Supplemental Information

Human mutational constraint as a tool to understand biology of rare and emerging bone marrow failure syndromes

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Supplemental Table S1: Demographic Data For 125,748 Exomes in gnomAD v2.1.1[1,2]

Sex	
Males	67,691
Females	57,787
Ethnicity	
African American	8,128
Latino	17,296
Ashkenazi Jewish	5,040
East Asian	9,197
Finnish	10,824
Non-Finnish European	56,885
South Asian	15,308
Other	3,070
Age	
<30	2,547
30-39	8,069
40-49	18,842
50-59	24,626
60-69	19,416
70-79	10,127
>80	1,935

[1] Karczewski KJ, Francioli LC, Tiao G, et al. The mutational constraint spectrum quantified from variation in 141,456 humans. *Nature*. 2020;581(7809):434-443.
[2] https://gnomad.broadinstitute.org/faq

Supplemental Table S2: Cohorts from which gnomAD exomes and genomes were derived[3,4]

1000 Genomes
1958 Birth Cohort
African American Coronary Artery Calcification project (AACAC)
ALSGEN
Alzheimer's Disease Sequencing Project (ADSP)
Atrial Fibrillation Genetics Consortium (AFGen)
    Duke Catheterization Genetics (CATHGEN)
Bangladesh Risk of Acute Vascular Events (BRAVE) Study
BioMe Biobank
Bulgarian Trios
COPD-Gene
Estonian Genome Center, University of Tartu (EGCUT)
Finland-United States Investigation of NIDDM Genetics (FUSION)
Finnish Migraine Study
Finnish Twin Cohort Study
FINN-ADGEN
FINRISK
Framingham Heart Study
Genetics of Cardiometabolic Health in the Amish
Génome Québec - Genizon Biobank
Genomic Psychiatry Cohort
GoT2D
Genotype-Tissue Expression Project (GTEx)
Health2000
Inflammatory Bowel Disease:
    1000IBD project
    Helsinki University Hospital Finland
    NIDDK IBD Genetics Consortium
    Quebec IBD Genetics Consortium
Jackson Heart Study
Jewish Genome Project - funded by Bonei Olam

[3] Karczewski KJ, Francioli LC, Tiao G, et al. The mutational constraint spectrum quantified from variation in 141,456 humans. *Nature*. 2020;581(7809):434-443.
[4] https://gnomad.broadinstitute.org/about

Kuopio Alzheimer Study
LifeLines Cohort
Lung Tissue Research Consortium (LTRC)
McLean Program for Neuropsychiatric Research, Psychotic Disorders Division
MESTA
METabolic Syndrome In Men (METSIM)
Multi-Ethnic Study of Atherosclerosis (MESA)
Myocardial Infarction Genetics Consortium (MIGen):
    Leicester Exome Seq
    North German MI Study
    Ottawa Genomics Heart Study
    Pakistan Risk of Myocardial Infarction Study (PROMIS)
    Precocious Coronary Artery Disease Study (PROCARDIS)
    Registre Gironi del COR (REGICOR)
    South German MI Study
    Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO)
National Institute of Mental Health (NIMH) Controls
NHGRI CCDG
NHLBI-GO Exome Sequencing Project (ESP)
NHLBI TOPMed
Population Architecture Using Genomics and Epidemiology (PAGE) Consortium
Pritzker Neuropsychiatric Disorders Research Consortium
Schizophrenia Trios from Taiwan
Sequencing Initiative Suomi (SiSu)
SIGMA-T2D
SubPopulations and InteRmediate Outcome Measures In COPD Study (SPIROMICS)
Swedish Schizophrenia & Bipolar Studies
T2D-GENES
    GoDARTS
T2D-SEARCH
The Cancer Genome Atlas (TCGA)
Whole Genome Sequencing in Psychiatric Disorders (WGSPD)
Women's Health Initiative (WHI)

Supplemental Table S3: Observed unique pLoF Variants in 125,748 exomes of gnomAD v2.1.1 compared to 71,702 genomes of gnomAD v3.0

Gene	OMIM	Observed Unique pLoF (SNVs) in gnomAD 2.1.1 exomes (n=125,748)	Prevalence of unique pLoF in gnomAD 2.1.1 exomes	Observed Unique pLoF (SNVs) in gnomAD 3.0 (n=71,702)	Prevalence of unique PLoF in gnomAD 3.0 genomes	Observed Unique pLoF (SNVs) in gnomAD 2.1.1 genomes (n=15,708)	Prevalence of unique pLoF in gnomAD 2.1.1 genomes
MDM4	602704	0	0.0	0	0.0		
TERT	187270	7	$5.6x10^{-5}$	6	$8.4x10^{-5}$		
NAF1	617868	2	$1.6x10^{-5}$	3	$4.2x10^{-5}$		
ZCCHC8	616381	5	$4.0x10^{-5}$	5	$7.0x10^{-5}$		
POT1	606478	6	$4.8x10^{-5}$	6	$8.4x10^{-5}$		
RTEL1	608833	29	$2.3x10^{-4}$	14	$2.0x10^{-4}$		
PARN	604212	14	$1.1x10^{-4}$	10	$1.4x10^{-4}$		
TINF2	604319	9	$7.2x10^{-5}$	7	$9.8x10^{-5}$		
ACD	609377	21	$1.7x10^{-4}$	***	***	4	$2.5x10^{-4}$
DKC1	300126	1	$8.0x10^{-6}$	1	$1.4x10^{-5}$		
WRAP53	612661	12	$9.5x10^{-5}$	***	***	2	$1.3x10^{-4}$
CTC1	613129	29	$2.3x10^{-4}$	***	***	6	$3.8x10^{-4}$
STN1	613128	17	$1.4x10^{-4}$	9	$1.3x10^{-4}$		
NOP10	606471	0	0.0	2	$2.8x10^{-5}$		
NHP2	606470	3	$2.4x10^{-5}$	3	$4.2x10^{-5}$		
SRP54	604857	2	$1.6x10^{-5}$	***	***	0	0.0
GFI1	600871	4	$3.2x10^{-5}$	***	***	1	$6.4x10^{-5}$
WAS	300392	0	0.0	0	0.0		
TAZ	300394	2	$1.6x10^{-5}$	1	$1.4x10^{-5}$		
WIPF1	602357	2	$1.6x10^{-5}$	2	$2.8x10^{-5}$		
LYST	606897	44	$3.5x10^{-4}$	25	$3.5x10^{-4}$		
VPS45	610035	15	$1.2x10^{-4}$	***	***	3	$1.9x10^{-4}$
VPS13B	607817	105	$8.4x10^{-4}$	70	$9.8x10^{-4}$		
DNAJC21	617048	17	$1.4x10^{-4}$	***	***	8	$5.1x10^{-4}$
CSF3R	138971	23	$1.8x10^{-4}$	***	***	1	$6.4x10^{-5}$
USB1	613276	7	$5.6x10^{-5}$	3	$4.2x10^{-5}$		
G6PC3	611045	11	$8.7x10^{-5}$	5	$7.0x10^{-5}$		
SBDS	607444	8	$6.4x10^{-5}$	7	$9.8x10^{-5}$		
HAX1	605998	12	$9.5x10^{-5}$	3	$4.2x10^{-5}$		
RAB27A	603868	10	$8.0x10^{-5}$	***	***	2	$1.3x10^{-4}$
LAMTOR2	610389	2	$1.6x10^{-5}$	1	$1.4x10^{-5}$		
KIF23	605064	4	$3.2x10^{-5}$	3	$4.2x10^{-5}$		
RPL5	603634	0	0.0	***	***	0	0.0
SLC2A1	138140	1	$8.0x10^{-6}$	0	0.0		
RPL19	180466	0	0.0	1	$1.4x10^{-5}$		
RPL15	604174	0	0.0	***	***	0	0.0
RPL18	618310	0	0.0	1	$1.4x10^{-5}$		
RPS7	603658	0	0.0	0	0.0		

