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Supplemental Data

DrGaP: A Powerful Tool for Identifying Driver Genes and Pathways in Cancer Sequencing Studies

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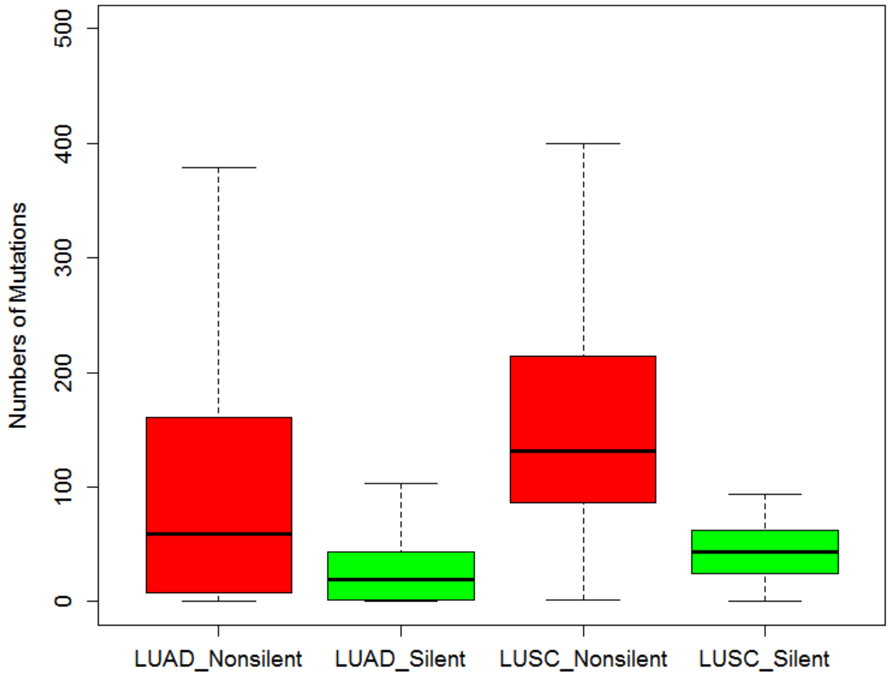

Figure S1. Numbers of somatic mutations in CDS per lung cancer exome. As of Dec 2011, 119 lung adenocarcinoma (LUAD) and 127 lung squamous cell carcinoma (LUSC) exomes in the format of BAM files from TCGA were downloaded and analyzed by our in-house analysis pipeline for cancer genome sequencing data (Liu et al. Carcinogenesis. 33(7):1270-6, 2012). Briefly, after alignment, PCR duplicates will be removed by Picard (http://picard.sourceforge.net). SNVs will be called by both SomaticSniper (Larson et al. Bioinformatics 28, 311-317, 2012) and VarScan (Koboldt et al. Genome Res 22, 568-576, 2012). We defined high-quality SNVs as those detected by both SomaticSniper with Somatic Score > 40 and mapping quality > 40 and VarScan with somatic p value < 0.05. To minimize false positives, we adopted a stringent set of criteria: 1) minimum coverage of a specific position as 8X in normal and 8X in tumor, 2) minimum reads of variant allele as 3 and minimum proportion of variant allele as 15% in tumor, and 3) minimum number of 1 reads supporting the variant allele per strand. For small insertion and deletions (indels), we further removed them with any support reads from its matched normal control. Such filtering criteria ensure a high validation rate for somatic mutations at about 90%. The lists of SNVs/indels were finally annotated by using ANNOVAR (Wang Nucleic Acids Research 38, e164, 2010). We first filtered SNVs/indels by various public databases including dbSNP, 1000 genomes and HapMap exome Project. After filtering, these novel SNVs/indels were subject to functional annotation using the NCBI refseq gene database (http://www.ncbi.nlm.nih.gov/gene). After gene annotation, somatic mutations in a gene were counted and classified into silent, missense, nonsense, splicing mutations, in-frame and out-of-frame indels; each type of mutations except indels are further classified into nine of nucleotide types based on the base of interest and its flanking bases and location of CpG islands.

