Beyond Traditional Morphological Characterization of Lung Neuroendocrine Neoplasms: In Silico Study of Next-Generation Sequencing Mutations Analysis across the Four World Health Organization Defined Groups

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Table S1. Genes Frequently mutated in Typical Carcinoids (TCs).

Mutation Rate %	Original	Entrez	Gene	Gene
4.84	EIF1AX	1964	EIF1AX	eukaryotic translation initiation factor 1A X-linked [Source: HGNC Symbol; Acc: HGNC: 3250]
4.71	ARID1A	8289	ARID1A	AT-rich interaction domain 1A [Source: HGNC Symbol;Acc: HGNC: 11110]
4.35	LRP1B	53353	LRP1B	LDL receptor related protein 1B [Source: HGNC Symbol; Acc: HGNC: 6693]
3.53	NF1	4763	NF1	neurofibromin 1 [Source: HGNC Symbol;Acc: HGNC: 7765]
2.90	DSCAML1	57453	DSCAML1	DS cell adhesion molecule like 1 [Source: HGNC Symbol; Acc: HGNC: 14656]
2.90	DST	667	DST	dystonin [Source: HGNC Symbol;Acc: HGNC: 1090]
2.90	FANCD2	2177	FANCD2	FA complementation group D2 [Source: HGNC Symbol; Acc: HGNC: 3585]
2.90	PCLO	27445	PCLO	piccolo presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 13406]
2.44	ERBB2	2064	ERBB2	erb-b2 receptor tyrosine kinase 2 [Source: HGNC Symbol; Acc: HGNC: 3430]
2.35	BAP1	8314	BAP1	BRCA1 associated protein 1 [Source: HGNC Symbol; Acc: HGNC: 950]
2.35	CIC	23152	CIC	capicua transcriptional repressor [Source: HGNC Symbol; Acc: HGNC: 14214]
2.35	EPHA3	2042	EPHA3	EPH receptor A3 [Source: HGNC Symbol; Acc: HGNC: 3387]
2.35	MLL3	58508	KMT2C	lysine methyltransferase 2C [Source: HGNC Symbol; Acc: HGNC: 13726]
2.35	PDGFRB	5159	PDGFRB	platelet derived growth factor receptor beta [Source: HGNC Symbol; Acc: HGNC: 8804]
2.35	ROS1	6098	ROS1	ROS proto-oncogene 1, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 10261]
2.17	APBB1IP	54518	APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein [Source: HGNC Symbol; Acc: HGNC: 17379]
2.17	ATP1A2	477	ATP1A2	ATPase Na+/K+ transporting subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 800]
2.17	CNTNAP2	26047	CNTNAP2	contactin associated protein like 2 [Source: HGNC Symbol; Acc: HGNC: 13830]
2.17	HECW2	57520	HECW2	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2 [Source: HGNC Symbol;Acc: HGNC: 29853]
2.17	LAMA1	284217	LAMA1	laminin subunit alpha 1 [Source: HGNC Symbol; Acc: HGNC: 6481]
2.17	MDN1	23195	MDN1	midasin AAA ATPase 1 [Source: HGNC Symbol; Acc: HGNC: 18302]
2.17	MSH3	4437	MSH3	mutS homolog 3 [Source: HGNC Symbol; Acc: HGNC: 7326]
2.17	NCOR2	9612	NCOR2	nuclear receptor corepressor 2 [Source: HGNC Symbol; Acc: HGNC: 7673]
2.17	SALL1	6299	SALL1	spalt like transcription factor 1 [Source: HGNC Symbol; Acc: HGNC: 10524]
1.96	APC	324	APC	APC regulator of WNT signaling pathway [Source: HGNC Symbol; Acc: HGNC: 583]

1.96	ATM	472	ATM	ATM serine/threonine kinase [Source: HGNC Symbol; Acc: HGNC: 795]
1.96	IDH1	3417	IDH1	isocitrate dehydrogenase (NADP(+)) 1 [Source: HGNC Symbol; Acc: HGNC: 5382]
1.63	KRAS	3845	KRAS	KRAS proto-oncogene, GTPase [Source: HGNC Symbol; Acc: HGNC: 6407]
1.63	SMAD4	4089	SMAD4	SMAD family member 4 [Source: HGNC Symbol; Acc: HGNC: 6770]
1.61	FAT1	2195	FAT1	FAT atypical cadherin 1 [Source: HGNC Symbol; Acc: HGNC: 3595]
1.61	NOTCH3	4854	NOTCH3	notch receptor 3 [Source: HGNC Symbol; Acc: HGNC: 7883]
1.61	PARP1	142	PARP1	poly(ADP-ribose) polymerase 1 [Source: HGNC Symbol; Acc: HGNC: 270]
1.61	POLE	5426	POLE	DNA polymerase epsilon, catalytic subunit [Source: HGNC Symbol; Acc: HGNC: 9177]
1.61	RAD51C	5889	RAD51C	RAD51 paralog C [Source: HGNC Symbol; Acc: HGNC: 9820]
1.61	SF3B1	23451	SF3B1	splicing factor 3b subunit 1 [Source: HGNC Symbol; Acc: HGNC: 10768]
1.45	CSMD3	114788	CSMD3	CUB and Sushi multiple domains 3 [Source: HGNC Symbol; Acc: HGNC: 19291]
1.45	KAT6B	23522	KAT6B	lysine acetyltransferase 6B [Source: HGNC Symbol; Acc: HGNC: 17582]
1.45	NCAM2	4685	NCAM2	neural cell adhesion molecule 2 [Source: HGNC Symbol; Acc: HGNC: 7657]
1.45	PDE4DIP	9659	PDE4DIP	phosphodiesterase 4D interacting protein [Source: HGNC Symbol; Acc: HGNC: 15580]
1.45	SPHKAP	80309	SPHKAP	SPHK1 interactor, AKAP domain containing [Source: HGNC Symbol; Acc: HGNC: 30619]
1.45	SYNE1	23345	SYNE1	spectrin repeat containing nuclear envelope protein 1 [Source: HGNC Symbol; Acc: HGNC: 17089]
1.45	TDRD7	23424	TDRD7	tudor domain containing 7 [Source: HGNC Symbol; Acc: HGNC: 30831]
1.27	KIT	3815	KIT	KIT proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 6342]
1.18	AR	367	AR	androgen receptor [Source: HGNC Symbol; Acc: HGNC: 644]
1.18	FLT1	2321	FLT1	fms related tyrosine kinase 1 [Source: HGNC Symbol; Acc: HGNC: 3763]
1.18	MEN1	4221	MEN1	menin 1 [Source: HGNC Symbol; Acc: HGNC: 7010]
1.18	NOTCH2	4853	NOTCH2	notch receptor 2 [Source: HGNC Symbol; Acc: HGNC: 7882]

Table S2. Genes Frequently mutated in Atypical Carcinoids (ACs).

Mutation Rate %	Original	Entrez	Gene	Gene
24.66	MEN1	4221	MEN1	menin 1 [Source: HGNC Symbol; Acc: HGNC: 7010]
18.18	ATP1A2	477	ATP1A2	ATPase Na+/K+ transporting subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 800]
16.67	EIF1AX	1964	EIF1AX	eukaryotic translation initiation factor 1A X-linked [Source: HGNC Symbol; Acc: HGNC: 3250]
12.82	SPHKAP	80309	SPHKAP	SPHK1 interactor, AKAP domain containing [Source: HGNC Symbol; Acc: HGNC: 30619]
9.59	ARID1A	8289	ARID1A	AT-rich interaction domain 1A [Source: HGNC Symbol; Acc: HGNC: 11110]
9.59	SMARCA4	6597	SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 [Source: HGNC Symbol; Acc: HGNC: 11100]
9.09	PKD1	5310	PKD1	polycystin 1, transient receptor potential channel interacting [Source: HGNC Symbol; Acc: HGNC: 9008]
8.33	AMER1	139285	AMER1	APC membrane recruitment protein 1 [Source: HGNC Symbol; Acc: HGNC: 26837]
8.33	RAD51C	5889	RAD51C	RAD51 paralog C [Source: HGNC Symbol; Acc: HGNC: 9820]
7.69	TDRD7	23424	TDRD7	tudor domain containing 7 [Source: HGNC Symbol; Acc: HGNC: 30831]
6.85	MLL3	58508	KMT2C	lysine methyltransferase 2C [Source: HGNC Symbol; Acc: HGNC: 13726]
6.85	NOTCH2	4853	NOTCH2	notch receptor 2 [Source: HGNC Symbol; Acc: HGNC: 7882]