RPS10	603632	0	0.0	***	***	0	0.0
RPL11	604175	0	0.0	0	0.0		
KLF1	600599	7	$5.6x10^{-5}$	7	$9.8x10^{-5}$		
RPS19	603474	0	0.0	0	0.0		
RPL26	603704	0	0.0	***	***	0	0.0
RPL35A	180468	0	0.0	0	0.0		
RPL27	607526	0	0.0	0	0.0		
RPS26	603701	0	0.0	0	0.0		
RPS27	603702	0	0.0	0	0.0		
RPL31	617415	0	0.0	0	0.0		
RPL35	618315	1	$8.0x10^{-6}$	1	$1.4x10^{-5}$		
RPS15A	603674	0	0.0	0	0.0		
RPS24	602412	1	$8.0x10^{-6}$	***	***	0	0.0
RPS29	603633	1	$8.0x10^{-6}$	***	***	0	0.0
RPS28	603685	0	0.0	0	0.0		
RPS17	180472	*	*	*	*	*	*
ALAS2	301300	0	0.0	0	0.0		
TSR2	300945	0	0.0	0	0.0		
CDAN1	607465	30	$2.4x10^{-4}$	24	$3.5x10^{-4}$		
SEC23B	610512	37	$2.9x10^{-4}$	***	***	8	$5.1x10^{-4}$
CECR1	607575	14	$1.1x10^{-4}$	***	***	3	$1.9x10^{-4}$
SLC25A38	610819	10	$8.0x10^{-5}$	***	***	3	$1.9x10^{-4}$
GLRX5	609588	0	0.0	2	$2.8x10^{-5}$		
FANCB	300515	1	$8.0x10^{-6}$	0	0.0		
RAD51	179617	6	$4.8x10^{-5}$	***	***	1	$6.4x10^{-5}$
NHEJ1	611290	7	$5.6x10^{-5}$	3	$4.2x10^{-5}$		
FANCM	609644	40	$3.2x10^{-4}$	23	$3.2x10^{-4}$		
BRCA2	600185	61	$4.9x10^{-4}$	45	$6.3x10^{-4}$		
ATM	607585	103	$8.2x10^{-4}$	72	$1.0x10^{-3}$		
ERCC6L2	615667	17	$1.4x10^{-4}$	***	***	8	$5.1x10^{-4}$
FANCD2	613984	60	$4.8x10^{-4}$	30	$4.2x10^{-4}$		
FANCE	613976	13	$1.0x10^{-4}$	11	$1.5x10^{-4}$		
SLX4	613278	45	$3.6x10^{-4}$	20	$2.8x10^{-4}$		
LIG4	601837	13	$1.0x10^{-4}$	3	$4.2x10^{-5}$		
ESCO2	609353	15	$1.2x10^{-4}$	6	$8.4x10^{-5}$		
ERCC4	133520	25	$2.0x10^{-4}$	17	$2.4x10^{-4}$		
FANCC	613899	24	$1.9x10^{-4}$	22	$3.1x10^{-4}$		
FANCI	611360	63	$5.0x10^{-4}$	32	$4.5x10^{-4}$		
NBN	602667	30	$2.4x10^{-4}$	16	$2.2x10^{-4}$		
DDX11	601150	40	$3.2x10^{-4}$	***	***	8	$5.1x10^{-4}$
PALB2	610355	35	$2.8x10^{-4}$	20	$2.8x10^{-4}$		
BRCA1	113705	55	$4.4x10^{-4}$	***	***	9	$5.7x10^{-4}$
FANCG	602956	25	$2.0x10^{-4}$	19	$2.6x10^{-4}$		
FANCA	607139	96	$7.6x10^{-4}$	47	$6.6x10^{-4}$		
RAD51C	602774	20	$1.6x10^{-4}$	13	$1.8x10^{-4}$		
FANCL	608111	31	$2.5x10^{-4}$	***	***	3	$1.9x10^{-4}$
FANCF	613897	0	0.0	0	0.0		
MECOM	165215	5	$4.0x10^{-5}$	***	***	0	0.0