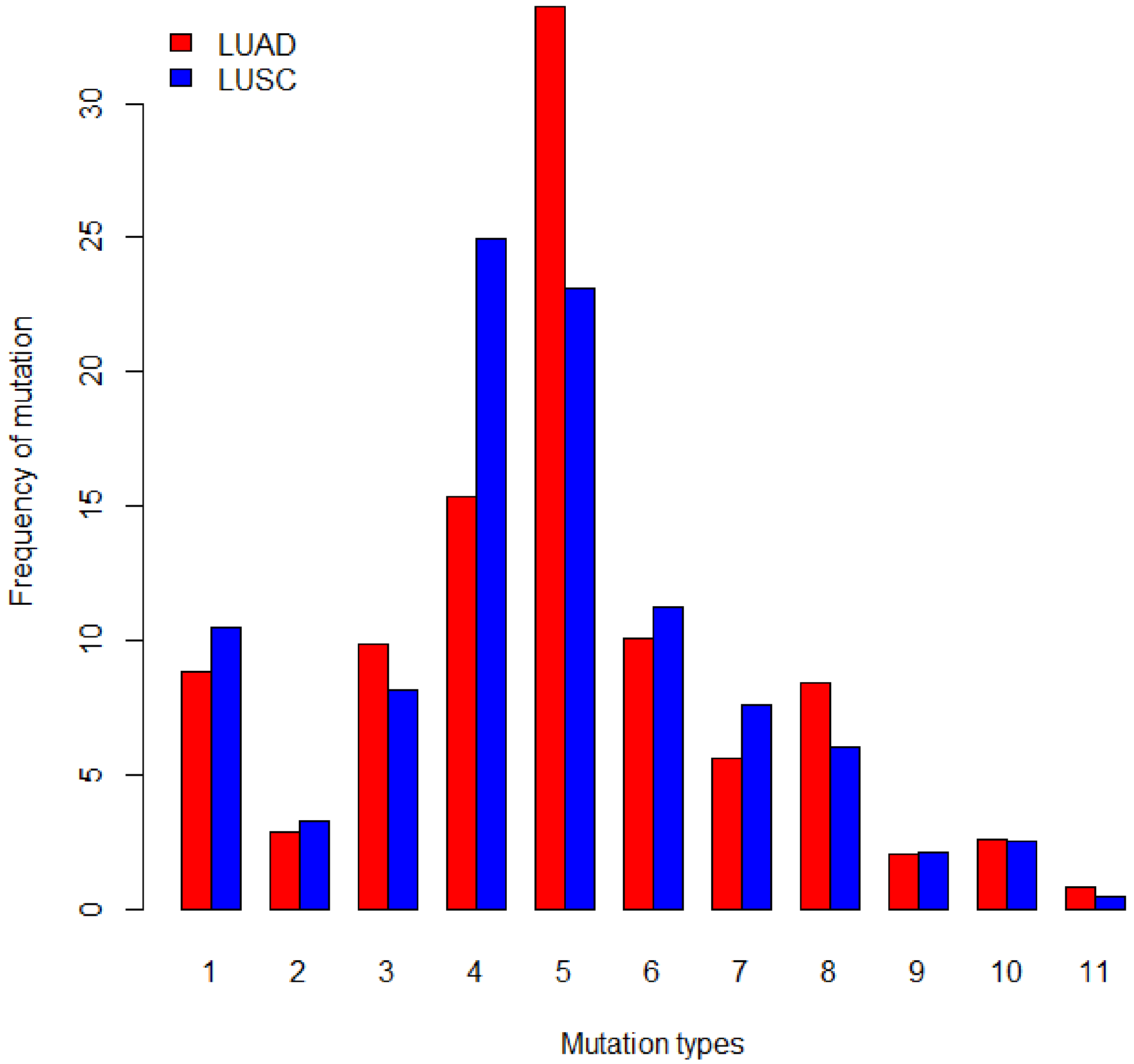

Figure S2. Somatic single-nucleotide mutation trends and patterns in lung cancer. The numbers 1 to 11 represent different types of mutation in Table S1: i.e., A/T→G/C , A/T→C/G, A/T→T/A, C/G→T/A at non CpG, C/G→A/T at non CpG, C/G→G/C at non CpG, C/G→T/A at CpG, C/G→A/T at CpG, C/G→G/C at CpG, in-frame indels, and out-of-frame indels.

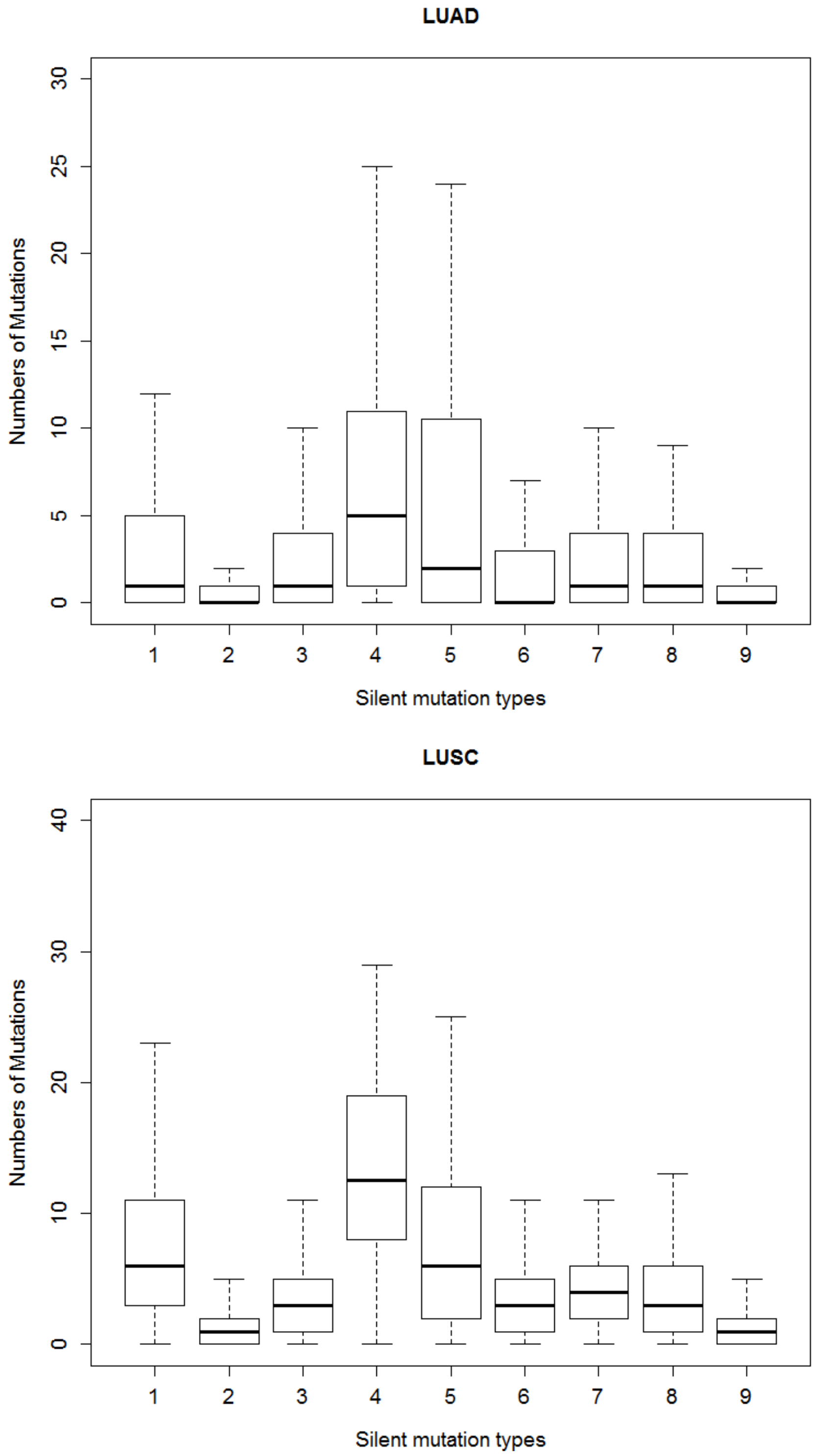

Figure S3. Numbers of different types of silent mutations per lung cancer exome. The numbers 1 to 9 represent different types of mutation except indels in Table S1.

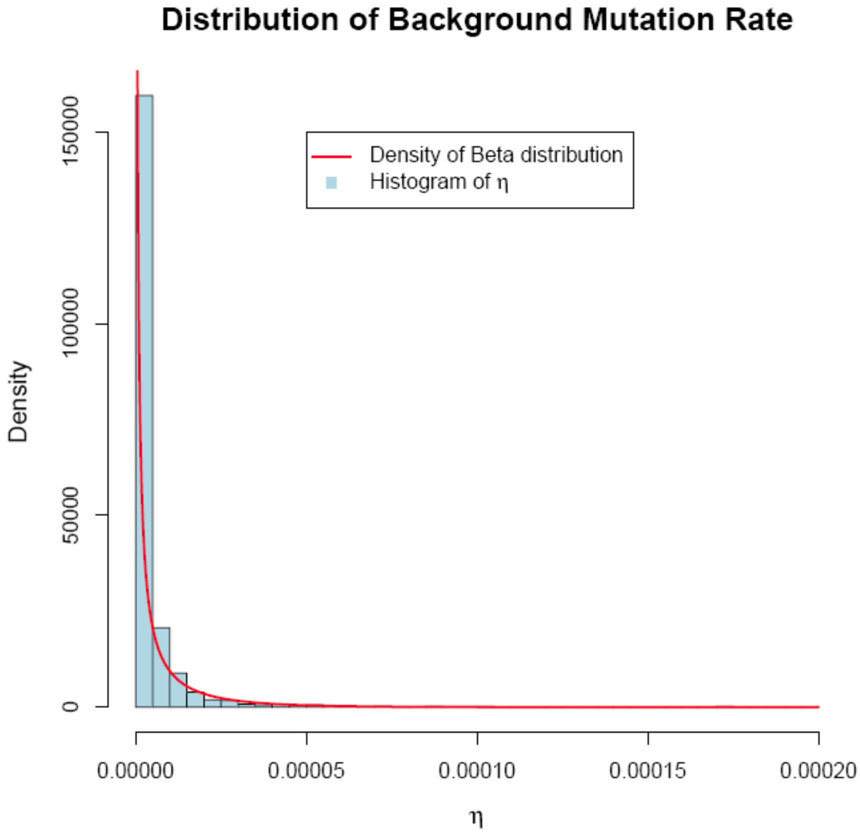

Figure S4. Beta prior of background mutation rates. Silent mutations identified in LUAD and LUSC were used for estimating background mutation rates.