5.80	APC	324	APC	APC regulator of WNT signaling pathway [Source: HGNC Symbol; Acc: HGNC: 583]
5.80	PDGFRA	5156	PDGFRA	platelet derived growth factor receptor alpha [Source: HGNC Symbol; Acc: HGNC: 8803]
5.77	MLL	4297	KMT2A	lysine methyltransferase 2A [Source: HGNC Symbol; Acc: HGNC: 7132]
5.48	MLL2	8085	KMT2D	lysine methyltransferase 2D [Source: HGNC Symbol; Acc: HGNC: 7133]
5.32	TP53	7157	TP53	tumor protein p53 [Source: HGNC Symbol; Acc: HGNC: 11998]
5.26	SF3B1	23451	SF3B1	splicing factor 3b subunit 1 [Source: HGNC Symbol; Acc: HGNC: 10768]
5.13	CSMD3	114788	CSMD3	CUB and Sushi multiple domains 3 [Source: HGNC Symbol; Acc: HGNC: 19291]
5.13	DSCAML1	57453	DSCAML1	DS cell adhesion molecule like 1 [Source: HGNC Symbol; Acc: HGNC: 14656]
5.13	NCAM2	4685	NCAM2	neural cell adhesion molecule 2 [Source: HGNC Symbol; Acc: HGNC: 7657]
5.13	PCLO	27445	PCLO	piccolo presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 13406]
5.13	PTPRZ1	5803	PTPRZ1	protein tyrosine phosphatase receptor type Z1 [Source: HGNC Symbol; Acc: HGNC: 9685]
4.35	HNF1A	6927	HNF1A	HNF1 homeobox A [Source: HGNC Symbol; Acc: HGNC: 11621]
4.35	KDR	3791	KDR	kinase insert domain receptor [Source: HGNC Symbol; Acc: HGNC: 6307]
4.17	EPHA5	2044	EPHA5	EPH receptor A5 [Source: HGNC Symbol; Acc: HGNC: 3389]
4.17	GRIN2A	2903	GRIN2A	glutamate ionotropic receptor NMDA type subunit 2A [Source: HGNC Symbol; Acc: HGNC: 4585]
3.85	ARID2	196528	ARID2	AT-rich interaction domain 2 [Source: HGNC Symbol; Acc: HGNC: 18037]
3.85	ATRX	546	ATRX	ATRX chromatin remodeler [Source: HGNC Symbol; Acc: HGNC: 886]
3.85	KDM5C	8242	KDM5C	lysine demethylase 5C [Source: HGNC Symbol; Acc: HGNC: 11114]
3.85	PTPRT	11122	PTPRT	protein tyrosine phosphatase receptor type T [Source: HGNC Symbol; Acc: HGNC: 9682]
3.85	SETD2	29072	SETD2	SET domain containing 2, histone lysine methyltransferase [Source: HGNC Symbol; Acc: HGNC: 18420]
3.64	KIT	3815	KIT	KIT proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 6342]
2.74	EGFR	1956	EGFR	epidermal growth factor receptor [Source: HGNC Symbol; Acc: HGNC: 3236]
2.74	ERBB2	2064	ERBB2	erb-b2 receptor tyrosine kinase 2 [Source: HGNC Symbol; Acc: HGNC: 3430]
2.74	ERBB4	2066	ERBB4	erb-b2 receptor tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3432]
2.74	FGFR1	2260	FGFR1	fibroblast growth factor receptor 1 [Source: HGNC Symbol; Acc: HGNC: 3688]
2.74	MET	4233	MET	MET proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 7029]
2.56	NUP98	4928	NUP98	nucleoporin 98 [Source: HGNC Symbol; Acc: HGNC: 8068]
2.56	RNF213	57674	RNF213	ring finger protein 213 [Source: HGNC Symbol; Acc: HGNC: 14539]
2.22	RB1	5925	RB1	RB transcriptional corepressor 1 [Source: HGNC Symbol; Acc: HGNC: 9884]
2.13	PIK3CA	5290	PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha [Source: HGNC Symbol; Acc: HGNC: 8975]
2.13	PTEN	5728	PTEN	phosphatase and tensin homolog [Source: HGNC Symbol; Acc: HGNC: 9588]
1.92	AR	367	AR	androgen receptor [Source: HGNC Symbol; Acc: HGNC: 644]
1.92	DICER1	23405	DICER1	dicer 1, ribonuclease III [Source: HGNC Symbol; Acc: HGNC: 17098]
1.92	EPHB1	2047	EPHB1	EPH receptor B1 [Source: HGNC Symbol; Acc: HGNC: 3392]
1.92	FLT4	2324	FLT4	fms related tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3767]
1.92	MDM4	4194	MDM4	MDM4 regulator of p53 [Source: HGNC Symbol; Acc: HGNC: 6974]
1.92	NF1	4763	NF1	neurofibromin 1 [Source: HGNC Symbol; Acc: HGNC: 7765]

1.92	NTRK3	4916	NTRK3	neurotrophic receptor tyrosine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 8033]
1.92	PTCH1	5727	PTCH1	patched 1 [Source: HGNC Symbol; Acc: HGNC: 9585]
1.92	TNFAIP3	7128	TNFAIP3	TNF alpha induced protein 3 [Source: HGNC Symbol; Acc: HGNC: 11896]
1.45	GNAS	2778	GNAS	GNAS complex locus [Source: HGNC Symbol; Acc: HGNC: 4392]
1.45	RET	5979	RET	ret proto-oncogene [Source: HGNC Symbol; Acc: HGNC: 9967]
1.45	SMARCB1	6598	SMARCB1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1 [Source: HGNC Symbol; Acc: HGNC: 11103]
1.45	SMO	6608	SMO	smoothened, frizzled class receptor [Source: HGNC Symbol; Acc: HGNC: 11119]
1.37	KRAS	3845	KRAS	KRAS proto-oncogene, GTPase [Source: HGNC Symbol; Acc: HGNC: 6407]

Table S3. Genes Frequently mutated in Large Cell Neuroendocrine Carcinomas (LCNECs).

Mutation Rate %	Original	Entrez	Gene	Gene
87.14	TP53	7157	TP53	tumor protein p53 [Source: HGNC Symbol; Acc: HGNC: 11998]
49.37	LRP1B	53353	LRP1B	LDL receptor related protein 1B [Source: HGNC Symbol; Acc: HGNC: 6693]
46.84	CSMD3	114788	CSMD3	CUB and Sushi multiple domains 3 [Source: HGNC Symbol; Acc: HGNC: 19291]
35.22	RB1	5925	RB1	RB transcriptional corepressor 1 [Source: HGNC Symbol; Acc: HGNC: 9884]
26.58	SYNE1	23345	SYNE1	spectrin repeat containing nuclear envelope protein 1 [Source: HGNC Symbol; Acc: HGNC: 17089]
21.67	ADAMTS12	81792	ADAMTS12	ADAM metallopeptidase with thrombospondin type 1 motif 12 [Source: HGNC Symbol; Acc: HGNC: 14605]
20.29	USH2A	7399	USH2A	usherin [Source: HGNC Symbol; Acc: HGNC: 12601]
19.91	KEAP1	9817	KEAP1	kelch like ECH associated protein 1 [Source: HGNC Symbol; Acc: HGNC: 23177]
19.49	STK11	6794	STK11	serine/threonine kinase 11 [Source: HGNC Symbol; Acc: HGNC: 11389]
18.84	DNAH9	1770	DNAH9	dynein axonemal heavy chain 9 [Source: HGNC Symbol; Acc: HGNC: 2953]
18.33	ADAMTS2	9509	ADAMTS2	ADAM metallopeptidase with thrombospondin type 1 motif 2 [Source: HGNC Symbol; Acc: HGNC: 218]
15.32	PTPRT	11122	PTPRT	protein tyrosine phosphatase receptor type T [Source: HGNC Symbol; Acc: HGNC: 9682]
14.52	PTPRD	5789	PTPRD	protein tyrosine phosphatase receptor type D [Source: HGNC Symbol; Acc: HGNC: 9668]
13.18	MLL3	58508	KMT2C	lysine methyltransferase 2C [Source: HGNC Symbol; Acc: HGNC: 13726]
12.38	GRIN2A	2903	GRIN2A	glutamate ionotropic receptor NMDA type subunit 2A [Source: HGNC Symbol; Acc: HGNC: 4585]
11.67	GAS7	8522	AC005747.1	growth arrest specific 7 [Source: NCBI gene; Acc: 8522]
11.67	NTM	50863	NTM	neurotrimin [Source: HGNC Symbol; Acc: HGNC: 17941]
10.93	FAT1	2195	FAT1	FAT atypical cadherin 1 [Source: HGNC Symbol; Acc: HGNC: 3595]
10.87	COL11A1	1301	COL11A1	collagen type XI alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 2186]
10.87	COL22A1	169044	COL22A1	collagen type XXII alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 22989]
10.87	ZFHX4	79776	ZFHX4	zinc finger homeobox 4 [Source: HGNC Symbol; Acc: HGNC: 30939]
10.48	EPHA3	2042	EPHA3	EPH receptor A3 [Source: HGNC Symbol; Acc: HGNC: 3387]
10.48	EPHA5	2044	EPHA5	EPH receptor A5 [Source: HGNC Symbol; Acc: HGNC: 3389]
10.14	LAMA2	3908	LAMA2	laminin subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 6482]
10.13	DST	667	DST	dystonin [Source: HGNC Symbol; Acc: HGNC: 1090]
10.00	BSN	8927	BSN	bassoon presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 1117]