PAX5	167414	0	0.0	0	0.0		
ETV6	600618	3	$2.4x10^{-5}$	3	$4.2x10^{-5}$		
GATA2	137295	1	$8.0x10^{-6}$	0	0.0		
FLI1	193067	2	$1.6x10^{-5}$	1	$1.4x10^{-5}$		
SRP72	602122	13	$1.0x10^{-4}$	***	***	1	$6.4x10^{-5}$
RUNX1	151385	0	0.0	3	$4.2x10^{-5}$		
CBL	165360	14	$1.1x10^{-4}$	9	$1.3x10^{-4}$		
DDX41	608170	18	$1.4x10^{-4}$	***	***	4	$2.5x10^{-4}$
GFI1B	604383	10	$8.0x10^{-5}$	5	7.0x10-5		
SAMD9L	611170	32	$2.5x10^{-4}$	20	$2.8x10^{-4}$		
SAMD9	610456	51	$4.1x10^{-4}$	38	$5.3x10^{-4}$		
HOXA11	142958	0	0.0	1	$1.4x10^{-5}$		
CEBPA	116897	0	0.0	1	$1.4x10^{-5}$		
GATA1	305371	0	0.0	0	0.0		
AK2	103020	8	$6.4x10^{-5}$	***	***	1	$6.4x10^{-5}$

*** For validation, we used two independent genome datasets of 71,702 sequenced genomes included in gnomAD v3.0 and 15,708 genomes included in gnomAD v.2.1.1. Using gnomAD v3.0 we were able to determine the number of high-confidence pLoF variants in 73/100 genes. The 27 genes that could not be accurately analyzed in gnomAD3.0 due to differeces in the genome builds and canonical transcript mapping, were analyzed using another cohort of 15,708 genomes included in gnomAD v.2.1.1. These genomes are in addition to the 125,748 exomes in gnomAD v2.1.1 that we analyzed in our manuscript and are included as a subset of the 71,702 genomes in v3.0. Notably, there are certain important limitations in making direct comparisons between v2.1.1. and v3.0 stemming from different genome builds (GRCh37/hg19 built with Gencode v19 and VEP v85 for v2.1.1 compared to GRCh38 built using Gencode v29 and VEP v95 for v3.0), and comparing exome to genome data. Rather, we present this as a survey to show that there are no significant enrichments or depletions of unique SNV pLoF variants in the gnomAD v2.1.1 exome cohort.

Supplemental Table S4: Demographic Data For 71,702 Genomes in gnomAD v3.0[5]

Sex	
Males	34,752
Females	36,950
Ethnicity	
African American	21,042
Amish	450
Latino	6,835
Ashkenazi Jewish	1,662
East Asian	1,567
Finnish	5,244
Non-Finnish European	32,399
South Asian	1,526
Other	1,077

[5] https://gnomad.broadinstitute.org/faq

Supplemental Table S5: Frequency of pLOF Variants in IBMF Genes Distributed By Decade of Life

Frequency of pLoF Variants Distributed By Age (n=85462)							
Gene	**Frequency <30 (n=2,547)**	**Frequency 30-39 (n=8069)**	**Frequency 40-49 (n=18842)**	**Frequency 50-59 (n=24626)**	**Frequency 60-69 (n=19416)**	**Frequency 70-79 (n=10127)**	**Frequency >80 (n=1,935)**
MDM4	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TERT	$3.93x10^{-4}$	$3.72x10^{-4}$	$2.12x10^{-4}$	$1.62x10^{-4}$	$2.58x10^{-4}$	$1.97x10^{-4}$	0.000
NAF1	0.000	0.000	$5.31x10^{-5}$	$4.06x10^{-5}$	$1.03x10^{-4}$	$1.97x10^{-4}$	0.000
ZCCHC8	$3.93x10^{-4}$	$1.24x10^{-4}$	$5.31x10^{-5}$	0.000	$1.03x10^{-4}$	0.000	0.000
POT1	$3.93x10^{-4}$	$4.96x10^{-4}$	$3.72x10^{-4}$	$1.22x10^{-4}$	$2.58x10^{-4}$	$9.87x10^{-5}$	$5.17x10^{-4}$
RTEL1	$3.93x10^{-4}$	$6.20x10^{-4}$	$5.84x10^{-4}$	$8.53x10^{-4}$	$4.64x10^{-4}$	$6.91x10^{-4}$	$1.03x10^{-3}$
PARN	0.000	$9.9x10^{-4}$	$1.06x10^{-4}$	$2.03x10^{-4}$	$1.03x10^{-4}$	$9.87x10^{-5}$	0.000
TINF2	$3.93x10^{-4}$	$1.24x10^{-4}$	$1.06x10^{-4}$	$1.22x10^{-4}$	0.000	$1.97x10^{-4}$	0.000
ACD	0.000	$7.44x10^{-4}$	$2.65x10^{-4}$	$2.03x10^{-4}$	$3.09x10^{-4}$	$4.94x10^{-4}$	$1.03x10^{-3}$
DKC1	0.000	0.000	0.000	0.000	0.000	0.000	0.000
NOP10	0.000	0.000	0.000	$4.06x10^{-5}$	0.000	0.000	$5.17x10^{-4}$
WRAP53	0.000	$6.20x10^{-4}$	$6.37x10^{-4}$	$2.84x10^{-4}$	$1.55x10^{-4}$	$3.95x10^{-4}$	$5.17x10^{-4}$
CTC1	$4.31x10^{-3}$	2.2310^{-3}	$2.97x10^{-3}$	$2.84x10^{-3}$	$2.99x10^{-3}$	$2.76x10^{-3}$	$1.55x10^{-3}$
STN1	0.000	$3.72x10^{-4}$	$4.25x10^{-4}$	$4.06x10^{-4}$	$3.09x10^{-4}$	$2.96x10^{-4}$	$5.17x10^{-4}$
NHP2	0.000	$2.48x10^{-4}$	$3.18x10^{-4}$	$4.06x10^{-4}$	$4.12x10^{-4}$	$4.94x10^{-4}$	$1.03x10^{-3}$
SRP54	$3.93x10^{-4}$	0.000	$5.31x10^{-5}$	$8.12x10^{-5}$	0.000	0.000	0.000
GFI1	0.000	0.000	$1.59x10^{-4}$	$4.06x10^{-5}$	$2.06x10^{-4}$	0.000	0.000
WAS	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TAZ	0.000	0.000	0.000	0.000	0.000	0.000	0.000
WIPF1	0.000	$1.24x10^{-4}$	0.000	$8.12x10^{-5}$	0.000	0.000	0.000
LYST	$1.18x10^{-3}$	$6.20x10^{-4}$	$6.90x10^{-4}$	$7.72x10^{-4}$	$6.18x10^{-4}$	$2.96x10^{-4}$	$5.17x10^{-4}$
VPS45	$7.85x10^{-4}$	$2.48x10^{-4}$	$4.25x10^{-4}$	$3.65x10^{-4}$	$5.67x10^{-4}$	$3.95x10^{-4}$	0.000
VPS13B	$2.36x10^{-3}$	$2.60x10^{-3}$	$3.45x10^{-3}$	$3.17x10^{-3}$	$3.86x10^{-3}$	$3.16x10^{-3}$	$1.03x10^{-3}$
DNAJC21	$1.57x10^{-3}$	$2.11x10^{-3}$	$1.33x10^{-3}$	$1.02x10^{-3}$	$1.39x10^{-3}$	$1.48x10^{-3}$	$1.03x10^{-3}$
CSF3R	$7.85x10^{-4}$	$6.20x10^{-4}$	$1.01x10^{-3}$	$8.12x10^{-4}$	$7.73x10^{-4}$	$8.89x10^{-4}$	$1.03x10^{-3}$
LAMTOR2	0.000	0.000	$5.31x10^{-5}$	0.000	$5.15x10^{-5}$	$9.87x10^{-5}$	0.000
USB1	0.000	$7.44x10^{-4}$	$5.31x10^{-5}$	$2.84x10^{-4}$	$2.57x10^{-4}$	$1.97x10^{-4}$	$5.17x10^{-4}$
G6PC3	$7.85x10^{-4}$	$2.48x10^{-4}$	$8.49x10^{-4}$	$5.28x10^{-4}$	$5.67x10^{-4}$	$6.91x10^{-4}$	$5.17x10^{-4}$
SBDS	$7.07x10^{-3}$	$8.43x10^{-3}$	$7.96x10^{-3}$	$8.41x10^{-3}$	$8.45x10^{-3}$	$7.90x10^{-3}$	$6.72x10^{-3}$
HAX1	$1.57x10^{-3}$	$8.68x10^{-4}$	$6.37x10^{-4}$	$6.09x10^{-4}$	$1.24x10^{-3}$	$1.88x10^{-3}$	$5.17x10^{-4}$
RAB27A	0.000	$6.20x10^{-4}$	$6.37x10^{-4}$	$3.65x10^{-4}$	$3.09x10^{-4}$	$5.92x10^{-4}$	$1.03x10^{-3}$
KIF23	0.000	$1.24x10^{-4}$	$5.31x10^{-5}$	0.000	$5.15x10^{-5}$	$1.97x10^{-4}$	0.000
RPL5	0.000	0.000	0.000	0.000	0.000	0.000	0.000
SLC2A1	0.000	0.000	0.000	$4.06x10^{-5}$	0.000	0.000	0.000
RPL19	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL15	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL18	0.000	0.000	0.000	0.000	0.000	0.000	0.000