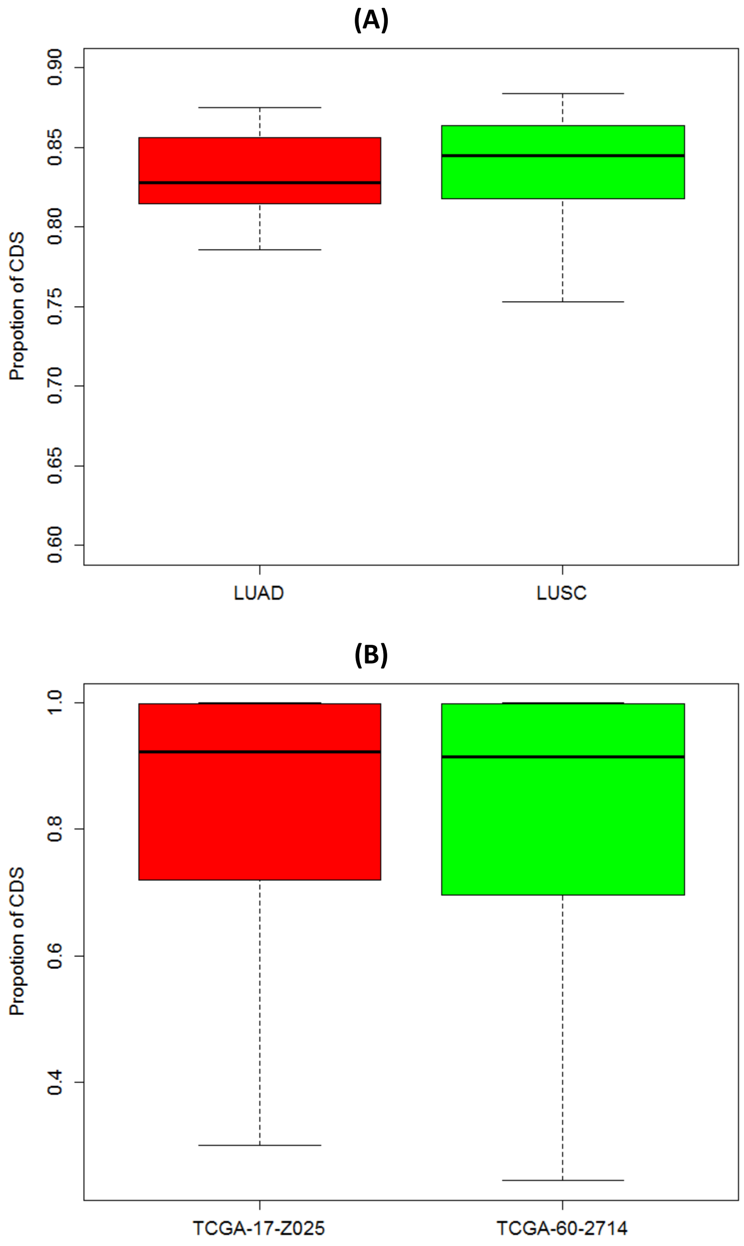

Figure S5. Proportion of CDS with >= 8x in both tumor and normal DNAs. (**A**) The proportion of CDS was plotted against all LUAD and LUSC samples. (**B**) The proportion of CDS was plotted against all of the genes within the same samples; one representative sample from LUAD and one from LUSC were presented. The software for estimating sequence coverage in tumor and normal matched samples, pairdoc is available at http://code.google.com/p/pairdoc/.

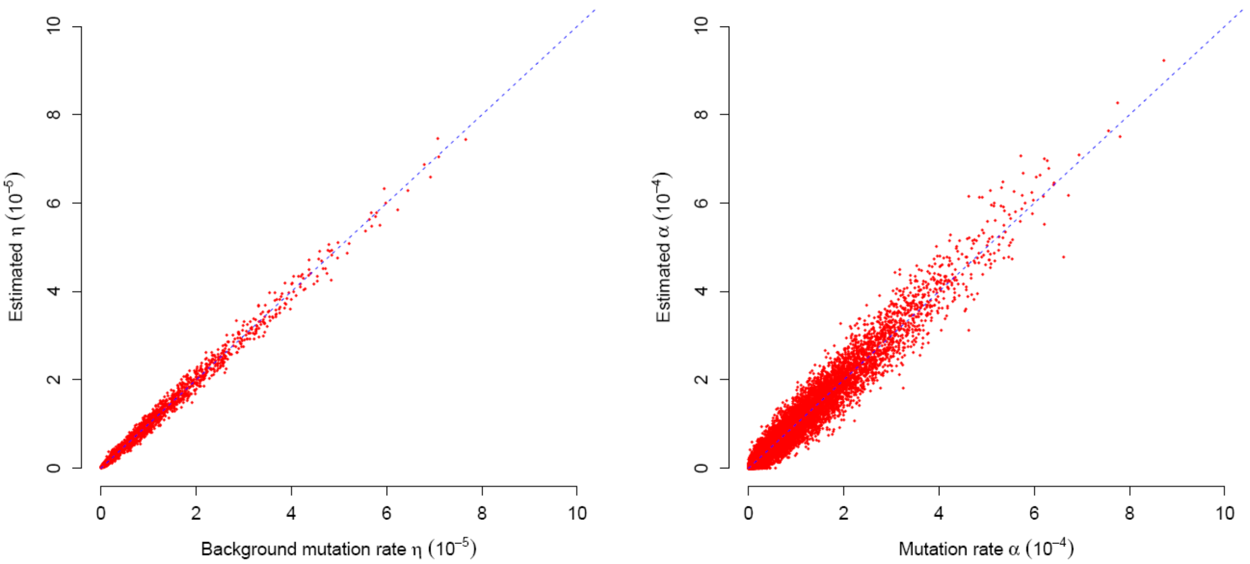

Figure S6. Parameter estimation of η and α when at least one type of driver mutations occurr in tumor samples.