10.00	FAP	2191	FAP	fibroblast activation protein alpha [Source: HGNC Symbol; Acc: HGNC: 3590]
9.95	NOTCH1	4851	NOTCH1	notch receptor 1 [Source: HGNC Symbol; Acc: HGNC: 7881]
9.55	ARID1A	8289	ARID1A	AT-rich interaction domain 1A [Source: HGNC Symbol; Acc: HGNC: 11110]
9.55	MLL2	8085	KMT2D	lysine methyltransferase 2D [Source: HGNC Symbol; Acc: HGNC: 7133]
8.92	PDE4DIP	9659	PDE4DIP	phosphodiesterase 4D interacting protein [Source: HGNC Symbol; Acc: HGNC: 15580]
8.91	NF1	4763	NF1	neurofibromin 1 [Source: HGNC Symbol; Acc: HGNC: 7765]
8.70	CNTNAP2	26047	CNTNAP2	contactin associated protein like 2 [Source: HGNC Symbol; Acc: HGNC: 13830]
8.57	PAK7	57144	PAK5	p21 (RAC1) activated kinase 5 [Source: HGNC Symbol; Acc: HGNC: 15916]
8.57	POLE	5426	POLE	DNA polymerase epsilon, catalytic subunit [Source: HGNC Symbol; Acc: HGNC: 9177]
8.33	ALMS1	7840	ALMS1	ALMS1 centrosome and basal body associated protein [Source: HGNC Symbol; Acc: HGNC: 428]
8.33	COL5A3	50509	COL5A3	collagen type V alpha 3 chain [Source: HGNC Symbol; Acc: HGNC: 14864]
8.18	SMARCA4	6597	SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 [Source: HGNC Symbol; Acc: HGNC: 11100]
8.06	NOTCH4	4855	NOTCH4	notch receptor 4 [Source: HGNC Symbol; Acc: HGNC: 7884]
7.97	LRFN5	145581	LRFN5	leucine rich repeat and fibronectin type III domain containing 5 [Source: HGNC Symbol; Acc: HGNC: 20360]
7.97	STAB2	55576	STAB2	stabilin 2 [Source: HGNC Symbol; Acc: HGNC: 18629]
7.91	KRAS	3845	KRAS	KRAS proto-oncogene, GTPase [Source: HGNC Symbol; Acc: HGNC: 6407]
7.69	ERBB4	2066	ERBB4	erb-b2 receptor tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3432]
7.62	STAG2	10735	STAG2	stromal antigen 2 [Source: HGNC Symbol; Acc: HGNC: 11355]
7.59	PTPRZ1	5803	PTPRZ1	protein tyrosine phosphatase receptor type Z1 [Source: HGNC Symbol; Acc: HGNC: 9685]
7.43	APC	324	APC	APC regulator of WNT signaling pathway [Source: HGNC Symbol; Acc: HGNC: 583]
7.43	NTRK3	4916	NTRK3	neurotrophic receptor tyrosine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 8033]
6.79	ATM	472	ATM	ATM serine/threonine kinase [Source: HGNC Symbol; Acc: HGNC: 795]
6.67	FMN2	56776	FMN2	formin 2 [Source: HGNC Symbol; Acc: HGNC: 14074]
6.67	IRS1	3667	IRS1	insulin receptor substrate 1 [Source: HGNC Symbol; Acc: HGNC: 6125]
6.67	KIAA1324L	222223	KIAA1324L	KIAA1324 like [Source: HGNC Symbol; Acc: HGNC: 21945]
6.67	PKD1	5310	PKD1	polycystin 1, transient receptor potential channel interacting [Source: HGNC Symbol; Acc: HGNC: 9008]
6.56	BRCA2	675	BRCA2	BRCA2 DNA repair associated [Source: HGNC Symbol; Acc: HGNC: 1101]
6.52	ASPM	259266	ASPM	abnormal spindle microtubule assembly [Source: HGNC Symbol; Acc: HGNC: 19048]
6.52	LAMA1	284217	LAMA1	laminin subunit alpha 1 [Source: HGNC Symbol; Acc: HGNC: 6481]
6.37	ZNF521	25925	ZNF521	zinc finger protein 521 [Source: HGNC Symbol; Acc: HGNC: 24605]
6.34	MEN1	4221	MEN1	menin 1 [Source: HGNC Symbol; Acc: HGNC: 7010]
6.33	KAT6B	23522	KAT6B	lysine acetyltransferase 6B [Source: HGNC Symbol; Acc: HGNC: 17582]
5.80	SALL1	6299	SALL1	spalt like transcription factor 1 [Source: HGNC Symbol; Acc: HGNC: 10524]
5.65	IL7R	3575	IL7R	interleukin 7 receptor [Source: HGNC Symbol; Acc: HGNC: 6024]
5.54	PTEN	5728	PTEN	phosphatase and tensin homolog [Source: HGNC Symbol; Acc: HGNC: 9588]
5.46	NOTCH3	4854	NOTCH3	notch receptor 3 [Source: HGNC Symbol; Acc: HGNC: 7883]

5.43	SMARCA2	6595	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2 [Source: HGNC Symbol; Acc: HGNC: 11098]
5.10	PCLO	27445	PCLO	piccolo presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 13406]
5.07	PRIC285	85441	HELZ2	helicase with zinc finger 2 [Source: HGNC Symbol; Acc: HGNC: 30021]
5.06	DSCAML1	57453	DSCAML1	DS cell adhesion molecule like 1 [Source: HGNC Symbol; Acc: HGNC: 14656]
5.06	SPHKAP	80309	SPHKAP	SPHK1 interactor, AKAP domain containing [Source: HGNC Symbol; Acc: HGNC: 30619]
5.06	THSD7B	80731	THSD7B	thrombospondin type 1 domain containing 7B [Source: HGNC Symbol; Acc: HGNC: 29348]
5.00	HECW2	57520	HECW2	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2 [Source: HGNC Symbol; Acc: HGNC: 29853]
5.00	KIAA1211	57482	CRACD	capping protein inhibiting regulator of actin dynamics [Source: HGNC Symbol; Acc: HGNC: 29219]
5.00	MAP3K4	4216	MAP3K4	mitogen-activated protein kinase kinase kinase 4 [Source: HGNC Symbol; Acc: HGNC: 6856]
5.00	VPS13A	23230	VPS13A	vacuolar protein sorting 13 homolog A [Source: HGNC Symbol; Acc: HGNC: 1908]
5.00	XRN1	54464	XRN1	5'-3' exoribonuclease 1 [Source: HGNC Symbol; Acc: HGNC: 30654]
4.98	FLT3	2322	FLT3	fms related tyrosine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 3765]
4.95	ATRX	546	ATRX	ATRX chromatin remodeler [Source: HGNC Symbol; Acc: HGNC: 886]
4.95	FLT1	2321	FLT1	fms related tyrosine kinase 1 [Source: HGNC Symbol; Acc: HGNC: 3763]
4.95	MLL	4297	KMT2A	lysine methyltransferase 2A [Source: HGNC Symbol; Acc: HGNC: 7132]
4.92	MED12	9968	MED12	mediator complex subunit 12 [Source: HGNC Symbol; Acc: HGNC: 11957]
4.84	ARID2	196528	ARID2	AT-rich interaction domain 2 [Source: HGNC Symbol; Acc: HGNC: 18037]
4.84	GATA3	2625	GATA3	GATA binding protein 3 [Source: HGNC Symbol; Acc: HGNC: 4172]
4.84	PIK3CG	5294	PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma [Source: HGNC Symbol; Acc: HGNC: 8978]
4.80	PIK3CA	5290	PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha [Source: HGNC Symbol; Acc: HGNC: 8975]
4.76	PARK2	5071	PRKN	parkin RBR E3 ubiquitin protein ligase [Source: HGNC Symbol; Acc: HGNC: 8607]
4.76	PIK3C2G	5288	PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma [Source: HGNC Symbol; Acc: HGNC: 8973]
4.52	KDR	3791	KDR	kinase insert domain receptor [Source: HGNC Symbol; Acc: HGNC: 6307]
4.46	CREBBP	1387	CREBBP	CREB binding protein [Source: HGNC Symbol; Acc: HGNC: 2348]
4.46	DNMT3A	1788	DNMT3A	DNA methyltransferase 3 alpha [Source: HGNC Symbol; Acc: HGNC: 2978]
4.37	INSR	3643	INSR	insulin receptor [Source: HGNC Symbol; Acc: HGNC: 6091]
4.35	COL18A1	80781	COL18A1	collagen type XVIII alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 2195]
4.35	MDN1	23195	MDN1	midasin AAA ATPase 1 [Source: HGNC Symbol; Acc: HGNC: 18302]
4.35	PDGFRA	5156	PDGFRA	platelet derived growth factor receptor alpha [Source: HGNC Symbol; Acc: HGNC: 8803]
4.35	ZDBF2	57683	ZDBF2	zinc finger DBF-type containing 2 [Source: HGNC Symbol; Acc: HGNC: 29313]
4.09	NOTCH2	4853	NOTCH2	notch receptor 2 [Source: HGNC Symbol; Acc: HGNC: 7882]
4.03	NFE2L2	4780	NFE2L2	nuclear factor, erythroid 2 like 2 [Source: HGNC Symbol; Acc: HGNC: 7782]
4.03	AR	367	AR	androgen receptor [Source: HGNC Symbol; Acc: HGNC: 644]