RPS7	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS10	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL11	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS19	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL26	0.000	0.000	0.000	0.000	5.15×10^{-5}	0.000	0.000
RPL35A	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL27	0.000	0.000	0.000	4.06×10^{-5}	0.000	0.000	0.000
RPS26	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS27	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL31	0.000	0.000	0.000	0.000	0.000	9.87×10^{-5}	0.000
RPL35	0.000	0.000	0.000	0.000	0.000	9.87×10^{-5}	0.000
RPS15A	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS24	0.000	0.000	0.000	0.000	5.15×10^{-5}	0.000	0.000
RPS29	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS28	0.000	0.000	0.000	0.000	0.000	0.000	0.000
KLF1	0.000	1.24×10^{-4}	2.65×10^{-4}	2.03×10^{-4}	5.15×10^{-5}	1.97×10^{-4}	0.000
RPS17	0.000	0.000	0.000	0.000	0.000	0.000	0.000
ALAS2	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TSR2	0.000	0.000	0.000	0.000	0.000	0.000	0.000
GLRX5	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CDAN1	1.18×10^{-3}	4.96×10^{-4}	9.02×10^{-4}	1.02×10^{-3}	3.61×10^{-4}	1.18×10^{-3}	5.17×10^{-4}
SEC23B	1.18×10^{-3}	1.49×10^{-3}	1.43×10^{-3}	1.42×10^{-3}	1.75×10^{-3}	8.89×10^{-4}	2.07×10^{-3}
CECR1	7.85×10^{-4}	8.68×10^{-4}	5.84×10^{-4}	4.06×10^{-4}	8.24×10^{-4}	8.89×10^{-4}	5.17×10^{-4}
SLC25A38	0.000	7.44×10^{-4}	4.78×10^{-4}	6.90×10^{-4}	6.18×10^{-4}	1.09×10^{-3}	0.000