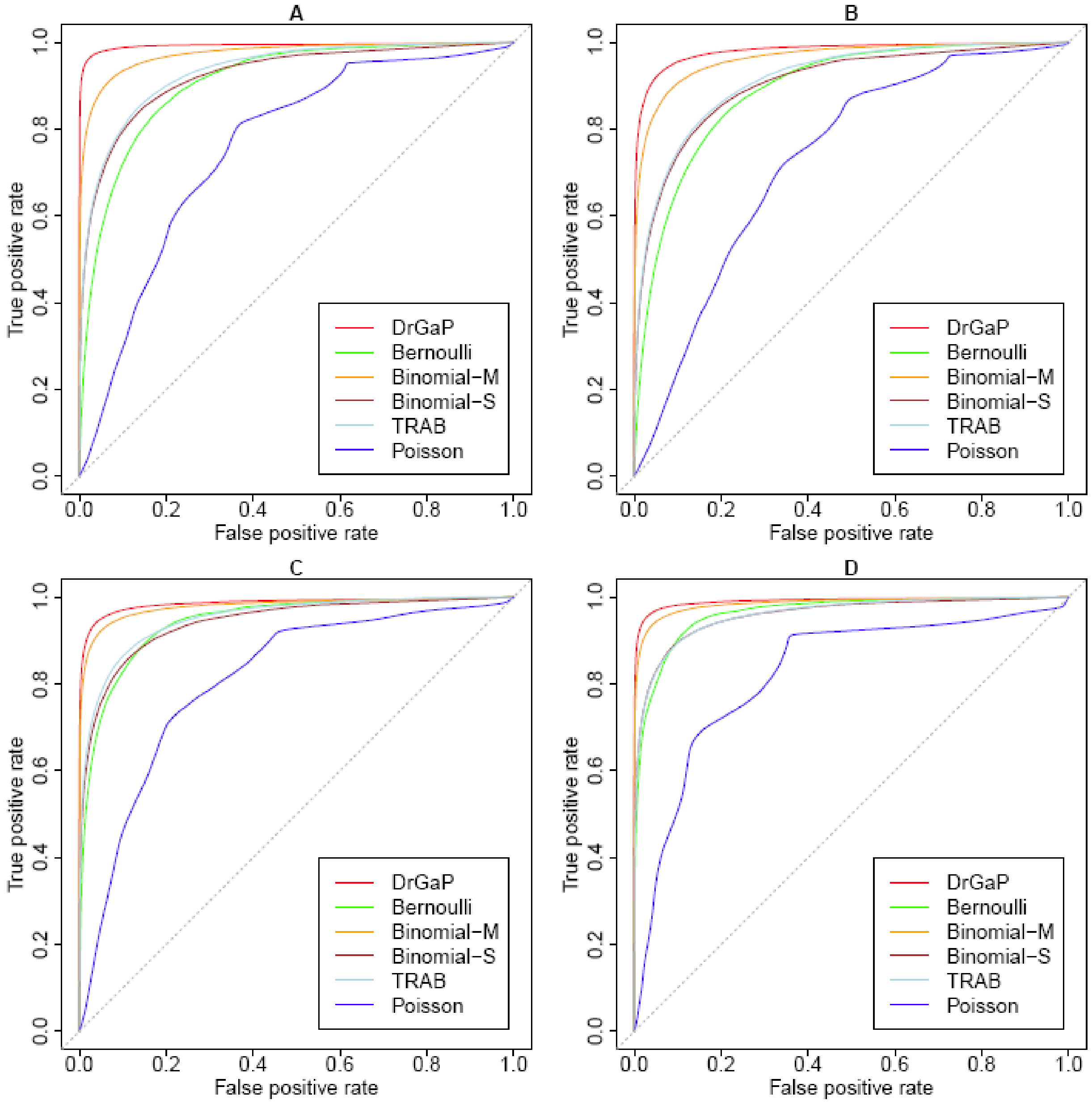

Figure S7. ROC plots of sensitivity and specificity of six statistical methods in TCGA-simulated data. (**A**) LUAD, (**B**) LUSC, (**C**) Non-hypermutated CRC, and (**D**) HGS-OvCa.

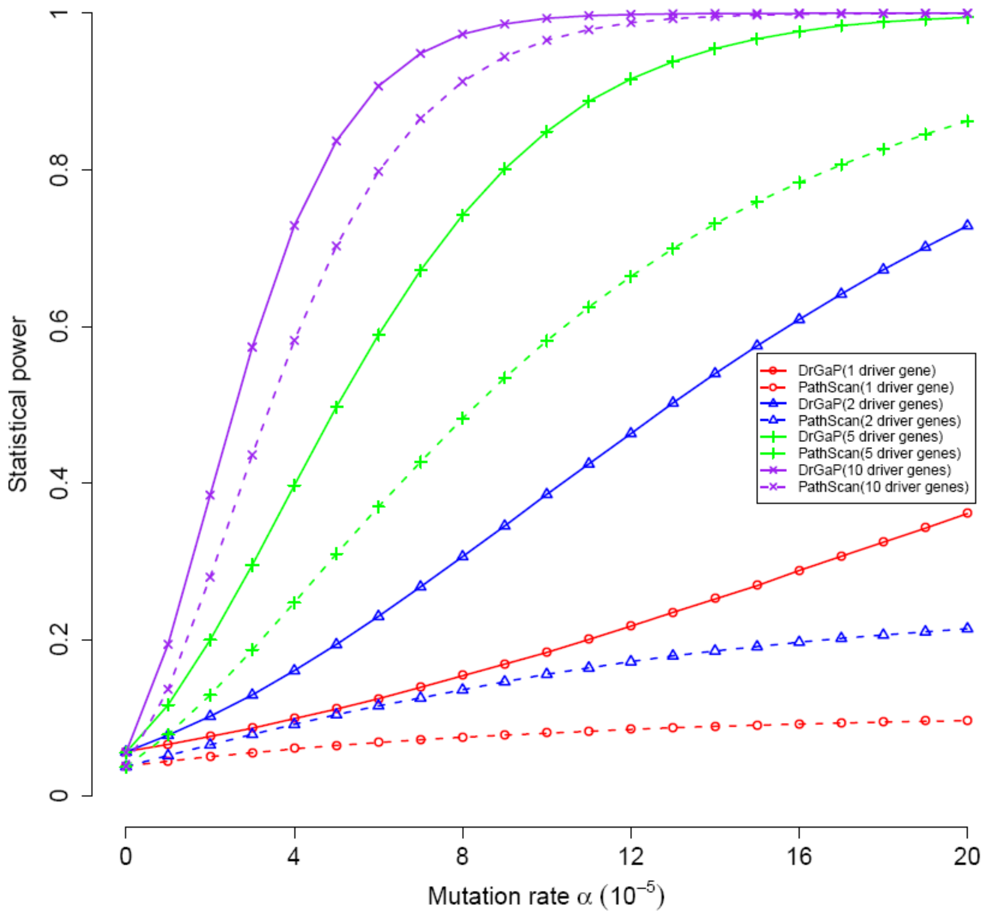

Figure S8. Comparison of DrGaP with PathScan for identifying driver pathways. Twenty genes in a pathway were simulated. 1, 2, 5 and 10 genes were simulated to be driver genes in the pathway.

Table S1 Mutation types

A/T→G/C
A/T→C/G
A/T→T/A
C/G→T/A at non *CpG*
C/G→A/T at non *CpG*
C/G→G/C at non *CpG*
C/G→T/A at *CpG*
C/G→A/T at *CpG*
C/G→G/C at *CpG*
In-frame indels
Out-of-frame indels

*Except indel, all mutation types are further classified into silent, missense, nonsense and splicing mutations.

