

Table S5: Compound heterozygous SNVs/Indels

Patient	Gene	mRNA Expression in Tumor	Protein Atlas/Likelihood	Variant Type	Reference Sequence	Nucleotide Change	Protein Change	Maximum minor allele frequency (in all databases)	SIFT	PolypheS, HADY	CADD_pReid	Gene Description	Disease Name/Inheritance/OMIM	Presence of the variant in Somatic Mutations in Cancer (COSMIC)	# Gene mutations in lung adenocarcinoma (COSMIC database)	Percentage of SNVs and indels in all lung cancer samples tested in COSMIC (n=10,000)	LINK disease: presence in genome informatics (MG)	Presence of the variant in the Catalogue of Somatic Mutations in Cancer (TCGA)	APC/MUC2/BAAC/SCC (Mutations in TCGA database)	Percentage of SNVs and indels in all lung cancer samples tested in TCGA for a given gene	Phenotypes described in the Incohering Disorders (IDD) project	ISP_AR	ISP_JAE	
CPAM2	LZTSL1	YES	ND	missense	NM_021020	c.1367G>A	p.R456H	0.001029	D	D	34.0	leucine zipper tumor suppressor 1	Esophageal squamous cell carcinoma/AD/133239	Reported in 1 lung adenocarcinoma patient COSM335951	26/0/0/2	1.14	ND	ND	70/6/15/16	0.51	ND	0.08093	0.03918	
		NO/YES	NO/YES	missense	NM_001142769	c.4537A>G	p.K1513E	0.000580	D	B	19.9	protocadherin related 15	Deafness/AR/609533; Usher syndrome1D/F digenic/AD/601067; Usher syndrome1F/AR/602083	Reported in 1 colon adenocarcinoma patient COSM2147499	203/0/0/52	9.43	ND	ND	371/50/107/158	4.30	ND	0.10415	0.82105	
CPAM4	VWA8	YES	ND	missense	NM_015058	c.4721G>C	p.G1574A	0.007042	D	P	29.1	von Willebrand factor	ND	ND	0/0/0/0	74(KIAA056)	ND	ND	153/15/11/22	0.45	ND	0.07414	0.01582	
		ND	ND	missense	NM_001272046	c.2445G>A	p.D82N	0.001968	D	D	32.0	A domain containing 8	ND	ND	19/0/0/1	0.72	ND	ND	51/5/5/11	0.18	ND	0.01892	0.01702	
CPAM6	DYNC2H1	YES	ND	missense	NM_001377	c.5177G>A	p.R1726Q	0.005102	D	D	34.0	dynein cytoplasmic 2 heavy chain 1	Short-rib thoracic dysplasia 3 with or without polydactyly/AR-AD/613091; Short-rib-polydactyly syndrome-III/615087 and -III/263510	ND	25/0/0/6	0.93	abnormal lung lobe morphology, aorta pulmonary collateral arteries, tracheoesophageal fistula, abnormal respiratory system morphology	ND	246/34/33/52	1.17	SHORT RIB	0.02974	0.04391	
		ND	ND	missense	NM_001377	c.7576A>G	p.I2526V	0.008637	T	B	5.1	connector enhancer of kinase suppressor of Ras 1 (Approved)	ND	ND	15/0/0/1	0.71	ND	ND	64/13/12/14	0.37	AL RETARD	0.01051	0.00654	
CPAM11	CNKSR1	YES	ND	missense	NM_001297647	c.1058C>G	p.P353R	N	D	P	10.3	connector enhancer of kinase suppressor of Ras 1 (Approved)	ND	ND	15/0/0/1	0.71	ND	ND	64/13/12/14	0.37	AL RETARD	0.01051	0.00654	