RAD51	3.93×10^{-4}	0.000	1.06×10^{-4}	0.000	5.15×10^{-5}	0.000	0.000
FANCB	0.000	0.000	0.000	0.000	0.000	0.000	0.000
NHEJ1	0.000	3.72×10^{-4}	1.06×10^{-4}	4.06×10^{-5}	0.000	0.000	0.000
FANCM	4.32×10^{-3}	2.72×10^{-3}	2.87×10^{-3}	3.65×10^{-3}	2.99×10^{-3}	3.16×10^{-3}	2.58×10^{-3}
BRCA2	7.85×10^{-4}	7.44×10^{-4}	8.49×10^{-4}	8.12×10^{-4}	4.12×10^{-4}	8.89×10^{-4}	0.000
ATM	3.14×10^{-3}	2.85×10^{-3}	2.60×10^{-3}	2.55×10^{-3}	2.88×10^{-3}	2.07×10^{-3}	2.58×10^{-3}
ERCC6L2	3.93×10^{-3}	2.11×10^{-3}	1.22×10^{-3}	1.14×10^{-3}	1.08×10^{-3}	1.08×10^{-3}	5.17×10^{-4}
FANCD2	1.18×10^{-3}	1.24×10^{-3}	1.59×10^{-3}	1.30×10^{-3}	1.44×10^{-3}	1.88×10^{-3}	1.03×10^{-3}
FANCE	1.18×10^{-3}	8.68×10^{-4}	4.78×10^{-4}	5.28×10^{-4}	5.67×10^{-4}	1.97×10^{-4}	0.000
SLX4	3.93×10^{-4}	1.24×10^{-3}	1.49×10^{-3}	1.42×10^{-3}	1.60×10^{-3}	7.90×10^{-4}	1.03×10^{-3}
LIG4	2.36×10^{-3}	1.36×10^{-3}	1.06×10^{-3}	1.38×10^{-3}	1.24×10^{-3}	2.07×10^{-3}	1.03×10^{-3}
ESCO2	0.000	0.000	3.18×10^{-4}	1.22×10^{-4}	1.55×10^{-4}	0.000	0.000
ERCC4	3.93×10^{-4}	9.91×10^{-4}	9.55×10^{-4}	6.90×10^{-4}	6.18×10^{-4}	1.38×10^{-3}	1.55×10^{-3}
FANCC	7.85×10^{-4}	1.61×10^{-3}	9.02×10^{-4}	6.50×10^{-4}	5.67×10^{-4}	5.92×10^{-4}	1.03×10^{-3}
FANCI	1.57×10^{-3}	2.97×10^{-3}	2.02×10^{-3}	1.75×10^{-3}	1.96×10^{-3}	2.57×10^{-3}	5.17×10^{-4}
NBN	1.18×10^{-3}	9.91×10^{-4}	7.43×10^{-4}	8.53×10^{-4}	8.24×10^{-4}	6.91×10^{-4}	5.17×10^{-4}
DDX11	5.1×10^{-3}	1.24×10^{-3}	1.38×10^{-3}	1.54×10^{-3}	1.96×10^{-3}	1.88×10^{-3}	3.62×10^{-3}
PALB2	0.000	2.48×10^{-4}	3.72×10^{-4}	2.84×10^{-4}	3.61×10^{-4}	3.95×10^{-4}	0.000
BRCA1	7.85×10^{-4}	9.91×10^{-4}	1.27×10^{-3}	6.90×10^{-4}	1.03×10^{-3}	1.09×10^{-3}	2.07×10^{-3}
FANCG	1.57×10^{-3}	9.91×10^{-4}	9.55×10^{-4}	8.12×10^{-4}	8.76×10^{-4}	3.95×10^{-4}	1.03×10^{-3}
FANCA	1.18×10^{-3}	2.35×10^{-3}	2.97×10^{-3}	2.23×10^{-3}	1.75×10^{-3}	3.16×10^{-3}	3.10×10^{-3}
RAD51C	1.57×10^{-3}	7.44×10^{-4}	1.22×10^{-3}	1.02×10^{-3}	8.24×10^{-4}	1.09×10^{-3}	0.000
FANCL	3.93×10^{-4}	7.44×10^{-4}	7.96×10^{-4}	4.06×10^{-5}	6.60×10^{-4}	6.91×10^{-4}	1.03×10^{-3}
FANCF	0.000	0.000	0.000	0.000	0.000	0.000	0.000

MECOM	0.000	1.24×10^{-4}	5.31×10^{-5}	4.06×10^{-5}	0.000	2.96×10^{-4}	0.000
PAX5	0.000	1.24×10^{-4}	5.31×10^{-5}	8.12×10^{-5}	5.15×10^{-5}	0.000	0.000
ETV6	3.93×10^{-4}	0	5.31×10^{-5}	4.06×10^{-5}	1.03×10^{-4}	0.000	5.17×10^{-4}
GATA2	0.000	0.000	0.000	0.000	5.15×10^{-5}	0.000	0.000
FLI1	0.000	0.000	0.000	4.06×10^{-5}	0.000	9.87×10^{-5}	0.000
SRP72	0.000	1.24×10^{-4}	2.65×10^{-4}	1.62×10^{-4}	3.09×10^{-4}	1.97×10^{-4}	0.000
HOXA11	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RUNX1	0.000	0.000	2.65×10^{-4}	4.06×10^{-5}	5.15×10^{-5}	0.000	0.000
CBL	0.000	7.44×10^{-4}	3.18×10^{-4}	3.65×10^{-4}	3.09×10^{-4}	2.96×10^{-4}	0.000
DDX41	1.57×10^{-3}	2.48×10^{-4}	4.25×10^{-4}	9.34×10^{-4}	1.13×10^{-3}	7.90×10^{-4}	1.03×10^{-3}
GFI1B	3.92×10^{-4}	2.48×10^{-4}	2.12×10^{-4}	3.65×10^{-4}	3.61×10^{-4}	2.96×10^{-4}	5.17×10^{-4}
CEBPA	0.000	0.000	0.000	0.000	0.000	0.000	0.000
GATA1	0.000	0.000	0.000	0.000	0.000	0.000	0.000
AK2	3.92×10^{-4}	2.48×10^{-4}	1.59×10^{-4}	2.03×10^{-4}	1.03×10^{-4}	0.000	0.000

Supplemental Table S6: Frequency Accumulation of pLOF Variants in IBMF Genes By Age