Table S2 CDS coverage in both tumor and its matched normal DNAs from LUAD samples*

LUAD_samples	Total_bases	Avgerage	Median	>=1	>=5	>=8	>=10	>=15	>=20
TCGA-05-4244	8,550,199,268	241	100	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-05-4249	8,141,453,137	230	95	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-05-4250	8,857,970,361	250	100	0.91	0.88	0.86	0.85	0.83	0.80
TCGA-05-4382	6,248,490,266	176	74	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-05-4389	6,504,954,943	183	77	0.91	0.87	0.86	0.84	0.81	0.79
TCGA-05-4395	6,412,601,231	181	75	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-05-4397	6,474,290,614	183	76	0.91	0.87	0.85	0.84	0.81	0.79
TCGA-05-4398	6,976,210,852	197	83	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-05-4402	6,952,905,850	196	83	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-05-4403	6,695,121,803	189	81	0.91	0.88	0.86	0.85	0.82	0.79
TCGA-05-4418	6,885,546,507	194	82	0.91	0.88	0.86	0.85	0.82	0.79
TCGA-05-4420	6,633,581,234	187	78	0.91	0.88	0.86	0.84	0.82	0.79
TCGA-05-4422	6,947,237,050	196	82	0.91	0.88	0.86	0.85	0.82	0.79
TCGA-05-4426	6,628,626,221	187	79	0.91	0.88	0.86	0.85	0.82	0.79
TCGA-05-4430	6,781,440,027	191	81	0.91	0.87	0.86	0.85	0.82	0.80
TCGA-05-4432	6,176,128,303	174	74	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-05-4434	6,639,013,847	187	79	0.91	0.87	0.85	0.84	0.82	0.79
TCGA-17-Z000	5,024,987,113	142	54	0.95	0.86	0.83	0.81	0.77	0.73
TCGA-17-Z001	4,990,575,011	141	53	0.94	0.86	0.82	0.80	0.76	0.72
TCGA-17-Z002	5,286,576,569	149	53	0.94	0.85	0.82	0.80	0.76	0.72
TCGA-17-Z003	4,890,993,570	138	52	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z004	4,253,794,618	120	44	0.93	0.84	0.80	0.78	0.72	0.67
TCGA-17-Z005	4,955,294,618	140	52	0.94	0.85	0.82	0.80	0.76	0.72
TCGA-17-Z007	6,320,802,262	178	61	0.94	0.85	0.82	0.80	0.76	0.72
TCGA-17-Z008	4,256,828,926	120	44	0.93	0.84	0.81	0.79	0.73	0.68
TCGA-17-Z009	5,000,269,099	141	51	0.93	0.85	0.81	0.79	0.74	0.70
TCGA-17-Z010	4,762,475,869	134	50	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z011	4,794,352,581	135	49	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z012	4,468,995,068	126	47	0.94	0.85	0.81	0.79	0.75	0.70
TCGA-17-Z013	5,098,751,396	144	53	0.93	0.85	0.81	0.79	0.75	0.71
TCGA-17-Z014	5,019,432,334	142	49	0.93	0.84	0.81	0.79	0.74	0.70
TCGA-17-Z015	5,031,885,599	142	49	0.93	0.84	0.81	0.79	0.74	0.70
TCGA-17-Z016	6,118,743,175	173	60	0.94	0.86	0.82	0.80	0.76	0.71
TCGA-17-Z017	4,636,259,660	131	48	0.93	0.84	0.80	0.78	0.73	0.68
TCGA-17-Z018	4,941,386,804	139	53	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z019	5,266,514,641	149	53	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z020	6,159,700,966	174	66	0.95	0.87	0.83	0.81	0.78	0.74
TCGA-17-Z021	6,301,328,765	178	64	0.94	0.86	0.83	0.81	0.77	0.73
TCGA-17-Z022	6,869,694,781	194	66	0.95	0.86	0.82	0.80	0.75	0.70
TCGA-17-Z023	5,063,382,776	143	52	0.94	0.86	0.82	0.80	0.76	0.71
TCGA-17-Z025	4,690,704,370	132	47	0.93	0.84	0.80	0.78	0.73	0.68

TCGA-17-Z026	5,002,245,683	141	53	0.94	0.85	0.82	0.80	0.75	0.71
TCGA-17-Z027	5,124,355,996	145	50	0.94	0.85	0.81	0.79	0.75	0.70
TCGA-17-Z028	4,893,270,031	138	51	0.94	0.85	0.81	0.79	0.75	0.71
TCGA-17-Z030	5,356,783,935	151	55	0.94	0.86	0.82	0.80	0.76	0.72
TCGA-17-Z031	6,148,899,918	173	61	0.94	0.86	0.83	0.81	0.77	0.73
TCGA-17-Z032	8,100,544,291	228	77	0.95	0.88	0.85	0.83	0.79	0.76
TCGA-17-Z033	5,028,644,814	142	53	0.94	0.85	0.82	0.80	0.76	0.71
TCGA-17-Z035	4,407,434,150	124	44	0.93	0.84	0.81	0.78	0.74	0.69
TCGA-17-Z036	4,222,579,044	119	39	0.93	0.83	0.79	0.76	0.70	0.65
TCGA-17-Z037	4,731,735,024	133	50	0.94	0.86	0.82	0.80	0.76	0.72
TCGA-17-Z039	5,092,766,204	144	52	0.94	0.86	0.82	0.80	0.76	0.72
TCGA-17-Z040	7,445,428,825	210	76	0.95	0.88	0.84	0.82	0.78	0.75
TCGA-17-Z041	7,368,632,488	208	70	0.95	0.86	0.83	0.81	0.77	0.74
TCGA-17-Z042	4,332,427,729	122	46	0.94	0.85	0.81	0.79	0.74	0.69
TCGA-17-Z043	5,138,559,822	145	54	0.94	0.86	0.83	0.81	0.76	0.71
TCGA-17-Z044	5,138,266,971	145	51	0.93	0.84	0.81	0.79	0.74	0.70
TCGA-17-Z045	4,373,263,065	123	46	0.94	0.84	0.81	0.79	0.74	0.69
TCGA-17-Z046	11,412,066,473	322	113	0.90	0.86	0.84	0.83	0.80	0.78
TCGA-17-Z047	9,415,360,551	266	89	0.90	0.85	0.82	0.81	0.78	0.75
TCGA-17-Z048	9,934,284,549	280	99	0.90	0.86	0.83	0.82	0.79	0.77
TCGA-17-Z049	11,572,097,978	326	120	0.90	0.87	0.85	0.84	0.81	0.79
TCGA-17-Z050	10,392,925,407	293	97	0.90	0.85	0.83	0.82	0.79	0.77
TCGA-17-Z051	10,762,406,491	304	104	0.90	0.86	0.84	0.82	0.80	0.77
TCGA-17-Z052	8,326,221,706	235	74	0.90	0.85	0.82	0.81	0.77	0.73
TCGA-17-Z053	10,908,464,344	308	100	0.90	0.85	0.83	0.82	0.79	0.76
TCGA-17-Z054	10,255,724,852	289	96	0.90	0.85	0.82	0.81	0.78	0.75
TCGA-17-Z056	10,343,720,841	292	99	0.90	0.85	0.83	0.82	0.79	0.76
TCGA-17-Z058	10,277,990,763	290	97	0.90	0.85	0.83	0.82	0.79	0.76
TCGA-17-Z059	10,345,560,251	292	91	0.89	0.85	0.82	0.81	0.78	0.75
TCGA-17-Z060	11,687,955,784	330	116	0.90	0.86	0.84	0.83	0.80	0.78
TCGA-17-Z061	8,617,309,330	243	78	0.89	0.83	0.81	0.79	0.76	0.73
TCGA-17-Z062	9,428,428,654	266	92	0.90	0.85	0.83	0.82	0.79	0.76
TCGA-35-3615	11,560,329,590	326	103	0.91	0.85	0.83	0.82	0.79	0.77
TCGA-35-4122	7,706,957,527	217	92	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-35-4123	8,448,084,395	238	100	0.91	0.89	0.87	0.87	0.84	0.82
TCGA-38-4628	7,097,414,068	200	83	0.91	0.87	0.86	0.85	0.82	0.80
TCGA-38-4629	7,093,186,083	200	86	0.91	0.88	0.86	0.85	0.83	0.80
TCGA-38-4630	6,628,555,257	187	76	0.91	0.87	0.85	0.84	0.81	0.79
TCGA-44-2655	12,124,112,677	342	112	0.90	0.84	0.82	0.81	0.79	0.77
TCGA-44-2656	11,612,984,586	328	99	0.90	0.83	0.81	0.80	0.77	0.75
TCGA-44-2657	8,731,442,439	246	104	0.91	0.89	0.87	0.86	0.84	0.82
TCGA-44-2659	12,874,000,185	363	103	0.88	0.83	0.81	0.79	0.77	0.74
TCGA-44-2661	8,709,735,208	246	101	0.91	0.89	0.87	0.86	0.84	0.82
TCGA-44-2662	11,054,468,462	312	94	0.90	0.84	0.81	0.80	0.77	0.75