4.03	DICER1	23405	DICER1	dicer 1, ribonuclease III [Source: HGNC Symbol; Acc: HGNC: 17098]
4.03	KDM5C	8242	KDM5C	lysine demethylase 5C [Source: HGNC Symbol; Acc: HGNC: 11114]
4.03	PAX5	5079	PAX5	paired box 5 [Source: HGNC Symbol; Acc: HGNC: 8619]
4.03	TET1	80312	TET1	tet methylcytosine dioxygenase 1 [Source: HGNC Symbol; Acc: HGNC: 29484]
3.96	ROS1	6098	ROS1	ROS proto-oncogene 1, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 10261]
3.95	MET	4233	MET	MET proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 7029]
3.82	NCAM2	4685	NCAM2	neural cell adhesion molecule 2 [Source: HGNC Symbol; Acc: HGNC: 7657]
3.81	AMER1	139285	AMER1	APC membrane recruitment protein 1 [Source: HGNC Symbol; Acc: HGNC: 26837]
3.80	RIN3	79890	AL159141.1	Ras and Rab interactor 3 [Source: NCBI gene; Acc: 79890]
3.63	KIT	3815	KIT	KIT proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 6342]
3.62	AHNAK2	113146	AHNAK2	AHNAK nucleoprotein 2 [Source: HGNC Symbol; Acc: HGNC: 20125]
3.62	KIAA0226	9711	RUBCN	rubicon autophagy regulator [Source: HGNC Symbol; Acc: HGNC: 28991]
3.62	OR5D14	219436	OR5D14	olfactory receptor family 5 subfamily D member 14 [Source: HGNC Symbol; Acc: HGNC: 15281]
3.62	VWDE	221806	VWDE	von Willebrand factor D and EGF domains [Source: HGNC Symbol; Acc: HGNC: 21897]
3.56	EGFR	1956	EGFR	epidermal growth factor receptor [Source: HGNC Symbol; Acc: HGNC: 3236]
3.47	IGF1R	3480	IGF1R	insulin like growth factor 1 receptor [Source: HGNC Symbol; Acc: HGNC: 5465]
3.36	PARP1	142	PARP1	poly(ADP-ribose) polymerase 1 [Source: HGNC Symbol; Acc: HGNC: 270]
3.36	SF3B1	23451	SF3B1	splicing factor 3b subunit 1 [Source: HGNC Symbol; Acc: HGNC: 10768]
3.33	APBB1IP	54518	APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein [Source: HGNC Symbol; Acc: HGNC: 17379]
3.33	ARHGAP4	393	ARHGAP4	Rho GTPase activating protein 4 [Source: HGNC Symbol; Acc: HGNC: 674]
3.33	CEP128	145508	CEP128	centrosomal protein 128 [Source: HGNC Symbol; Acc: HGNC: 20359]
3.33	FPR1	2357	FPR1	formyl peptide receptor 1 [Source: HGNC Symbol; Acc: HGNC: 3826]
3.33	RAD51C	5889	RAD51C	RAD51 paralog C [Source: HGNC Symbol; Acc: HGNC: 9820]
3.33	TP73	7161	TP73	tumor protein p73 [Source: HGNC Symbol; Acc: HGNC: 12003]
3.28	BCOR	54880	BCOR	BCL6 corepressor [Source: HGNC Symbol; Acc: HGNC: 20893]
3.23	BAP1	8314	BAP1	BRCA1 associated protein 1 [Source: HGNC Symbol; Acc: HGNC: 950]
3.23	IRS2	8660	IRS2	insulin receptor substrate 2 [Source: HGNC Symbol; Acc: HGNC: 6126]
3.23	PIK3CD	5293	PIK3CD	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta [Source: HGNC Symbol; Acc: HGNC: 8977]
3.23	WT1	7490	WT1	WT1 transcription factor [Source: HGNC Symbol; Acc: HGNC: 12796]
3.18	RNF213	57674	RNF213	ring finger protein 213 [Source: HGNC Symbol; Acc: HGNC: 14539]
2.97	EPHB1	2047	EPHB1	EPH receptor B1 [Source: HGNC Symbol; Acc: HGNC: 3392]
2.97	FLT4	2324	FLT4	fms related tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3767]
2.97	SETD2	29072	SETD2	SET domain containing 2, histone lysine methyltransferase [Source: HGNC Symbol; Acc: HGNC: 18420]
2.97	TSC2	7249	TSC2	TSC complex subunit 2 [Source: HGNC Symbol; Acc: HGNC: 12363]
2.90	ACSM2B	348158	ACSM2B	acyl-CoA synthetase medium chain family member 2B [Source: HGNC Symbol; Acc: HGNC: 30931]

2.90	DCHS1	8642	DCHS1	dachsous cadherin-related 1 [Source: HGNC Symbol; Acc: HGNC: 13681]
2.90	KIF1A	547	KIF1A	kinesin family member 1A [Source: HGNC Symbol; Acc: HGNC: 888]
2.90	MEGF8	1954	MEGF8	multiple EGF like domains 8 [Source: HGNC Symbol; Acc: HGNC: 3233]
2.90	PLEC	5339	PLEC	plectin [Source: HGNC Symbol; Acc: HGNC: 9069]
2.86	INPP4A	3631	INPP4A	inositol polyphosphate-4-phosphatase type I A [Source: HGNC Symbol; Acc: HGNC: 6074]
2.80	HNF1A	6927	HNF1A	HNF1 homeobox A [Source: HGNC Symbol; Acc: HGNC: 11621]
2.80	SMO	6608	SMO	smoothened, frizzled class receptor [Source: HGNC Symbol; Acc: HGNC: 11119]
2.77	ALK	238	ALK	ALK receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 427]
2.73	ETV6	2120	ETV6	ETS variant transcription factor 6 [Source: HGNC Symbol; Acc: HGNC: 3495]
2.71	ABL1	25	ABL1	ABL proto-oncogene 1, non-receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 76]
2.53	FANCD2	2177	FANCD2	FA complementation group D2 [Source: HGNC Symbol; Acc: HGNC: 3585]
2.48	EP300	2033	EP300	E1A binding protein p300 [Source: HGNC Symbol; Acc: HGNC: 3373]
2.42	CBL	867	CBL	Cbl proto-oncogene [Source: HGNC Symbol; Acc: HGNC: 1541]
2.42	CCND2	894	CCND2	cyclin D2 [Source: HGNC Symbol; Acc: HGNC: 1583]
2.42	CDC73	79577	CDC73	cell division cycle 73 [Source: HGNC Symbol; Acc: HGNC: 16783]
2.42	CDK12	51755	CDK12	cyclin dependent kinase 12 [Source: HGNC Symbol; Acc: HGNC: 24224]
2.42	ERCC5	2073	ERCC5	ERCC excision repair 5, endonuclease [Source: HGNC Symbol; Acc: HGNC: 3437]
2.42	ETV1	2115	ETV1	ETS variant transcription factor 1 [Source: HGNC Symbol; Acc: HGNC: 3490]
2.42	IKZF1	10320	IKZF1	IKAROS family zinc finger 1 [Source: HGNC Symbol; Acc: HGNC: 13176]
2.42	MDM4	4194	MDM4	MDM4 regulator of p53 [Source: HGNC Symbol; Acc: HGNC: 6974]
2.42	TNFAIP3	7128	TNFAIP3	TNF alpha induced protein 3 [Source: HGNC Symbol; Acc: HGNC: 11896]
2.37	BRAF	673	BRAF	B-Raf proto-oncogene, serine/threonine kinase [Source: HGNC Symbol; Acc: HGNC: 1097]
2.37	ERBB2	2064	ERBB2	erb-b2 receptor tyrosine kinase 2 [Source: HGNC Symbol; Acc: HGNC: 3430]
2.26	FGFR1	2260	FGFR1	fibroblast growth factor receptor 1 [Source: HGNC Symbol; Acc: HGNC: 3688]
2.19	BRCA1	672	BRCA1	BRCA1 DNA repair associated [Source: HGNC Symbol; Acc: HGNC: 1100]
2.19	RICTOR	253260	RICTOR	RPTOR independent companion of MTOR complex 2 [Source: HGNC Symbol; Acc: HGNC: 28611]
2.10	CDKN2A	1029	CDKN2A	cyclin dependent kinase inhibitor 2A [Source: HGNC Symbol; Acc: HGNC: 1787]
1.98	MTOR	2475	MTOR	mechanistic target of rapamycin kinase [Source: HGNC Symbol; Acc: HGNC: 3942]
1.98	NTRK1	4914	NTRK1	neurotrophic receptor tyrosine kinase 1 [Source: HGNC Symbol; Acc: HGNC: 8031]
1.98	TSC1	7248	TSC1	TSC complex subunit 1 [Source: HGNC Symbol; Acc: HGNC: 12362]
1.98	GNAS	2778	GNAS	GNAS complex locus [Source: HGNC Symbol; Acc: HGNC: 4392]
1.91	AKAP9	10142	AKAP9	A-kinase anchoring protein 9 [Source: HGNC Symbol; Acc: HGNC: 379]
1.81	HRAS	3265	HRAS	HRas proto-oncogene, GTPase [Source: HGNC Symbol; Acc: HGNC: 5173]
1.67	ATP1A2	477	ATP1A2	ATPase Na+/K+ transporting subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 800]
1.67	EPG5	57724	EPG5	ectopic P-granules autophagy protein 5 homolog [Source: HGNC Symbol; Acc: HGNC: 29331]

