	RT		54	7.7	1.1E-7	1.1E-4
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">extracellular matrix structural constituent</a>	RT		16	2.3	4.3E-7	2.7E-4
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">cell adhesion</a>	RT		38	5.4	5.5E-7	6.6E-5
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">plasma membrane</a>	RT		180	25.6	2.1E-6	8.3E-4
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF038286:preferentially expressed antigen of melanoma (PRAME) family protein	RT		8	1.1	3.3E-6	7.5E-4
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">disulfide bond</a>	RT		149	21.2	4.8E-6	4.7E-4
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">homophilic cell adhesion</a>	RT		17	2.4	1.5E-5	9.6E-3
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cell-cell adhesion</a>	RT		26	3.7	1.5E-5	7.6E-3
<input type="checkbox"/>	INTERPRO	<a href="#">EGF-like, type 3</a>	RT		21	3.0	2.7E-5	1.3E-2
<input type="checkbox"/>	INTERPRO	<a href="#">MAGE protein</a>	RT		9	1.3	2.8E-5	9.2E-3
<input type="checkbox"/>	KEGG_PATHWAY	<a href="#">Graft-versus-host disease</a>	RT		9	1.3	4.0E-5	5.3E-3
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">tumor antigen</a>	RT		9	1.3	4.9E-5	4.0E-3
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">egf-like domain</a>	RT		22	3.1	8.7E-5	6.0E-3
<input type="checkbox"/>	INTERPRO	<a href="#">Neuroblastoma breakpoint family</a>	RT		5	0.7	1.1E-4	2.6E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cellular component morphogenesis</a>	RT		30	4.3	1.7E-4	6.6E-2
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF003152:G protein-coupled olfactory receptor, class II	RT		26	3.7	2.8E-4	3.2E-2
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF800006:rhodopsin-like G protein-coupled receptors	RT		41	5.8	3.1E-4	2.3E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">sensory perception of smell</a>	RT		31	4.4	3.1E-4	9.7E-2
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">coiled coil</a>	RT		102	14.5	3.2E-4	1.9E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cell morphogenesis</a>	RT		27	3.8	3.7E-4	1.0E-1
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">sensory perception of chemical stimulus</a>	RT		33	4.7	4.0E-4	9.3E-2
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">olfaction</a>	RT		30	4.3	4.0E-4	2.1E-2
<input type="checkbox"/>	KEGG_PATHWAY	<a href="#">Olfactory transduction</a>	RT		27	3.8	4.3E-4	2.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	<a href="#">Antigen processing and presentation</a>	RT		11	1.6	4.7E-4	2.1E-2
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF005491:tumor associated protein MAGE	RT		6	0.9	5.2E-4	2.9E-2

**Current Gene List: z.premature.list****Current Background: Homo sapiens****86 DAVID IDs****Options**

Rerun Using Options

Create Sublist

**43 chart records** **Download File**

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF800006:rhodopsin-like G protein-coupled receptors	<a href="#">RT</a>		12	14.0	1.3E-5	3.2E-4
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">olfactory receptor activity</a>	<a href="#">RT</a>		10	11.6	4.0E-5	5.3E-3
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">sensory perception of smell</a>	<a href="#">RT</a>		10	11.6	5.4E-5	1.7E-2
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">olfaction</a>	<a href="#">RT</a>		10	11.6	7.3E-5	9.2E-3
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">sensory perception of chemical stimulus</a>	<a href="#">RT</a>		10	11.6	1.2E-4	1.9E-2
<input type="checkbox"/>	INTERPRO	<a href="#">Olfactory receptor</a>	<a href="#">RT</a>		10	11.6	1.4E-4	2.4E-2
<input type="checkbox"/>	PIR_SUPERFAMILY	PIRSF003152:G protein-coupled olfactory receptor, class II	<a href="#">RT</a>		8	9.3	2.1E-4	2.5E-3
<input type="checkbox"/>	KEGG_PATHWAY	<a href="#">Olfactory transduction</a>	<a href="#">RT</a>		9	10.5	4.2E-4	1.7E-2
<input type="checkbox"/>	INTERPRO	<a href="#">GPCR, rhodopsin-like superfamily</a>	<a href="#">RT</a>		12	14.0	4.3E-4	3.7E-2
<input type="checkbox"/>	INTERPRO	<a href="#">7TM GPCR, rhodopsin-like</a>	<a href="#">RT</a>		12	14.0	4.4E-4	2.5E-2
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">g-protein coupled receptor</a>	<a href="#">RT</a>		12	14.0	8.2E-4	5.1E-2
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">sensory transduction</a>	<a href="#">RT</a>		10	11.6	1.1E-3	4.7E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">sensory perception</a>	<a href="#">RT</a>		11	12.8	1.4E-3	1.4E-1
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">transducer</a>	<a href="#">RT</a>		12	14.0	1.4E-3	4.4E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">G-protein coupled receptor protein signaling pathway</a>	<a href="#">RT</a>		13	15.1	1.6E-3	1.2E-1
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">disulfide bond</a>	<a href="#">RT</a>		24	27.9	2.9E-3	7.0E-2
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cognition</a>	<a href="#">RT</a>		11	12.8	3.3E-3	1.9E-1
<input type="checkbox"/>	UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	<a href="#">RT</a>		30	34.9	3.6E-3	7.1E-1
<input type="checkbox"/>	UP_SEQ_FEATURE	disulfide bond	<a href="#">RT</a>		23	26.7	3.7E-3	4.7E-1
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">glycoprotein</a>	<a href="#">RT</a>		31	36.0	3.9E-3	7.8E-2
<input type="checkbox"/>	UP_SEQ_FEATURE	transmembrane region	<a href="#">RT</a>		33	38.4	6.7E-3	5.4E-1
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">neurological system process</a>	<a href="#">RT</a>		12	14.0	8.5E-3	3.7E-1
<input type="checkbox"/>	SP_PIR_KEYWORDS	<a href="#">transmembrane</a>	<a href="#">RT</a>		33	38.4	9.0E-3	1.5E-1