TCGA-44-2665	12,568,984,832	354	118	0.90	0.84	0.82	0.81	0.79	0.77
TCGA-44-2666	11,694,650,525	330	107	0.91	0.85	0.83	0.82	0.79	0.77
TCGA-44-2668	12,467,883,648	352	119	0.90	0.85	0.83	0.82	0.80	0.78
TCGA-44-3396	7,196,119,294	203	87	0.91	0.88	0.86	0.85	0.83	0.81
TCGA-44-3398	8,532,105,328	241	101	0.91	0.89	0.87	0.86	0.84	0.82
TCGA-44-3918	8,370,998,041	236	95	0.91	0.88	0.87	0.86	0.84	0.81
TCGA-44-3919	8,511,443,441	240	99	0.91	0.89	0.87	0.86	0.84	0.82
TCGA-44-4112	8,280,325,124	234	94	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-49-4486	6,517,437,373	184	78	0.91	0.87	0.86	0.84	0.82	0.79
TCGA-49-4494	6,803,747,371	192	82	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-49-4501	6,734,942,016	190	80	0.91	0.87	0.86	0.84	0.82	0.79
TCGA-49-4505	7,132,867,043	201	85	0.91	0.87	0.86	0.85	0.82	0.80
TCGA-49-4506	5,971,246,966	168	73	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-49-4507	6,995,098,538	197	83	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-49-4510	6,669,396,239	188	78	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-55-1592	10,723,489,826	302	101	0.90	0.84	0.82	0.80	0.78	0.75
TCGA-55-1594	12,620,553,666	356	101	0.89	0.83	0.81	0.80	0.77	0.74
TCGA-55-1596	11,811,121,232	333	103	0.89	0.83	0.81	0.80	0.77	0.75
TCGA-64-1676	12,615,433,577	356	104	0.90	0.84	0.82	0.80	0.77	0.75
TCGA-64-1677	12,345,468,065	348	116	0.90	0.84	0.82	0.81	0.79	0.77
TCGA-64-1678	10,579,415,707	298	100	0.90	0.83	0.81	0.80	0.77	0.74
TCGA-64-1680	10,560,204,019	298	94	0.89	0.83	0.81	0.79	0.76	0.73
TCGA-67-3770	11,470,031,108	323	93	0.89	0.82	0.79	0.78	0.75	0.72
TCGA-67-3771	12,299,443,410	347	97	0.89	0.83	0.80	0.79	0.76	0.74
TCGA-67-3772	12,641,429,079	357	99	0.89	0.83	0.80	0.79	0.76	0.73
TCGA-67-3773	11,989,756,211	338	103	0.89	0.83	0.81	0.80	0.77	0.75
TCGA-67-3774	11,359,935,626	320	95	0.89	0.83	0.80	0.79	0.76	0.74
TCGA-73-4659	6,812,839,840	192	82	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-73-4662	6,283,870,709	177	73	0.91	0.87	0.85	0.84	0.81	0.78
TCGA-73-4666	6,362,903,523	179	75	0.91	0.87	0.85	0.84	0.82	0.79
TCGA-73-4668	7,098,167,843	200	85	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-73-4670	6,780,832,816	191	80	0.91	0.88	0.86	0.85	0.82	0.80
TCGA-73-4675	6,296,382,658	178	75	0.91	0.88	0.86	0.85	0.82	0.79
TCGA-73-4677	6,991,264,920	197	83	0.91	0.87	0.86	0.84	0.82	0.79

***Note:** CDS size was estimated as 35,457,434 bp based on Ensembl annotation (GRCh37.64). CDS coverage was estimated from paired tumor and its matched normal samples from the same patient. For example, ">=8" is the proportion of CDS that has at least 8x in both tumor and its matched normal DNA samples. If a tumor has 8x and 0x at positions A and B; and its matched normal has 0x and 8x at positions A and B, the coverage at positions A and B will be 0x for the paired sample.

Table S3 CDS coverage in both tumor and its matched normal DNAs from LUSC samples