1.67	NCOR2	9612	NCOR2	nuclear receptor corepressor 2 [Source: HGNC Symbol; Acc: HGNC: 7673]
1.67	PSMD2	5708	PSMD2	proteasome 26S subunit, non-ATPase 2 [Source: HGNC Symbol; Acc: HGNC: 9559]
1.67	PTGFRN	5738	PTGFRN	prostaglandin F2 receptor inhibitor [Source: HGNC Symbol; Acc: HGNC: 9601]
1.67	RBL1	5933	RBL1	RB transcriptional corepressor like 1 [Source: HGNC Symbol; Acc: HGNC: 9893]
1.67	SPATA6	54558	SPATA6	spermatogenesis associated 6 [Source: HGNC Symbol; Acc: HGNC: 18309]
1.67	TRAPPC9	83696	TRAPPC9	trafficking protein particle complex 9 [Source: HGNC Symbol; Acc: HGNC: 30832]
1.67	YTHDC2	64848	YTHDC2	YTH domain containing 2 [Source: HGNC Symbol; Acc: HGNC: 24721]
1.61	CIC	23152	CIC	capicua transcriptional repressor [Source: HGNC Symbol; Acc: HGNC: 14214]
1.61	PALB2	79728	PALB2	partner and localizer of BRCA2 [Source: HGNC Symbol; Acc: HGNC: 26144]
1.61	PTCH1	5727	PTCH1	patched 1 [Source: HGNC Symbol; Acc: HGNC: 9585]
1.52	SOX2	6657	SOX2	SRY-box transcription factor 2 [Source: HGNC Symbol; Acc: HGNC: 11195]
1.49	AKT3	10000	AKT3	AKT serine/threonine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 393]
1.45	CHD7	55636	CHD7	chromodomain helicase DNA binding protein 7 [Source: HGNC Symbol; Acc: HGNC: 20626]
1.45	CLTCL1	8218	CLTCL1	clathrin heavy chain like 1 [Source: HGNC Symbol; Acc: HGNC: 2093]
1.45	MUC12	10071	MUC12	mucin 12, cell surface associated [Source: HGNC Symbol; Acc: HGNC: 7510]
1.45	RGS7	6000	RGS7	regulator of G protein signaling 7 [Source: HGNC Symbol; Acc: HGNC: 10003]
1.45	ZNF208	7757	ZNF208	zinc finger protein 208 [Source: HGNC Symbol; Acc: HGNC: 12999]
1.36	JAK2	3717	JAK2	Janus kinase 2 [Source: HGNC Symbol; Acc: HGNC: 6192]
1.36	RET	5979	RET	ret proto-oncogene [Source: HGNC Symbol; Acc: HGNC: 9967]
1.27	TDRD7	23424	TDRD7	tudor domain containing 7 [Source: HGNC Symbol; Acc: HGNC: 30831]
1.14	SMAD4	4089	SMAD4	SMAD family member 4 [Source: HGNC Symbol; Acc: HGNC: 6770]

Table S4. Genes Frequently mutated in Small Cell Lung Carcinomas (SCLCs).

Mutation Rate %	Original	Entrez	Gene	Gene
92.76	TP53	7157	TP53	tumor protein p53 [Source: HGNC Symbol; Acc: HGNC: 11998]
66.67	LRP1B	53353	LRP1B	LDL receptor related protein 1B [Source: HGNC Symbol; Acc: HGNC: 6693]
60.18	RB1	5925	RB1	RB transcriptional corepressor 1 [Source: HGNC Symbol; Acc: HGNC: 9884]
55.26	CSMD3	114788	CSMD3	CUB and Sushi multiple domains 3 [Source: HGNC Symbol; Acc: HGNC: 19291]
33.50	ZFHX4	79776	ZFHX4	zinc finger homeobox 4 [Source: HGNC Symbol; Acc: HGNC: 30939]
33.33	SYNE1	23345	SYNE1	spectrin repeat containing nuclear envelope protein 1 [Source: HGNC Symbol; Acc: HGNC: 17089]
29.00	USH2A	7399	USH2A	usherin [Source: HGNC Symbol; Acc: HGNC: 12601]
23.68	SPHKAP	80309	SPHKAP	SPHK1 interactor, AKAP domain containing [Source: HGNC Symbol; Acc: HGNC: 30619]
21.08	MLL2	8085	KMT2D	lysine methyltransferase 2D [Source: HGNC Symbol; Acc: HGNC: 7133]
19.09	KIAA1211	57482	CRACD	capping protein inhibiting regulator of actin dynamics [Source: HGNC Symbol; Acc: HGNC: 29219]
18.50	COL11A1	1301	COL11A1	collagen type XI alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 2186]
18.18	FMN2	56776	FMN2	formin 2 [Source: HGNC Symbol; Acc: HGNC: 14074]