Gene	Frequency >80 (n=1935)	Frequency >70 (n=12,062)	Frequency>60 (n=31,478)	Frequency>50 (n=56,104)	Frequency >40 (n=74,946)	Frequency >30 (n=83,015)	Frequency All (n=85,562)
MDM4	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TERT	0.000	$1.97x10^{-04}$	$4.55x10^{-04}$	$6.17x10^{-04}$	$8.29x10^{-04}$	$1.20x10^{-03}$	$1.59x10^{-03}$
NAF1	0.000	$1.97x10^{-04}$	$3.00x10^{-04}$	$3.41x10^{-04}$	$3.94x10^{-04}$	$3.94x10^{-04}$	$3.94x10^{-04}$
ZCCHC8	0.000	0.000	$1.03x10^{-04}$	$1.03x10^{-04}$	$1.56x10^{-04}$	$2.80x10^{-04}$	$6.73x10^{-04}$
POT1	$5.17x10^{-04}$	$6.16x10^{-04}$	$8.73x10^{-04}$	$9.95x10^{-04}$	$1.37x10^{-03}$	$1.86x10^{-03}$	$2.25x10^{-03}$
RTEL1	$1.03x10^{-03}$	$1.72x10^{-03}$	$2.19x10^{-03}$	$3.04x10^{-03}$	$3.62x10^{-03}$	$4.24x10^{-03}$	$4.64x10^{-03}$
PARN	0.000	$9.87x10^{-05}$	$2.02x10^{-04}$	$4.05x10^{-04}$	$5.11x10^{-04}$	$1.50x10^{-03}$	$1.50x10^{-03}$
TINF2	0.000	$1.97x10^{-04}$	$1.97x10^{-04}$	$3.19x10^{-04}$	$4.25x10^{-04}$	$5.49x10^{-04}$	$9.42x10^{-04}$
ACD	$1.03x10^{-03}$	$1.52x10^{-03}$	$1.83x10^{-03}$	$2.04x10^{-03}$	$2.30x10^{-03}$	$3.05x10^{-03}$	$3.05x10^{-03}$
DKC1	0.000	0.000	0.000	0.000	0.000	0.000	0.000
NOP10	$5.17x10^{-04}$	$5.17x10^{-04}$	$5.17x10^{-04}$	$5.58x10^{-04}$	$5.58x10^{-04}$	$5.58x10^{-04}$	$5.58x10^{-04}$
WRAP53	$5.17x10^{-04}$	$9.12x10^{-04}$	$1.07x10^{-03}$	$1.35x10^{-03}$	$1.99x10^{-03}$	$2.61x10^{-03}$	$2.61x10^{-03}$
CTC1	$1.55x10^{-03}$	$4.31x10^{-03}$	$7.30x10^{-03}$	$1.01x10^{-02}$	$1.31x10^{-02}$	$1.31x10^{-02}$	$1.74x10^{-02}$
STN1	$5.17x10^{-04}$	$8.13x10^{-04}$	$1.12x10^{-03}$	$1.53x10^{-03}$	$1.95x10^{-03}$	$2.32x10^{-03}$	$2.32x10^{-03}$
NHP2	$1.03x10^{-03}$	$1.52x10^{-03}$	$1.94x10^{-03}$	$2.34x10^{-03}$	$2.66x10^{-03}$	$2.91x10^{-03}$	$2.91x10^{-03}$
SRP54	0.000	0.000	0.000	$8.12x10^{-05}$	$1.34x10^{-04}$	$1.34x10^{-04}$	$5.27x10^{-04}$
GFI1	0.000	0.000	$2.06x10^{-04}$	$2.47x10^{-04}$	$4.06x10^{-04}$	$4.06x10^{-04}$	$4.06x10^{-04}$
WAS	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TAZ	0.000	0.000	0.000	0.000	0.000	0.000	0.000
WIPF1	0.000	0.000	0.000	$8.12x10^{-05}$	$8.12x10^{-05}$	$2.05x10^{-04}$	$2.05x10^{-04}$
LYST	$5.17x10^{-04}$	$8.13x10^{-04}$	$1.43x10^{-03}$	$2.20x10^{-03}$	$2.89x10^{-03}$	$3.51x10^{-03}$	$4.69x10^{-03}$
VPS45	0.000	$3.95x10^{-04}$	$9.62x10^{-04}$	$1.33x10^{-03}$	$1.75x10^{-03}$	$2.00x10^{-03}$	$2.79x10^{-03}$

VPS13B	$1.03x10^{-03}$	$4.19x10^{-03}$	$8.05x10^{-03}$	$1.12x10^{-02}$	$1.47x10^{-02}$	$1.73x10^{-02}$	$1.96x10^{-02}$
DNAJC21	$1.03x10^{-03}$	$2.51x10^{-03}$	$3.91x10^{-03}$	$4.92x10^{-03}$	$6.25x10^{-03}$	$8.35x10^{-03}$	$9.92x10^{-03}$
CSF3R	$1.03x10^{-03}$	$1.92x10^{-03}$	$2.69x10^{-03}$	$3.50x10^{-03}$	$4.51x10^{-03}$	$5.13x10^{-03}$	$5.92x10^{-03}$
LAMTOR2	0.000	$9.87x10^{-05}$	$1.50x10^{-04}$	$1.50x10^{-04}$	$2.03x10^{-04}$	$2.03x10^{-04}$	$2.03x10^{-04}$
USB1	$5.17x10^{-04}$	$7.14x10^{-04}$	$9.71x10^{-04}$	$1.26x10^{-03}$	$1.31x10^{-03}$	$2.05x10^{-03}$	$2.05x10^{-03}$
G6PC3	$5.17x10^{-04}$	$1.21x10^{-03}$	$1.78x10^{-03}$	$2.30x10^{-03}$	$3.15x10^{-03}$	$3.40x10^{-03}$	$4.19x10^{-03}$
SBDS	$6.72x10^{-03}$	$1.46x10^{-02}$	$2.31x10^{-02}$	$3.15x10^{-02}$	$3.94x10^{-02}$	$4.79x10^{-02}$	$5.49x10^{-02}$
HAX1	$5.17x10^{-04}$	$2.40x10^{-03}$	$3.64x10^{-03}$	$4.25x10^{-03}$	$4.88x10^{-03}$	$5.75x10^{-03}$	$7.32x10^{-03}$
RAB27A	$1.03x10^{-03}$	$1.62x10^{-03}$	$1.93x10^{-03}$	$2.30x10^{-03}$	$2.93x10^{-03}$	$3.55x10^{-03}$	$3.55x10^{-03}$

KIF23	0.000	$1.97x10^{-04}$	$2.49x10^{-04}$	$2.49x10^{-04}$	$3.02x10^{-04}$	$4.26x10^{-04}$	$4.26x10^{-04}$
RPL5	0.000	0.000	0.000	0.000	0.000	0.000	0.000
SLC2A1	0.000	0.000	0.000	$4.06x10^{-05}$	$4.06x10^{-05}$	$4.06x10^{-05}$	$4.06x10^{-05}$
RPL19	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL15	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL18	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS7	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS10	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL11	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS19	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL26	0.000	0.000	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$
RPL35A	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL27	0.000	0.000	0.000	$4.06x10^{-05}$	$4.06x10^{-05}$	$4.06x10^{-05}$	$4.06x10^{-05}$
RPS26	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS27	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPL31	0.000	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$
RPL35	0.000	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$	$9.87x10^{-05}$
RPS15A	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS24	0.000	0.000	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$