LUSC_samples	Total	Average	Median	>=1	>=5	>=8	>=10	>=15	>=20
TCGA-18-3406	4,300,752,666	121	51	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-18-3407	4,059,509,780	114	48	0.96	0.88	0.84	0.82	0.78	0.73
TCGA-18-3408	4,343,893,828	123	48	0.96	0.88	0.84	0.82	0.76	0.70
TCGA-18-3409	3,817,011,933	108	46	0.96	0.88	0.84	0.82	0.78	0.74
TCGA-18-3410	3,948,145,452	111	47	0.96	0.88	0.84	0.82	0.78	0.73
TCGA-18-3411	4,569,248,613	129	53	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-18-3412	4,193,452,570	118	49	0.96	0.88	0.84	0.82	0.78	0.73
TCGA-18-3414	4,125,678,520	116	48	0.96	0.88	0.85	0.83	0.79	0.74
TCGA-18-3415	4,398,630,337	124	53	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-18-3416	4,202,188,982	119	49	0.96	0.88	0.84	0.82	0.77	0.73
TCGA-18-3417	8,650,795,965	244	107	0.90	0.88	0.86	0.85	0.83	0.81
TCGA-18-3419	4,629,764,688	131	55	0.96	0.89	0.85	0.84	0.80	0.76
TCGA-18-3421	4,281,665,673	121	50	0.96	0.88	0.85	0.83	0.79	0.74
TCGA-18-4083	10,089,511,804	285	109	0.91	0.88	0.87	0.86	0.84	0.81
TCGA-18-4086	4,820,495,385	136	59	0.90	0.86	0.84	0.83	0.80	0.76
TCGA-18-4721	8,487,725,365	239	108	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-21-1080	9,647,132,798	272	93	0.88	0.84	0.82	0.80	0.78	0.75
TCGA-21-1081	12,568,030,854	354	125	0.92	0.86	0.84	0.83	0.81	0.78
TCGA-21-1082	14,530,863,104	410	143	0.92	0.87	0.85	0.83	0.81	0.79
TCGA-21-1083	12,681,663,741	358	118	0.91	0.85	0.83	0.82	0.79	0.77
TCGA-22-1002	9,843,518,242	278	90	0.91	0.85	0.82	0.81	0.78	0.75
TCGA-22-1005	10,603,037,112	299	104	0.91	0.85	0.83	0.82	0.79	0.76
TCGA-22-1011	10,954,591,457	309	109	0.91	0.86	0.84	0.83	0.80	0.78
TCGA-22-4591	12,534,879,137	354	118	0.91	0.88	0.86	0.85	0.82	0.78
TCGA-22-4594	13,491,546,377	380	158	0.91	0.89	0.88	0.87	0.86	0.84
TCGA-22-4595	12,432,029,879	351	144	0.91	0.89	0.88	0.87	0.85	0.84
TCGA-22-4596	12,385,631,121	349	137	0.91	0.89	0.88	0.87	0.85	0.84
TCGA-22-4599	8,894,468,819	251	109	0.90	0.88	0.86	0.85	0.83	0.82
TCGA-22-4601	8,395,595,800	237	100	0.91	0.88	0.86	0.85	0.83	0.81
TCGA-22-4604	15,170,631,034	428	177	0.92	0.89	0.88	0.88	0.86	0.85
TCGA-22-4607	10,637,895,391	300	113	0.91	0.89	0.87	0.86	0.84	0.81
TCGA-22-4613	8,811,730,283	249	108	0.91	0.88	0.86	0.86	0.83	0.82
TCGA-33-4532	12,845,783,726	362	144	0.92	0.89	0.88	0.88	0.86	0.85
TCGA-33-4538	8,297,405,731	234	91	0.91	0.88	0.87	0.86	0.83	0.80
TCGA-33-4547	9,908,499,518	279	103	0.91	0.89	0.87	0.86	0.83	0.81
TCGA-33-4566	8,603,614,058	243	108	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-33-4582	7,070,268,491	199	87	0.90	0.87	0.85	0.84	0.82	0.79
TCGA-33-4583	7,635,042,622	215	97	0.91	0.88	0.87	0.86	0.84	0.81
TCGA-33-4586	7,572,561,398	214	95	0.92	0.88	0.87	0.86	0.83	0.81
TCGA-33-4589	7,981,758,118	225	102	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-34-5240	8,545,634,066	241	104	0.90	0.88	0.86	0.85	0.83	0.82

TCGA-37-3783	12,415,899,795	350	147	0.91	0.89	0.88	0.87	0.86	0.84
TCGA-37-3789	4,161,575,983	117	49	0.96	0.88	0.84	0.82	0.77	0.72
TCGA-37-3792	4,017,519,976	113	48	0.96	0.88	0.84	0.83	0.78	0.74
TCGA-37-4129	9,979,067,424	281	112	0.90	0.87	0.85	0.83	0.81	0.79
TCGA-37-4130	13,303,796,722	375	145	0.91	0.88	0.86	0.85	0.83	0.82
TCGA-37-4132	14,301,981,463	403	167	0.91	0.89	0.88	0.87	0.85	0.84
TCGA-37-4133	14,297,535,368	403	160	0.91	0.89	0.87	0.86	0.85	0.83
TCGA-37-4135	12,442,598,168	351	133	0.91	0.88	0.86	0.85	0.83	0.81
TCGA-37-4141	14,836,607,744	418	171	0.91	0.89	0.87	0.87	0.85	0.84
TCGA-39-5016	7,835,857,571	221	97	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-39-5021	7,283,299,503	205	92	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-39-5029	9,051,040,263	255	113	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-39-5031	8,313,103,918	234	104	0.91	0.88	0.86	0.85	0.83	0.82
TCGA-39-5034	8,050,934,046	227	101	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-39-5036	8,608,779,071	243	108	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-39-5037	7,484,557,856	211	92	0.91	0.88	0.87	0.86	0.83	0.81
TCGA-39-5039	8,239,229,818	232	104	0.91	0.88	0.86	0.86	0.83	0.82
TCGA-43-3394	4,256,241,544	120	49	0.96	0.88	0.85	0.83	0.79	0.74
TCGA-43-3920	4,071,027,701	115	48	0.96	0.88	0.84	0.82	0.78	0.73
TCGA-46-3765	4,402,275,644	124	52	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-46-3766	4,311,189,086	122	52	0.96	0.88	0.85	0.83	0.79	0.76
TCGA-46-3767	4,184,819,144	118	51	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-46-3768	4,111,319,395	116	47	0.96	0.87	0.84	0.82	0.77	0.73
TCGA-46-3769	4,095,369,802	116	49	0.96	0.88	0.85	0.83	0.78	0.74
TCGA-60-2710	10,098,222,285	285	83	0.89	0.83	0.80	0.78	0.75	0.72
TCGA-60-2712	14,227,023,353	401	126	0.92	0.86	0.83	0.82	0.79	0.77
TCGA-60-2713	13,028,285,011	367	115	0.91	0.85	0.83	0.81	0.79	0.76
TCGA-60-2714	9,351,256,094	264	79	0.89	0.82	0.79	0.78	0.74	0.71
TCGA-60-2725	14,222,069,039	401	161	0.91	0.89	0.87	0.87	0.85	0.83
TCGA-63-5131	8,604,111,212	243	108	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-66-2727	4,416,764,391	125	52	0.96	0.89	0.85	0.84	0.80	0.76
TCGA-66-2734	4,302,040,338	121	51	0.96	0.89	0.85	0.83	0.79	0.75
TCGA-66-2744	4,218,038,586	119	50	0.96	0.88	0.85	0.83	0.79	0.74
TCGA-66-2754	4,210,956,262	119	50	0.96	0.88	0.85	0.83	0.78	0.74
TCGA-66-2763	10,736,508,568	303	98	0.88	0.84	0.82	0.80	0.78	0.75
TCGA-66-2771	4,079,286,873	115	48	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-66-2773	13,694,424,493	386	159	0.92	0.89	0.88	0.87	0.86	0.84
TCGA-66-2786	9,055,557,868	255	81	0.88	0.83	0.81	0.79	0.76	0.73
TCGA-66-2787	4,104,207,344	116	49	0.96	0.88	0.84	0.82	0.78	0.74
TCGA-66-2788	4,539,552,175	128	55	0.96	0.89	0.86	0.84	0.80	0.77
TCGA-66-2789	4,212,564,207	119	50	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-66-2791	4,156,739,917	117	50	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-66-2792	4,493,422,516	127	52	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-66-2793	9,753,884,949	275	96	0.91	0.88	0.86	0.85	0.82	0.79