16.36	ADAMTS 12	81792	ADAMTS12	ADAM metallopeptidase with thrombospondin type 1 motif 12 [Source: HGNC Symbol; Acc: HGNC: 14605]
15.79	DST	667	DST	dystonin [Source: HGNC Symbol; Acc: HGNC: 1090]
15.20	PCLO	27445	PCLO	piccolo presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 13406]
14.22	NCAM2	4685	NCAM2	neural cell adhesion molecule 2 [Source: HGNC Symbol; Acc: HGNC: 7657]
14.04	THSD7B	80731	THSD7B	thrombospondin type 1 domain containing 7B [Source: HGNC Symbol; Acc: HGNC: 29348]
12.73	EPHA5	2044	EPHA5	EPH receptor A5 [Source: HGNC Symbol; Acc: HGNC: 3389]
11.82	ALMS1	7840	ALMS1	ALMS1 centrosome and basal body associated protein [Source: HGNC Symbol; Acc: HGNC: 428]
11.50	COL22A1	169044	COL22A1	collagen type XXII alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 22989]
11.40	PTPRD	5789	PTPRD	protein tyrosine phosphatase receptor type D [Source: HGNC Symbol; Acc: HGNC: 9668]
11.40	PTPRT	11122	PTPRT	protein tyrosine phosphatase receptor type T [Source: HGNC Symbol; Acc: HGNC: 9682]
10.50	LAMA1	284217	LAMA1	laminin subunit alpha 1 [Source: HGNC Symbol; Acc: HGNC: 6481]
10.50	LAMA2	3908	LAMA2	laminin subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 6482]
10.50	PLEC	5339	PLEC	plectin [Source: HGNC Symbol; Acc: HGNC: 9069]
10.50	ZNF208	7757	ZNF208	zinc finger protein 208 [Source: HGNC Symbol; Acc: HGNC: 12999]
10.29	MLL3	58508	KMT2C	lysine methyltransferase 2C [Source: HGNC Symbol; Acc: HGNC: 13726]
10.00	ASPM	259266	ASPM	abnormal spindle microtubule assembly [Source: HGNC Symbol; Acc: HGNC: 19048]
10.00	DNAH9	1770	DNAH9	dynein axonemal heavy chain 9 [Source: HGNC Symbol; Acc: HGNC: 2953]
10.00	STAB2	55576	STAB2	stabilin 2 [Source: HGNC Symbol; Acc: HGNC: 18629]
9.50	NOTCH1	4851	NOTCH1	notch receptor 1 [Source: HGNC Symbol; Acc: HGNC: 7881]
9.09	GRIN2A	2903	GRIN2A	glutamate ionotropic receptor NMDA type subunit 2A [Source: HGNC Symbol; Acc: HGNC: 4585]
9.00	FAT1	2195	FAT1	FAT atypical cadherin 1 [Source: HGNC Symbol; Acc: HGNC: 3595]
8.50	CHD7	55636	CHD7	chromodomain helicase DNA binding protein 7 [Source: HGNC Symbol; Acc: HGNC: 20626]
8.33	ZNF521	25925	ZNF521	zinc finger protein 521 [Source: HGNC Symbol; Acc: HGNC: 24605]
8.18	XRN1	54464	XRN1	5'-3' exoribonuclease 1 [Source: HGNC Symbol; Acc: HGNC: 30654]
8.00	AHNAK2	113146	AHNAK2	AHNAK nucleoprotein 2 [Source: HGNC Symbol; Acc: HGNC: 20125]
8.00	GPR98	84059	ADGRV1	adhesion G protein-coupled receptor V1 [Source: HGNC Symbol; Acc: HGNC: 17416]
8.00	LRFN5	145581	LRFN5	leucine rich repeat and fibronectin type III domain containing 5 [Source: HGNC Symbol; Acc: HGNC: 20360]
7.84	CREBBP	1387	CREBBP	CREB binding protein [Source: HGNC Symbol; Acc: HGNC: 2348]
7.50	NOTCH3	4854	NOTCH3	notch receptor 3 [Source: HGNC Symbol; Acc: HGNC: 7883]
7.35	EP300	2033	EP300	E1A binding protein p300 [Source: HGNC Symbol; Acc: HGNC: 3373]
7.27	BSN	8927	BSN	bassoon presynaptic cytomatrix protein [Source: HGNC Symbol; Acc: HGNC: 1117]
7.27	HECW2	57520	HECW2	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2 [Source: HGNC Symbol; Acc: HGNC: 29853]
7.27	PIK3C2G	5288	PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma [Source: HGNC Symbol; Acc: HGNC: 8973]
7.02	DSCAML1	57453	DSCAML1	DS cell adhesion molecule like 1 [Source: HGNC Symbol; Acc: HGNC: 14656]
7.02	PIK3CG	5294	PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma [Source: HGNC Symbol; Acc: HGNC: 8978]

7.02	PTPRZ1	5803	PTPRZ1	protein tyrosine phosphatase receptor type Z1 [Source: HGNC Symbol; Acc: HGNC: 9685]
7.00	DCHS1	8642	DCHS1	dachsous cadherin-related 1 [Source: HGNC Symbol; Acc: HGNC: 13681]
7.00	KIF1A	547	KIF1A	kinesin family member 1A [Source: HGNC Symbol; Acc: HGNC: 888]
6.37	PDE4DIP	9659	PDE4DIP	phosphodiesterase 4D interacting protein [Source: HGNC Symbol; Acc: HGNC: 15580]
6.36	COL5A3	50509	COL5A3	collagen type V alpha 3 chain [Source: HGNC Symbol; Acc: HGNC: 14864]
6.36	FPR1	2357	FPR1	formyl peptide receptor 1 [Source: HGNC Symbol; Acc: HGNC: 3826]
6.36	TRAPPC9	83696	TRAPPC9	trafficking protein particle complex 9 [Source: HGNC Symbol; Acc: HGNC: 30832]
6.36	VPS13A	23230	VPS13A	vacuolar protein sorting 13 homolog A [Source: HGNC Symbol; Acc: HGNC: 1908]
6.33	ERBB4	2066	ERBB4	erb-b2 receptor tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3432]
6.33	PIK3CA	5290	PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha [Source: HGNC Symbol; Acc: HGNC: 8975]
6.00	CNTNAP 2	26047	CNTNAP2	contactin associated protein like 2 [Source: HGNC Symbol; Acc: HGNC: 13830]
6.00	OR5D14	219436	OR5D14	olfactory receptor family 5 subfamily D member 14 [Source: HGNC Symbol; Acc: HGNC: 15281]
6.00	RGS7	6000	RGS7	regulator of G protein signaling 7 [Source: HGNC Symbol; Acc: HGNC: 10003]
5.88	ATRX	546	ATRX	ATRX chromatin remodeler [Source: HGNC Symbol; Acc: HGNC: 886]
5.50	MED12	9968	MED12	mediator complex subunit 12 [Source: HGNC Symbol; Acc: HGNC: 11957]
5.50	MUC12	10071	MUC12	mucin 12, cell surface associated [Source: HGNC Symbol; Acc: HGNC: 7510]
5.50	PRIC285	85441	HELZ2	helicase with zinc finger 2 [Source: HGNC Symbol; Acc: HGNC: 30021]
5.50	VWDE	221806	VWDE	von Willebrand factor D and EGF domains [Source: HGNC Symbol; Acc: HGNC: 21897]
5.45	ARHGAP 4	393	ARHGAP4	Rho GTPase activating protein 4 [Source: HGNC Symbol; Acc: HGNC: 674]
5.45	ATP1A2	477	ATP1A2	ATPase Na+/K+ transporting subunit alpha 2 [Source: HGNC Symbol; Acc: HGNC: 800]
5.45	CEP128	145508	CEP128	centrosomal protein 128 [Source: HGNC Symbol; Acc: HGNC: 20359]
5.45	EPG5	57724	EPG5	ectopic P-granules autophagy protein 5 homolog [Source: HGNC Symbol; Acc: HGNC: 29331]
5.45	KIAA1324 L	222223	KIAA1324L	KIAA1324 like [Source: HGNC Symbol; Acc: HGNC: 21945]
5.45	MAP3K4	4216	MAP3K4	mitogen-activated protein kinase kinase kinase 4 [Source: HGNC Symbol; Acc: HGNC: 6856]
5.45	PKD1	5310	PKD1	polycystin 1, transient receptor potential channel interacting [Source: HGNC Symbol; Acc: HGNC: 9008]
5.45	SMARCA 2	6595	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2 [Source: HGNC Symbol; Acc: HGNC: 11098]
5.45	SORL1	6653	SORL1	sortilin related receptor 1 [Source: HGNC Symbol; Acc: HGNC: 11185]
5.45	STAG2	10735	STAG2	stromal antigen 2 [Source: HGNC Symbol; Acc: HGNC: 11355]
5.45	TP73	7161	TP73	tumor protein p73 [Source: HGNC Symbol; Acc: HGNC: 12003]
5.43	PTEN	5728	PTEN	phosphatase and tensin homolog [Source: HGNC Symbol; Acc: HGNC: 9588]
4.98	ATM	472	ATM	ATM serine/threonine kinase [Source: HGNC Symbol; Acc: HGNC: 795]
4.98	RET	5979	RET	ret proto-oncogene [Source: HGNC Symbol; Acc: HGNC: 9967]
4.90	EPHB1	2047	EPHB1	EPH receptor B1 [Source: HGNC Symbol; Acc: HGNC: 3392]
4.58	APC	324	APC	APC regulator of WNT signaling pathway [Source: HGNC Symbol; Acc: HGNC: 583]

