

Supplemental Table 1: ASXL1 protein truncating variants in ExAC

Chrom	Position	Ref Allele	Alt Allele	HGVs Nucleotide	HGVs Protein	Annotation	Allele Count in ExAC	Ancestry	ExAC Global Allele Frequency	Cancer / Not cancer Cohort	Sex	Age (rounded)	Allele Balance (% Alt Allele)	Present in ClinVar	Notes
20	30947563	ATT	A	c.15_16delTT	p.Phe6CysfsTer62	frameshift	1	AFR	0.0000561	Cancer	Female	45	45%	no	Excluded - non-constitutive exon
20	30955528	A	G	c.141-2A>G		splice acceptor	2	SAS (2)	0.00001648	Not cancer Not cancer	Female Male	60 50	46% 47%	no	Excluded - non-constitutive exon
20	31016126	A	G	c.374-2A>G		splice acceptor	1	EUR	0.000008253	Cancer	Female	NA	42%	no	
20	31016127	G	A	c.374-1G>A		splice acceptor	1	EUR	0.000008254	Not cancer	Male	NA	45%	no	
20	31019423	CA	C	c.921delA	p.Leu308Ter	frameshift	1	EUR	0.000008239	Not cancer	Male	50	46%	no	
20	31021211	C	T	c.1210C>T	p.Arg404Ter	stop gained	7	EUR (4), AFR, EAS, FIN	0.00005767	Not cancer Not cancer Not cancer Not cancer Cancer Cancer Not cancer	Male Female Male Male Female Male Male	55 85 80 60 NA NA 70	23% 42% 19% 21% 43% 13% 12%	yes	
20	31021250	C	T	c.1249C>T	p.Arg417Ter	stop gained	9	EUR (6), FIN (2), EAS	0.00007414	Not cancer Not cancer Not cancer Not cancer Not cancer Not cancer Not cancer Not cancer Cancer	Male Male Male Male Male Female Male Female Male	65 55 55 80 75 85 65 NA 75	22% 40% 32% 25% 18% 30% 18% 20% 32%	no	
20	31021295	C	T	c.1294C>T	p.Gln432Ter	stop gained	3	EUR (3)	0.00002471	Not cancer Not cancer Cancer	Female Male Male	NA 50 80	23% 24% 31%	no	
20	31021332	C	G	c.1331C>G	p.Ser444Ter	stop gained	1	EUR	0.000008238	Not cancer	Male	80	30%	no	
20	31021439	G	T	c.1438G>T	p.Glu480Ter	stop gained	1	EUR	0.000008246	Not cancer	Female	50	17%	no	
20	31021535	C	T	c.1534C>T	p.Gln512Ter	stop gained	5	EUR (5)	0.00004123	Not cancer Not cancer Cancer Cancer Cancer	Female Male Male Male Male	55 45 65 NA NA	11% 25% 15% 29% 38%	no	
20	31021538	G	T	c.1537G>T	p.Glu513Ter	stop gained	1	EUR	0.000008245	Cancer	Female	65	46%	no	
20	31021565	C	T	c.1564C>T	p.Gln522Ter	stop gained	1	EUR	0.00000825	Not cancer	Male	55	39%	no	