		NO/NO	missense	NM_001040105	c.7733G>T	p.S2578I	0.000231	D	D	0.0	mucin 17, cell surface associated, probably	ND	ND	187/0/0/27	13.19	ND	ND	336/49/104/168	4.07	ND	0.03646	0.04953		
CPAM14	HELR2	YES	ND	missense	NM_001037335	c.4871C>T	p.L1624M	0.000274	D	D	24.4	helicase with zinc finger 2	ND	ND	0/0/0/0	95(PRIC28)	ND	ND	127/22/15/43	0.80	ND	0.10566	0.07884	
		ND	ND	missense	NM_015491	c.2350G>A	p.V784M	0.000231	T	B	14.4	FN1 interacting serine 23.5 and arginine rich	ND	ND	28/0/0/2	0.81	ND	ND	6/0/6/13	0.39	ND	0.03104	0.01262	
CPAM15	PNSR	YES	ND	missense	NM_015491	c.1360G>C	p.E454Q	0.001006	D	P	23.5	zinc finger protein 804B	ND	ND	89/0/0/15	7.15	ND	ND	195/25/49/123	2.59	ND	0.04171	0.02487	
		ND	ND	missense	NM_181644	c.592T>G	p.L198V	0.005114	T	D	0.6	zinc finger protein 804B	ND	ND	89/0/0/15	7.15	ND	ND	195/25/49/123	2.59	ND	0.04171	0.02487	
CPAM18	ZNF804B	YES	ND	missense	NM_181644	c.680T>G	p.V227G	0.000349	D	P	23.7	zinc finger protein 804B	ND	ND	89/0/0/15	7.15	ND	ND	195/25/49/123	2.59	ND	0.04171	0.02487	
		ND	ND	missense	NM_015057	c.939C>G	p.S3110C	0.000926	D	D	25.3	MYC binding protein 2, E3 ubiquitin protein	ND	ND	69/0/0/7	3.68	respiratory distress of	ND	231/44/36/76	1.48	ND	0.03268	0.10894	
CPAM19	MYCBP2	YES	ND	missense	NM_015057	c.6544A>G	p.I2182V	0.001279	T	B	4.8	E3 ubiquitin protein	ND	ND	69/0/0/7	3.68	respiratory distress of	ND	231/44/36/76	1.48	ND	0.03268	0.10894	
		ND	ND	missense	NM_174916	c.3934G>C	p.E1312Q	N	D	D	27.1	ubiquitin protein ligase E3 component n-recognin 1	Johanson-Bizzard syndrome/AR/243800	Somatic in 5 colon adenocarcinoma patients COSM4054765	33/0/0/2	1.69	ND	ND	101/15/13/19	0.47	JOHNSC	0.70122	0.66117	
CPAM20	MKI67	YES	ND	missense	NM_002417	c.5360C>T	p.P1787L	0.001006	T	B	11.7	marker of proliferation	ND	ND	127/0/0/8	4.27	ND	ND	217/43/33/85	1.50	ND	0.04496	0.07252	
		ND	ND	missense	NM_182961	c.890G>T	p.G297V	N	D	D	23.5	Ki-67	Emery-Dreifuss muscular dystrophy 4/AD/612998; Spinocerebellar ataxia/AR/610743	ND	ND	424/0/0/72	13.45	atelectasis, small lung	ND	525/9/176/282	4.79	SPINOCEF	0.04877	0.76574
CCAM22	SYNE1	YES	ND	missense	NM_182961	c.17053A>G	p.K568E	0.001166	D	P	29.0	spectrin repeat containing nuclear envelope protein 1	ND	ND	424/0/0/72	13.45	atelectasis, small lung	ND	525/9/176/282	4.79	SPINOCEF	0.04877	0.76574	
		ND	ND	missense	NM_001098623	c.8557A>G	p.T2853A	0.007166	D	B	10.5	envelope protein 1	ND	ND	264/2/0/27	9.18	ND	ND	472/76/87/126	3.08	ND	0.10292	0.07891	
CPAM23	OBSCN	YES	ND	missense	NM_001098623	c.3322T>A	p.Y1108N	0.003018	D	D	22.6	obscurin, cytoskeletal	ND	ND	264/2/0/27	9.18	ND	ND	472/76/87/126	3.08	ND	0.10292	0.07891	