4.55	ADAMTS2	9509	ADAMTS2	ADAM metallopeptidase with thrombospondin type 1 motif 2 [Source: HGNC Symbol; Acc: HGNC: 218]
4.55	APBB1IP	54518	APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein [Source: HGNC Symbol; Acc: HGNC: 17379]
4.55	EIF4G3	8672	EIF4G3	eukaryotic translation initiation factor 4 gamma 3 [Source: HGNC Symbol; Acc: HGNC: 3298]
4.55	FAP	2191	FAP	fibroblast activation protein alpha [Source: HGNC Symbol; Acc: HGNC: 3590]
4.55	NCOR2	9612	NCOR2	nuclear receptor corepressor 2 [Source: HGNC Symbol; Acc: HGNC: 7673]
4.55	POLE	5426	POLE	DNA polymerase epsilon, catalytic subunit [Source: HGNC Symbol; Acc: HGNC: 9177]
4.55	PSMD2	5708	PSMD2	proteasome 26S subunit, non-ATPase 2 [Source: HGNC Symbol; Acc: HGNC: 9559]
4.55	PTGFRN	5738	PTGFRN	prostaglandin F2 receptor inhibitor [Source: HGNC Symbol; Acc: HGNC: 9601]
4.55	SPATA6	54558	SPATA6	spermatogenesis associated 6 [Source: HGNC Symbol; Acc: HGNC: 18309]
4.52	ALK	238	ALK	ALK receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 427]
4.41	NF1	4763	NF1	neurofibromin 1 [Source: HGNC Symbol; Acc: HGNC: 7765]
4.41	NOTCH2	4853	NOTCH2	notch receptor 2 [Source: HGNC Symbol; Acc: HGNC: 7882]
4.41	ROS1	6098	ROS1	ROS proto-oncogene 1, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 10261]
4.39	AR	367	AR	androgen receptor [Source: HGNC Symbol; Acc: HGNC: 644]
4.39	CBL	867	CBL	Cbl proto-oncogene [Source: HGNC Symbol; Acc: HGNC: 1541]
4.39	NOTCH4	4855	NOTCH4	notch receptor 4 [Source: HGNC Symbol; Acc: HGNC: 7884]
4.39	WT1	7490	WT1	WT1 transcription factor [Source: HGNC Symbol; Acc: HGNC: 12796]
4.00	ACSM2B	348158	ACSM2B	acyl-CoA synthetase medium chain family member 2B [Source: HGNC Symbol; Acc: HGNC: 30931]
4.00	MDN1	23195	MDN1	midasin AAA ATPase 1 [Source: HGNC Symbol; Acc: HGNC: 18302]
4.00	MEGF8	1954	MEGF8	multiple EGF like domains 8 [Source: HGNC Symbol; Acc: HGNC: 3233]
3.92	AKAP9	10142	AKAP9	A-kinase anchoring protein 9 [Source: HGNC Symbol; Acc: HGNC: 379]
3.69	KIT	3815	KIT	KIT proto-oncogene, receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 6342]
3.64	RBL1	5933	RBL1	RB transcriptional corepressor like 1 [Source: HGNC Symbol; Acc: HGNC: 9893]
3.64	YTHDC2	64848	YTHDC2	YTH domain containing 2 [Source: HGNC Symbol; Acc: HGNC: 24721]
3.62	EGFR	1956	EGFR	epidermal growth factor receptor [Source: HGNC Symbol; Acc: HGNC: 3236]
3.62	KDR	3791	KDR	kinase insert domain receptor [Source: HGNC Symbol; Acc: HGNC: 6307]
3.62	PDGFRA	5156	PDGFRA	platelet derived growth factor receptor alpha [Source: HGNC Symbol; Acc: HGNC: 8803]
3.51	IL7R	3575	IL7R	interleukin 7 receptor [Source: HGNC Symbol; Acc: HGNC: 6024]
3.51	KEAP1	9817	KEAP1	kelch like ECH associated protein 1 [Source: HGNC Symbol; Acc: HGNC: 23177]
3.50	COL18A1	80781	COL18A1	collagen type XVIII alpha 1 chain [Source: HGNC Symbol; Acc: HGNC: 2195]
3.43	NTRK1	4914	NTRK1	neurotrophic receptor tyrosine kinase 1 [Source: HGNC Symbol; Acc: HGNC: 8031]
3.43	TSC2	7249	TSC2	TSC complex subunit 2 [Source: HGNC Symbol; Acc: HGNC: 12363]
3.17	GNAS	2778	GNAS	GNAS complex locus [Source: HGNC Symbol; Acc: HGNC: 4392]
3.00	CLTCL1	8218	CLTCL1	clathrin heavy chain like 1 [Source: HGNC Symbol; Acc: HGNC: 2093]
3.00	RBL2	5934	RBL2	RB transcriptional corepressor like 2 [Source: HGNC Symbol; Acc: HGNC: 9894]
3.00	SALL1	6299	SALL1	spalt like transcription factor 1 [Source: HGNC Symbol; Acc: HGNC: 10524]

2.94	ARID1A	8289	ARID1A	AT-rich interaction domain 1A [Source: HGNC Symbol; Acc: HGNC: 11110]
2.94	FLT1	2321	FLT1	fms related tyrosine kinase 1 [Source: HGNC Symbol; Acc: HGNC: 3763]
2.94	MLL	4297	KMT2A	lysine methyltransferase 2A [Source: HGNC Symbol; Acc: HGNC: 7132]
2.94	NUP98	4928	NUP98	nucleoporin 98 [Source: HGNC Symbol; Acc: HGNC: 8068]
2.94	SMARCA 4	6597	SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 [Source: HGNC Symbol; Acc: HGNC: 11100]
2.94	TSHR	7253	TSHR	thyroid stimulating hormone receptor [Source: HGNC Symbol; Acc: HGNC: 12373]
2.73	GAS7	8522	AC005747.1	growth arrest specific 7 [Source: NCBI gene; Acc: 8522]
2.73	INPP4A	3631	INPP4A	inositol polyphosphate-4-phosphatase type I A [Source: HGNC Symbol; Acc: HGNC: 6074]
2.73	IRS1	3667	IRS1	insulin receptor substrate 1 [Source: HGNC Symbol; Acc: HGNC: 6125]
2.73	PAK7	57144	PAK5	p21 (RAC1) activated kinase 5 [Source: HGNC Symbol; Acc: HGNC: 15916]
2.63	EPHA3	2042	EPHA3	EPH receptor A3 [Source: HGNC Symbol; Acc: HGNC: 3387]
2.63	GATA3	2625	GATA3	GATA binding protein 3 [Source: HGNC Symbol; Acc: HGNC: 4172]
2.63	IKZF1	10320	IKZF1	IKAROS family zinc finger 1 [Source: HGNC Symbol; Acc: HGNC: 13176]
2.63	PALB2	79728	PALB2	partner and localizer of BRCA2 [Source: HGNC Symbol; Acc: HGNC: 26144]
2.63	PAX5	5079	PAX5	paired box 5 [Source: HGNC Symbol; Acc: HGNC: 8619]
2.63	PTCH1	5727	PTCH1	patched 1 [Source: HGNC Symbol; Acc: HGNC: 9585]
2.63	TET1	80312	TET1	tet methylcytosine dioxygenase 1 [Source: HGNC Symbol; Acc: HGNC: 29484]
2.50	BCOR	54880	BCOR	BCL6 corepressor [Source: HGNC Symbol; Acc: HGNC: 20893]
2.50	INSR	3643	INSR	insulin receptor [Source: HGNC Symbol; Acc: HGNC: 6091]
2.50	MSH3	4437	MSH3	mutS homolog 3 [Source: HGNC Symbol; Acc: HGNC: 7326]
2.50	ZDBF2	57683	ZDBF2	zinc finger DBF-type containing 2 [Source: HGNC Symbol; Acc: HGNC: 29313]
2.50	ZNF195	7748	ZNF195	zinc finger protein 195 [Source: HGNC Symbol; Acc: HGNC: 12986]
2.45	DNMT3A	1788	DNMT3A	DNA methyltransferase 3 alpha [Source: HGNC Symbol; Acc: HGNC: 2978]
2.45	FLT4	2324	FLT4	fms related tyrosine kinase 4 [Source: HGNC Symbol; Acc: HGNC: 3767]
2.45	RNF213	57674	RNF213	ring finger protein 213 [Source: HGNC Symbol; Acc: HGNC: 14539]
2.29	CDKN2A	1029	CDKN2A	cyclin dependent kinase inhibitor 2A [Source: HGNC Symbol; Acc: HGNC: 1787]
2.29	IDH1	3417	IDH1	isocitrate dehydrogenase (NADP(+)) 1 [Source: HGNC Symbol; Acc: HGNC: 5382]
2.26	ERBB2	2064	ERBB2	erb-b2 receptor tyrosine kinase 2 [Source: HGNC Symbol; Acc: HGNC: 3430]
1.96	MTOR	2475	MTOR	mechanistic target of rapamycin kinase [Source: HGNC Symbol; Acc: HGNC: 3942]
1.96	NTRK3	4916	NTRK3	neurotrophic receptor tyrosine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 8033]
1.96	PDGFRB	5159	PDGFRB	platelet derived growth factor receptor beta [Source: HGNC Symbol; Acc: HGNC: 8804]
1.82	NTM	50863	NTM	neurotrimin [Source: HGNC Symbol; Acc: HGNC: 17941]
1.82	SF3B1	23451	SF3B1	splicing factor 3b subunit 1 [Source: HGNC Symbol; Acc: HGNC: 10768]
1.81	ABL1	25	ABL1	ABL proto-oncogene 1, non-receptor tyrosine kinase [Source: HGNC Symbol; Acc: HGNC: 76]
1.81	JAK3	3718	JAK3	Janus kinase 3 [Source: HGNC Symbol; Acc: HGNC: 6193]
1.75	CDK12	51755	CDK12	cyclin dependent kinase 12 [Source: HGNC Symbol; Acc: HGNC: 24224]
1.75	CIC	23152	CIC	capicua transcriptional repressor [Source: HGNC Symbol; Acc: HGNC: 14214]