RPS29	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RPS28	0.000	0.000	0.000	0.000	0.000	0.000	0.000
KLF1	0.000	$1.97x10^{-04}$	$2.49x10^{-04}$	$4.52x10^{-04}$	$7.17x10^{-04}$	$8.41x10^{-04}$	$8.41x10^{-04}$
RPS17	0.000	0.000	0.000	0.000	0.000	0.000	0.000
ALAS2	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TSR2	0.000	0.000	0.000	0.000	0.000	0.000	0.000
GLRX5	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CDAN1	$5.17x10^{-04}$	$1.70x10^{-03}$	$2.06x10^{-03}$	$3.08x10^{-03}$	$3.98x10^{-03}$	$4.48x10^{-03}$	$5.66x10^{-03}$
SEC23B	$2.07x10^{-03}$	$2.96x10^{-03}$	$4.71x10^{-03}$	$6.13x10^{-03}$	$7.56x10^{-03}$	$9.05x10^{-03}$	$1.02x10^{-02}$
CECR1	$5.17x10^{-04}$	$1.41x10^{-03}$	$2.23x10^{-03}$	$2.64x10^{-03}$	$3.22x10^{-03}$	$4.09x10^{-03}$	$4.87x10^{-03}$
SLC25A38	0.000	$1.09x10^{-03}$	$1.71x10^{-03}$	$2.40x10^{-03}$	$2.88x10^{-03}$	$3.62x10^{-03}$	$3.62x10^{-03}$

RAD51	0.000	0.000	$5.15x10^{-05}$	$5.15x10^{-05}$	$1.58x10^{-04}$	$1.58x10^{-04}$	$5.51x10^{-04}$
FANCB	0.000	0.000	0.000	0.000	0.000	0.000	0.000
NHEJ1	0.000	0.000	0.000	$4.06x10^{-05}$	$1.47x10^{-04}$	$5.19x10^{-04}$	$5.19x10^{-04}$
FANCM	$2.58x10^{-03}$	$5.74x10^{-03}$	$8.73x10^{-03}$	$1.24x10^{-02}$	$1.53x10^{-02}$	$1.80x10^{-02}$	$2.23x10^{-02}$
BRCA2	0.000	$8.89x10^{-04}$	$1.30x10^{-03}$	$2.11x10^{-03}$	$2.96x10^{-03}$	$3.71x10^{-03}$	$4.49x10^{-03}$
ATM	$2.58x10^{-03}$	$4.65x10^{-03}$	$7.53x10^{-03}$	$1.01x10^{-02}$	$1.27x10^{-02}$	$1.55x10^{-02}$	$1.87x10^{-02}$
ERCC6L2	$5.17x10^{-04}$	$1.60x10^{-03}$	$2.68x10^{-03}$	$3.82x10^{-03}$	$5.04x10^{-03}$	$7.15x10^{-03}$	$1.11x10^{-02}$
FANCD2	$1.03x10^{-03}$	$2.91x10^{-03}$	$4.35x10^{-03}$	$5.65x10^{-03}$	$7.24x10^{-03}$	$8.48x10^{-03}$	$9.66x10^{-03}$
FANCE	0.000	$1.97x10^{-04}$	$7.64x10^{-04}$	$1.29x10^{-03}$	$1.77x10^{-03}$	$2.64x10^{-03}$	$3.82x10^{-03}$
SLX4	$1.03x10^{-03}$	$1.82x10^{-03}$	$3.42x10^{-03}$	$4.84x10^{-03}$	$6.33x10^{-03}$	$7.57x10^{-03}$	$7.96x10^{-03}$
LIG4	$1.03x10^{-03}$	$3.10x10^{-03}$	$4.34x10^{-03}$	$5.72x10^{-03}$	$6.78x10^{-03}$	$8.14x10^{-03}$	$1.05x10^{-02}$
ESCO2	0.000	0.000	$1.55x10^{-04}$	$2.77x10^{-04}$	$5.95x10^{-04}$	$5.95x10^{-04}$	$5.95x10^{-04}$
ERCC4	$1.55x10^{-03}$	$2.93x10^{-03}$	$3.55x10^{-03}$	$4.24x10^{-03}$	$5.19x10^{-03}$	$6.18x10^{-03}$	$6.58x10^{-03}$
FANCC	$1.03x10^{-03}$	$1.62x10^{-03}$	$2.19x10^{-03}$	$2.84x10^{-03}$	$3.74x10^{-03}$	$5.35x10^{-03}$	$6.14x10^{-03}$
FANCI	$5.17x10^{-04}$	$3.09x10^{-03}$	$5.05x10^{-03}$	$6.80x10^{-03}$	$8.82x10^{-03}$	$1.18x10^{-02}$	$1.34x10^{-02}$
NBN	$5.17x10^{-04}$	$1.21x10^{-03}$	$2.03x10^{-03}$	$2.89x10^{-03}$	$3.63x10^{-03}$	$4.62x10^{-03}$	$5.80x10^{-03}$
DDX11	$3.62x10^{-03}$	$5.50x10^{-03}$	$7.46x10^{-03}$	$9.00x10^{-03}$	$1.04x10^{-02}$	$1.16x10^{-02}$	$1.67x10^{-02}$

PALB2	0.000	$3.95x10^{-04}$	$7.56x10^{-04}$	$1.04x10^{-03}$	$1.41x10^{-03}$	$1.66x10^{-03}$	$1.66x10^{-03}$
BRCA1	$2.07x10^{-03}$	$3.16x10^{-03}$	$4.19x10^{-03}$	$4.88x10^{-03}$	$6.15x10^{-03}$	$7.14x10^{-03}$	$7.93x10^{-03}$
FANCG	$1.03x10^{-03}$	$1.43x10^{-03}$	$2.30x10^{-03}$	$3.11x10^{-03}$	$4.07x10^{-03}$	$5.06x10^{-03}$	$6.63x10^{-03}$
FANCA	$3.10x10^{-03}$	$6.26x10^{-03}$	$8.01x10^{-03}$	$1.02x10^{-02}$	$1.32x10^{-02}$	$1.56x10^{-02}$	$1.67x10^{-02}$
RAD51C	0.000	$1.09x10^{-03}$	$1.91x10^{-03}$	$2.93x10^{-03}$	$4.15x10^{-03}$	$4.90x10^{-03}$	$6.47x10^{-03}$
FANCL	$1.03x10^{-03}$	$1.72x10^{-03}$	$2.38x10^{-03}$	$2.42x10^{-03}$	$3.22x10^{-03}$	$3.96x10^{-03}$	$4.35x10^{-03}$
FANCF	0.000	0.000	0.000	0.000	0.000	0.000	0.000