		ND	ND	missense	NM_000787	c.5867C>G	p.T1956S	0.001006	T	D	23.0	calmodulin and titin	ND	ND	264/2/0/27	9.18	ND	ND	472/76/87/126	3.08	ND	0.10292	0.07891	
CPAM23	DBH	YES	ND	missense	NM_000787	c.1088G>A	p.G363E	0.001740	D	D	26.3	dopamine beta-hydroxylase	Dopamine beta-hydroxylase deficiency/223360	Somatic in 1 malignant melanoma patient COSM4398533	29/0/0/4	1.02	ND	ND	55/14/11/11	0.29	ND	0.80889	0.76638	
		ND	ND	missense	NM_003330	c.1498C>G	p.L500V	0.000699	D	D	25.9	thioredoxin reductase	ND	ND	9/0/0/5	0.59	ND	ND	49/7/4/14	0.21	ND	0.09237	0.06038	
CPAM24	TXNRD1	YES	ND	missense	NM_003330	c.95T>C	p.I32T	0.001275	D	P	22.7	thioredoxin reductase	ND	ND	9/0/0/5	0.59	ND	ND	49/7/4/14	0.21	ND	0.09237	0.06038	
		ND	ND	missense	NM_001287212	c.1115A>G	p.D372G	0.001109	D	B	25.2	I	ND	ND	51/0/0/14	2.46	ND	ND	91/15/16/17	0.51	ND	0.03334	0.05653	
CPAM24	KIF17	YES	ND	splicing	NM_001287212	c.2492+1G>A	Gdonor	0.000347	NA	NA	23.5	kinesin family member 17, Cytoskeleton	ND	ND	51/0/0/14	2.46	ND	ND	91/15/16/17	0.51	ND	0.03334	0.05653	
		ND	ND	missense	NM_014935	c.913G>A	p.E305K	0.005679	T	D	25.0	I7, Cytoskeleton	ND	ND	51/0/0/14	2.46	ND	ND	91/15/16/17	0.51	ND	0.03334	0.05653	
CPAM28	PLEKHA6	YES	ND	missense	NM_014935	c.3019C>T	p.R1007C	0.000064	D	D	34.0	pleckstrin	ND	ND	24/0/0/5	1.82	ND	ND	122/24/13/25	0.45	ND	0.06985	0.0256	
		ND	ND	missense	NM_032119	c.2606A>C	p.H869P	0.002431	T	D	24.0	transmembrane 2C/AR or digenic/605472	Usher syndrome, type 2C/AR or digenic/605472	ND	ND	0/0/0/0	.86(GPR98)	ND	ND	334/50/50/137	2.55	ND	ND	ND
CPAM30	ADGRV1	YES	ND	missense	NM_032119	c.9701C>T	p.A3234V	0.003020	T	B	22.9	transmembrane 2C/AR or digenic/605472	Usher syndrome, type 2C/AR or digenic/605472	ND	ND	0/0/0/0	.86(GPR98)	ND	ND	334/50/50/137	2.55	ND	ND	ND
		ND	ND	missense	NM_173462	c.10448G>T	p.D3550Y	0.001006	D	P	13.5	receptor domain	ND	ND	49/0/0/6	0.72	ND	ND	84/20/8/21	0.41	ND	0.01895	0.00778	
CPAM31	PAPLN	YES	ND	missense	NM_173462	c.973C>G	p.R326G	0.001279	T	P	22.8	papilin, proteoglycan	ND	ND	49/0/0/6	0.72	ND	ND	84/20/8/21	0.41	ND	0.01895	0.00778	
		ND	ND	missense	NM_173462	c.2259C>A	p.N753K	0.001610	T	D	26.1	like sulfated	ND	ND	49/0/0/6	0.72	ND	ND	84/20/8/21	0.41	ND	0.01895	0.00778	

D: damaging; P: potentially damaging; T: tolerated; B: benign; ND: not described; NA: not applicable; AR: autosomal recessive; AD: autosomal dominant; ADC: Adenocarcinoma; MUC: Mucinous carcinoma; BAAC: Bronchioloalveolar adenocarcinoma; SCC: squamous cell/MUC: Cystic, Mucinous and Serous Neoplasms in TCGA; SCC*: Squamous Cell Neoplasms in TCGA.