1.75	IRS2	8660	IRS2	insulin receptor substrate 2 [Source: HGNC Symbol; Acc: HGNC: 6126]
1.75	KAT6B	23522	KAT6B	lysine acetyltransferase 6B [Source: HGNC Symbol; Acc: HGNC: 17582]
1.75	TDRD7	23424	TDRD7	tudor domain containing 7 [Source: HGNC Symbol; Acc: HGNC: 30831]
1.75	TNFAIP3	7128	TNFAIP3	TNF alpha induced protein 3 [Source: HGNC Symbol; Acc: HGNC: 11896]
1.53	HNF1A	6927	HNF1A	HNF1 homeobox A [Source: HGNC Symbol; Acc: HGNC: 11621]
1.53	SMAD4	4089	SMAD4	SMAD family member 4 [Source: HGNC Symbol; Acc: HGNC: 6770]
1.53	SMO	6608	SMO	smoothened, frizzled class receptor [Source: HGNC Symbol; Acc: HGNC: 11119]
1.50	ETV6	2120	ETV6	ETS variant transcription factor 6 [Source: HGNC Symbol; Acc: HGNC: 3495]
1.50	KIAA0226	9711	RUBCN	rubicon autophagy regulator [Source: HGNC Symbol; Acc: HGNC: 28991]
1.50	RICTOR	253260	RICTOR	RPTOR independent companion of MTOR complex 2 [Source: HGNC Symbol; Acc: HGNC: 28611]
1.47	IGF1R	3480	IGF1R	insulin like growth factor 1 receptor [Source: HGNC Symbol; Acc: HGNC: 5465]
1.47	SETD2	29072	SETD2	SET domain containing 2, histone lysine methyltransferase [Source: HGNC Symbol; Acc: HGNC: 18420]
1.36	FLT3	2322	FLT3	fms related tyrosine kinase 3 [Source: HGNC Symbol; Acc: HGNC: 3765]
1.36	JAK2	3717	JAK2	Janus kinase 2 [Source: HGNC Symbol; Acc: HGNC: 6192]

Table S5. Top 10 recurrently mutated genes among WHO histotypes.

Gene	All	NETs		NECs		*p*-Value*	*p*-Value#
		TCs	ACs	LCNECs	SCLCs		
Top10TCsRecurrentlyMutatedGenes							
EIF1AX	7/256(2.73)	3/62(4.84)	4/24(16.66)	0/60(0.0)	0/110(0.0)	0.0001	0.0004
ARID1A	38/582(6.52)	4/85(4.71)	7/73(9.59)	21/220(9.54)	6/204(2.94)	0.02	0.85
LRP1B	118/301(39.20)	3/69(4.34)	0/39(0.0)	39/79(49.36)	76/114(66.67)	<0.0001	<0.0001
NF1	31/543(5.70)	3/85(3.53)	1/52(1.92)	18/202(8.91)	9/204(4.41)	0.12	0.13
DSCAML1	16/301(5.31)	2/69(2.90)	2/39(5.12)	4/79(5.06)	8/114(7.01)	0.71	0.43
DST	28/301(9.30)	2/69(2.90)	0/39(0.0)	8/79(10.12)	18/114(15.78)	0.003	0.0006
FANCD2	4/301(1.32)	2/69(2.90)	0/39(0.0)	2/79(2.53)	0/114(0.0)	0.21	0.62
PCLO	43/469(9.16)	2/69(2.90)	2/39(5.12)	8/157(5.09)	31/204(15.19)	0.001	0.02
ERBB2	16/670(2.38)	3/123(2.43)	2/73(2.73)	6/253(2.37)	5/221(2.26)	1.00	0.79
BAP1	6/375(1.60)	2/85(2.35)	0/52(0.0)	4/124(3.22)	0/114(0.0)	0.17	1.00
Top10ACsRecurrentlyMutatedGenes							
MEN1	28/414(6.76)	1/85(1.17)	18/73(24.66)	9/142(6.33)	0/114(0.0)	<0.0001	0.001
ATP1A2	10/227(4.40)	1/46(2.17)	2/11(18.18)	1/60(1.66)	6/110(5.45)	0.10	0.71
EIF1AX	7/256(2.73)	3/62(4.84)	4/24(16.66)	0/60(0.0)	0/110(0.0)	0.0001	0.0004
SPHKAP	37/301(12.29)	1/69(1.44)	5/39(12.82)	4/79(5.06)	27/114(23.68)	<0.0001	0.009
ARID1A	38/582(6.52)	4/85(4.71)	7/73(9.59)	21/220(9.54)	6/204(2.94)	0.02	0.85
SMARCA4	31/582(5.32)	0/85(0.0)	7/73(9.59)	18/220(8.18)	6/204(2.94)	0.002	0.68
PKD1	11/227(4.84)	0/46(0.0)	1/11(9.09)	4/60(6.66)	6/110(5.45)	0.21	0.30
AMER1	6/301(1.99)	0/62(0.0)	2/24(8.33)	4/105(3.80)	0/110(0.0)	0.01	1.00
RAD51C	5/256(1.95)	1/62(1.61)	2/24(8.33)	2/60(3.33)	0/110(0.0)	0.02	0.34
TDRD7	7/301(2.32)	1/69(1.44)	3/39(7.69)	1/79(1.26)	2/114(1.75)	0.15	0.25
Top10LCNECsRecurrentlyMutatedGenes							
TP53	516/788(65.48)	1/123(0.81)	5/94(5.31)	305/350(87.14)	205/221(92.76)	<0.0001	<0.0001
LRP1B	118/301(39.20)	3/69(4.34)	0/39(0.0)	39/79(49.36)	76/114(66.67)	<0.0001	<0.0001
CSMD3	103/301(34.21)	1/69(1.44)	2/39(5.12)	37/79(46.83)	63/114(55.26)	<0.0001	<0.0001
RB1	248/731(33.92)	1/102(0.98)	2/90(2.22)	112/318(35.22)	133/221(60.18)	<0.0001	<0.0001
SYNE1	60/301(19.93)	1/69(1.44)	0/39(0.0)	21/79(26.58)	38/114(33.33)	<0.0001	<0.0001
ADAMTS12	31/227(13.65)	0/46(0.0)	0/11(0.0)	13/60(21.66)	18/110(16.36)	0.001	<0.0001
USH2A	86/395(21.76)	0/46(0.0)	0/11(0.0)	28/138(20.28)	58/200(29)	<0.0001	<0.0001
STK11	54/607(8.90)	0/114(0.0)	0/90(0.0)	53/272(19.49)	1/131(0.76)	<0.0001	<0.0001
KEAP1	48/480(10)	0/76(0.0)	0/69(0.0)	44/221(19.91)	4/114(3.50)	<0.0001	<0.0001
DNAH9	46/395(11.64)	0/46(0.0)	0/11(0.0)	26/138(18.84)	20/200(10)	0.001	0.0006
Top10SCLCsRecurrentlyMutatedGenes							

TP53	516/788(65.48)	1/123(0.81)	5/94(5.31)	305/350(87.14)	205/221(92.76)	<0.0001	<0.0001
LRP1B	118/301(39.20)	3/69(4.34)	0/39(0.0)	39/79(49.36)	76/114(66.67)	<0.0001	<0.0001
RB1	248/731(33.92)	1/102(0.98)	2/90(2.22)	112/318(35.22)	133/221(60.18)	<0.0001	<0.0001
CSMD3	103/301(34.21)	1/69(1.44)	2/39(5.12)	37/79(46.83)	63/114(55.26)	<0.0001	<0.0001
ZFHX4	82/395(20.75)	0/46(0.0)	0/11(0.0)	15/138(10.86)	67/200(33.50)	<0.0001	<0.0001
SYNE1	60/301(19.93)	1/69(1.44)	0/39(0.0)	21/79(26.58)	38/114(33.33)	<0.0001	<0.0001
USH2A	86/395(21.76)	0/46(0.0)	0/11(0.0)	28/138(20.28)	58/200(29)	<0.0001	<0.0001
SPHKAP	37/301(12.29)	1/69(1.44)	5/39(12.82)	4/79(5.06)	27/114(23.68)	<0.0001	0.009
KMT2D	68/582(11.68)	0/85(0.0)	4/73(5.48)	21/220(9.54)	43/204(21.07)	<0.0001	<0.0001
KIAA1211	24/227(10.57)	0/46(0.0)	0/11(0.0)	3/60(5)	21/110(19.09)	0.0004	0.0009

* *p*-value based on Fisher's exact for categorical variables between four WHO histological group; # *p*-value based on Fisher's exact for categorical variables between NET and NECs.