20	31021610	G	T	c.1609G>T	p.Glu537Ter	stop gained	1	EUR	0.000008282	Not cancer	Female	NA	37%	no	
20	31021627	T	TGAAGATC	c.1626delTinsTGAAGATC	p.Gln546ArgfsTer7	frameshift	1	EUR	0.0000083	Not cancer	Male	85	27%	no	
20	31021642	C	CT	c.1641_1642insT	p.Arg549SerfsTer2	frameshift	1	EUR	0.000008321	Cancer	Male	75	34%	no	
20	31022233	A	G	c.1720-2A>G		splice acceptor	2	EUR (2)	0.00001678	Not cancer Not cancer	Female Male	85 70	50% 11%	no	
20	31022238	C	T	c.1723C>T	p.Gln575Ter	stop gained	2	AFR, EUR	0.00001675	Not cancer Cancer	Male Male	75 75	15% 33%	no	
20	31022263	G	A	c.1748G>A	p.Trp583Ter	stop gained	2	EUR (2)	0.00001666	Not cancer Not cancer	Male Male	50 80	10% 41%	no	
20	31022265	G	GT	c.1750_1751insT	p.Val585GlyfsTer2	frameshift	1	EUR	0.000008325	Cancer	Female	NA	26%	no	
20	31022284	CTT	C	c.1770_1771delTT	p.Tyr591ProfTer27	frameshift	1	Other	0.00000831	Cancer	Male	55	33%	no	
20	31022288	C	A	c.1773C>A	p.Tyr591Ter	stop gained	4	EUR (3), SAS	0.00003326	Not cancer Not cancer Cancer Cancer	Male Male Female Male	45 70 NA NA	17% 11% 18% 26%	no	
20	31022288	C	G	c.1773C>G	p.Tyr591Ter	stop gained	3	EUR (3)	0.00002495	Not cancer Not cancer Cancer	Male Female Female	65 70 NA	12% 29% 13%	no	
20	31022297	C	A	c.1782C>A	p.Cys594Ter	stop gained	1	AFR	0.000008323	Not cancer	Male	45	16%	no	
20	31022365	T	TA	c.1850_1851insA	p.Lys618Ter	frameshift	1	AMR	0.000008494	Not cancer	Male	75	15%	no	
20	31022386	T	TC	c.1871_1872insC	p.Arg625ProfTer10	frameshift	1	EUR	0.000008824	Not cancer	Male	80	35%	no	
20	31022414	TAG	T	c.1900_1901delAG	p.Glu635GlyfsTer22	frameshift	1	EUR	0.000009443	Not cancer	Female	80	30%	no	
20	31022441	AGG	A	c.1926_1928delAGGinsA	p.Gly645TrpfsTer12	frameshift	1	EUR	0.00001238	Cancer	Male	60	18%	no	
20	31022592	C	T	c.2077C>T	p.Arg693Ter	stop gained	6	EUR (3), EAS (2), AFR	0.0000502	Not cancer Not cancer Not cancer Not cancer Not cancer	Male Female Female Female Male	60 55 65 75 65 60	13% 14% 59% 14% 19% 14%	no	
20	31022642	CG	C	c.2127_2128delCGinsC	p.Gly710GlyfsTer15	frameshift	1	SAS	0.00000828	Not cancer	Male	75	33%	no	