MECOM	0.000	$2.96x10^{-04}$	$2.96x10^{-04}$	$3.37x10^{-04}$	$3.90x10^{-04}$	$5.14x10^{-04}$	$5.14x10^{-04}$
PAX5	0.000	0.000	$5.15x10^{-05}$	$1.33x10^{-04}$	$1.86x10^{-04}$	$3.10x10^{-04}$	$3.10x10^{-04}$
ETV6	$5.17x10^{-04}$	$5.17x10^{-04}$	$6.20x10^{-04}$	$6.60x10^{-04}$	$7.13x10^{-04}$	$7.13x10^{-04}$	$1.11x10^{-03}$
GATA2	0.000	0.000	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$	$5.15x10^{-05}$
FLI1	0.000	$9.87x10^{-05}$	$9.87x10^{-05}$	$1.39x10^{-04}$	$1.39x10^{-04}$	$1.39x10^{-04}$	$1.39x10^{-04}$
SRP72	0.000	$1.97x10^{-04}$	$5.07x10^{-04}$	$6.69x10^{-04}$	$9.34x10^{-04}$	$1.06x10^{-03}$	$1.06x10^{-03}$
HOXA11	0.000	0.000	0.000	0.000	0.000	0.000	0.000
RUNX1	0.000	0.000	$5.15x10^{-05}$	$9.21x10^{-05}$	$3.57x10^{-04}$	$3.57x10^{-04}$	$3.57x10^{-04}$
CBL	0.000	$2.96x10^{-04}$	$6.05x10^{-04}$	$9.70x10^{-04}$	$1.29x10^{-03}$	$2.03x10^{-03}$	$2.03x10^{-03}$
DDX41	$1.03x10^{-03}$	$1.82x10^{-03}$	$2.95x10^{-03}$	$3.88x10^{-03}$	$4.31x10^{-03}$	$4.56x10^{-03}$	$6.13x10^{-03}$
GFI1B	$5.17x10^{-04}$	$8.13x10^{-04}$	$1.17x10^{-03}$	$1.54x10^{-03}$	$1.75x10^{-03}$	$2.00x10^{-03}$	$2.39x10^{-03}$
CEBPA	0.000	0.000	0.000	0.000	0.000	0.000	0.000
GATA1	0.000	0.000	0.000	0.000	0.000	0.000	0.000
AK2	0.000	0.000	$1.03x10^{-04}$	$3.06x10^{-04}$	$4.65x10^{-04}$	$7.13x10^{-04}$	$1.11x10^{-03}$

Supplemental Table S7 Loss-of-function Variants in DBA Genes in gnomAD

Gene	Chr	Position	rsID	Reference	Alternate	Protein Consequence	Transcript Consequence	Annotation	Exon	Age	Allele Count	Allele Number	Allele Frequency
RPS10	6	34389532	rs1373580194	ATC	A	p.Asp125Tyrfs Ter28	c.373_374delGA	frameshift_variant	4	n/a	1	251176	3.98127E-06
RPS10	6	34392618	rs779387874	CTG	C		c.151-3_151-2delCA	splice_acceptor_variant	3	n/a	1	248752	4.02007E-06
RPL26	17	8280963	rs778804923	G	A	p.Arg115Ter	c.342C>T	stop_gained	4	60-65	2	248858	8.03671E-06
RPL26	17	8280968	rs1325509343	T	TAACTCGCGCC CGTTCCCCATTC CCACGTTGTTGC CAAGTCTCCAG C	p.Ile118AlafsT er39	c.351_352insGCTG GAGACTTGGCAA CAACGTGGGAAT GGGGAACGGGCG CGAGTT	frameshift_variant	4	60-65	1	249288	4.01142E-06
RPL26	17	8281022	rs781337048	TAAGAAA AAAACAC TCCCAAG CTTTAAAT AATCACT AAAACAC AAGGGAA AGCCCAA CATTC	T		c.142-41_161delGAATGT TGGGCTTTCCCTT GTGTTTTAGTGAT TATTTAAAGCTTG GGAGTGTTTTTTT CTT	splice_acceptor_variant	4	30-35	1	238292	4.19653E-06
RPL27	17	41154800	rs746070243	G	GGTAAGTA		c.362+2_362+8dupT AAGTAG	stop_gained	4	50-55	1	251482	3.97643E-06
RPS24	10	79814287	rs1228580232	A	T		c.391-2A>T	splice_acceptor_variant	4	55-60	1	143222	6.98217E-06
RPS29	14	50044573	rs1354511680	T	G		c.163-2A>C	splice_acceptor_variant	3	n/a	1	204148	4.89841E-06

Supplemental Table S8: Loss-of-function Variants in *SRP54* in gnomAD

Gene	Chr	Position	rsID	Reference	Alternate	Protein Consequence	Transcript Consequence	Annotation	Exon	Age	Allele Count	Allele Number	Allele Frequency
SRP54	14	35465938	rs771241246	G	GA	p.Ile10AsnfsTer16	c.28dupA	frameshift_variant	2	50-55	1	251354	3.97845E-06
SRP54	14	35476529	rs753087160	GA	G	p.Lys100AsnfsTer4	c.300delA	frameshift_variant	5	<30	1	248880	4.018E-06
SRP54	14	35480732	rs1357701182	CT	C	p.Val169SerfsTer8	c.504delT	frameshift_variant	8	n/a	1	238176	4.19858E-06
SRP54	14	35482701	rs1335654383	G	A		c.785+1G>A	splice_donor_variant	9	45-50	1	250940	3.98502E-06
SRP54	14	35488185	rs1408854882	GT	G	p.Phe355LeufsTer6	c.1065delT	frameshift_variant	13	n/a	1	31398	3.18492E-05
SRP54	14	35488227	rs767844326	C	A	p.Ser368Ter	c.1103C>A	stop_gained	13	55-60	1	251214	3.98067E-06