20	31022669	AG	A	c.2155delG	p.Glu719ArgfsTer6	frameshift	1	AFR	0.00008267	Cancer	Male	60	34%	no	
20	31022688	A	T	c.2173A>T	p.Arg725Ter	stop gained	1	EUR	0.00008263	Not cancer	Male	75	25%	no	
20	31022711	AC	A	c.2197delC	p.Gln733ArgfsTer11	frameshift	1	EUR	0.0000826	Cancer	Female	NA	36%	no	
20	31022817	C	T	c.2302C>T	p.Gln768Ter	stop gained	2	EUR (2)	0.0000165	Not cancer	Female	75	42%	no	
										Cancer	Female	NA	28%		
20	31022839	T	G	c.2324T>G	p.Leu775Ter	stop gained	1	EUR	0.00008253	Cancer	Female	55	19%	no	
20	31022853	C	T	c.2338C>T	p.Gln780Ter	stop gained	1	AMR	0.00008262	Not cancer	Female	70	31%	no	
20	31022922	C	T	c.2407C>T	p.Gln803Ter	stop gained	3	AMR (2), EUR	0.00002485	Not cancer	Male	75	18%	no	
										Not cancer	Male	55	30%		
										Not cancer	Male	60	11%		
20	31022981	AT	A	c.2467delT	p.Leu823Ter	frameshift	2	AFR, EUR	0.00001656	Not cancer	Female	80	43%	no	
										Not cancer	Female	60	9%		
20	31022991	G	T	c.2476G>T	p.Gly826Ter	stop gained	1	EUR	0.0000828	Not cancer	Female	80	13%	no	
20	31023083	C	A	c.2568C>A	p.Cys856Ter	stop gained	1	EUR	0.00008247	Not cancer	Male	NA	18%	no	
20	31023156	A	T	c.2641A>T	p.Arg881Ter	stop gained	1	EUR	0.00008236	Not cancer	Male	75	30%	no	
20	31023209	G	A	c.2694G>A	p.Trp898Ter	stop gained	2	EUR (2)	0.00001648	Not cancer	Female	70	21%	no	
										Cancer	Male	NA	15%		
20	31023271	T	TA	c.2756delTinsTA	p.Pro920ThrfsTer4	frameshift	1	AMR	0.00008242	Not cancer	Male	85	22%	no	
20	31023408	C	T	c.2893_2896delCGAGinsTGAG	p.Arg965Ter	stop gained	1	EUR	0.00008244	Not cancer	Female	85	21%	yes	
20	31023446	GGT	G	c.2931_2933delGGTinsG	p.Val978GlyfsTer3	frameshift	1	EUR	0.00008241	Not cancer	Female	60	18%	no	
20	31023473	C	CGT	c.2958delCinsCGT	p.Gly987ValfsTer7	frameshift	1	EUR	0.00008241	Not cancer	Female	60	18%	no	
20	31023717	C	T	c.3202C>T	p.Arg1068Ter	stop gained	1	EUR	0.00008238	Not cancer	Male	65	22%	no	
20	31024165	C	CAA	c.3650_3651insAA	p.Asn1218LysfsTer63	frameshift	1	EUR	0.00008272	Not cancer	Female	45	51%	no	
20	31024273	G	GC	c.3758_3759insC	p.Asn1254Ter	frameshift	1	EUR	0.00008249	Not cancer	Male	70	49%	no	
20	31024279	CA	C	c.3765delA	p.Asn1256MetfsTer24	frameshift	1	EUR	0.00008241	Not cancer	Female	75	36%	no	
20	31024499	GA	G	c.3985delA	p.Ile1329SerfsTer121	frameshift	2	SAS (2)	0.00001655	Not cancer	Male	70	46%	no	Excluded - complex indel with variant below
										Not cancer	Male	75	36%		
20	31024502	C	CA	c.3987_3988insA	p.Pro1330ThrfsTer41	frameshift	2	SAS (2)	0.00001654	Not cancer	Male	70	45%	no	Excluded - complex indel with variant above
										Not cancer	Male	75	37%		
20	31024563	C	T	c.4048C>T	p.Gln1350Ter	stop gained	1	AMR	0.00008258	Cancer	Female	NA	56%	no	
20	31025057	CAT	C	c.4542_4544delCATinsC	p.Met1515ValfsTer11	frameshift	1	EUR	0.00008246	Not cancer	Male	NA	45%	no	

Data averaged across individuals

20	31022441	A	AG	c.1926_1928delAGGinsAGGG	p.Gly646TrpfsTer12	frameshift	132	EUR (95), SAS (13), AFR (12), AMR (7), EAS (3), Other (2)	0.001634	Majority Cancer (66%) Cancer Not cancer	Female (72%)	64.8 (data available for 36%) 67.9 (data available for 8%) 64.3 (data available for 91%)	24% (median 21.8%) 22.7% (median 21.4%) 26.4% (median 23.1%)	no	Excluded - homopolymer region
20	31022441	AG	A	c.1926_1928delAGGinsAG	p.Gly645ValfsTer58	frameshift	118	EUR (58), SAS (24), AMR (17), EAS (11), AFR (7), FIN (1)	0.00146	Majority Not cancer (92%) Cancer Not cancer	Male (62%)	56.8 (data available for 85%) 65.0 (data available for 50%) 56.3 (data available for 88%)	16.9% (median 15.4%) 16.3% (median 16.7%) 17.0% (median 15.2%)	no	Excluded - homopolymer region

Legend: Samples in figure 2 are marked in bold in columns K through N.