TCGA-66-2794	12,397,201,961	350	139	0.91	0.88	0.87	0.86	0.84	0.82
TCGA-66-2795	4,366,012,613	123	51	0.96	0.88	0.85	0.83	0.79	0.75
TCGA-66-2800	12,633,768,174	356	143	0.91	0.89	0.88	0.87	0.85	0.83
TCGA-21-1070	10,840,578,700	306	104	0.91	0.85	0.82	0.81	0.78	0.75
TCGA-21-1071	10,569,758,173	298	101	0.91	0.85	0.82	0.81	0.78	0.76
TCGA-21-1075	11,041,900,432	311	105	0.91	0.85	0.83	0.82	0.79	0.76
TCGA-21-1076	11,242,814,951	317	108	0.91	0.84	0.82	0.81	0.78	0.75
TCGA-21-1077	11,220,170,037	316	111	0.91	0.86	0.83	0.82	0.80	0.77
TCGA-21-1078	7,000,932,359	197	55	0.88	0.79	0.75	0.73	0.68	0.63
TCGA-21-1079	2,946,369,183	83	38	0.88	0.81	0.77	0.75	0.70	0.64
TCGA-22-0940	10,897,440,268	307	101	0.91	0.84	0.82	0.80	0.77	0.75
TCGA-22-0944	10,179,610,174	287	72	0.70	0.66	0.64	0.63	0.61	0.60
TCGA-22-1000	9,661,496,257	272	96	0.91	0.86	0.83	0.82	0.79	0.77
TCGA-22-1012	10,561,504,077	298	103	0.91	0.86	0.83	0.82	0.79	0.77
TCGA-22-1016	10,558,829,761	298	92	0.90	0.84	0.81	0.80	0.76	0.73
TCGA-34-2596	11,000,206,013	310	97	0.90	0.84	0.81	0.80	0.77	0.74
TCGA-43-2576	10,234,315,776	289	73	0.89	0.81	0.78	0.76	0.72	0.69
TCGA-43-2578	11,463,152,944	323	102	0.90	0.84	0.82	0.81	0.78	0.75
TCGA-43-2581	10,983,203,424	310	99	0.91	0.85	0.82	0.81	0.78	0.76
TCGA-56-1622	10,583,297,149	298	99	0.91	0.85	0.83	0.81	0.78	0.76
TCGA-60-2695	10,465,019,022	295	94	0.90	0.84	0.81	0.80	0.77	0.74
TCGA-60-2696	10,573,536,860	298	91	0.90	0.84	0.81	0.79	0.76	0.73
TCGA-60-2698	11,137,370,949	314	99	0.90	0.84	0.82	0.80	0.77	0.75
TCGA-60-2706	5,655,220,094	159	7	0.67	0.28	0.15	0.10	0.04	0.02
TCGA-60-2707	7,111,733,866	201	59	0.88	0.81	0.77	0.75	0.71	0.68
TCGA-60-2708	7,695,626,963	217	63	0.88	0.81	0.78	0.76	0.72	0.69
TCGA-60-2711	5,622,363,484	159	27	0.84	0.71	0.63	0.58	0.46	0.37
TCGA-60-2715	5,243,020,011	148	26	0.83	0.68	0.60	0.54	0.43	0.33
TCGA-60-2716	11,335,839,649	320	98	0.90	0.84	0.81	0.80	0.77	0.75
TCGA-60-2720	3,056,333,066	86	35	0.86	0.78	0.74	0.71	0.66	0.61
TCGA-60-2721	2,734,315,330	77	33	0.87	0.78	0.73	0.71	0.65	0.59
TCGA-60-2722	10,289,975,661	290	84	0.90	0.83	0.80	0.79	0.76	0.73
TCGA-60-2723	10,975,250,101	310	100	0.90	0.84	0.82	0.81	0.78	0.75
TCGA-60-2724	10,752,143,362	303	99	0.90	0.84	0.81	0.80	0.77	0.75
TCGA-60-2726	10,601,802,168	299	95	0.90	0.84	0.81	0.80	0.77	0.74
TCGA-66-2756	10,398,860,675	293	87	0.88	0.83	0.80	0.79	0.76	0.73
TCGA-66-2759	7,694,961,304	217	64	0.87	0.81	0.78	0.76	0.72	0.68
TCGA-66-2765	5,621,684,473	159	12	0.75	0.46	0.31	0.24	0.13	0.08
TCGA-66-2766	8,896,963,614	251	71	0.88	0.82	0.79	0.78	0.74	0.71
TCGA-66-2769	5,713,005,697	161	41	0.86	0.78	0.73	0.71	0.64	0.57
TCGA-66-2780	8,169,834,940	230	68	0.86	0.80	0.77	0.75	0.71	0.68
TCGA-66-2781	5,479,945,892	155	25	0.82	0.68	0.59	0.54	0.42	0.32

Table S4 Summary of analysis datasets

Datasets	Number of sample	Number of genes
Ding's[1]	**188**	**623**
LUAD[2]	**119**	**7,755**
LUSC[3]	**127**	**11,125**
Non-hypermutated CRC[4]	**194**	**9,252**
HGS-OvCa[5]	**316**	**9,965**

1. Ding, L., Getz, G., Wheeler, D.A., Mardis, E.R., McLellan, M.D., Cibulskis, K., Sougnez, C., Greulich, H., Muzny, D.M., Morgan, M.B., et al. (2008). Somatic mutations affect key pathways in lung adenocarcinoma. Nature 455, 1069-1075.
2. The TCGA database: http://cancergenome.nih.gov/.
3. Cancer Genome Atlas Research Network. (2012). Comprehensive genomic characterization of squamous cell lung cancers. Nature 489, 519-525.
4. Cancer Genome Atlas Research Network. (2012). Comprehensive molecular characterization of human colon and rectal cancer. Nature 487, 330-337.
5. Cancer Genome Atlas Research Network. (2011). Integrated genomic analyses of ovarian carcinoma. Nature 474, 609-615.

Table S5 Driver genes in the study of Ding *et al.*

Gene	Silent	Missense	Nonsense	Splicing	Fs_Indel	nFs_Indel	avg_alpha	#_pa	p_adj	Methods
KRAS	1	61	0	0	0	0	4.22E-04	4	8.4E-129	Both
TP53	1	41	10	6	6	1	2.94E-04	18	4.4E-102	Both
STK11	0	9	9	5	9	0	1.95E-04	14	2.42E-52	Both
EGFR	0	21	0	0	0	13	1.73E-05	5	1.73E-49	Both
NF1	0	6	4	5	1	0	6.26E-05	11	1.89E-11	Both
CDKN2A	0	7	0	0	2	0	3.64E-05	7	2.29E-09	Both
INSRR	3	5	0	1	0	0	8.35E-05	5	1.72E-07	DrGaP
APC	0	5	3	1	3	1	5.92E-05	8	1.43E-06	Both
ATM	0	10	1	1	2	0	1.45E-05	11	2.16E-06	Both
PTPRD	3	10	0	0	0	0	2.06E-05	7	2.18E-06	Both
RB1	0	0	4	2	1	0	1.63E-04	6	2.37E-06	Both
EPHA3	0	11	0	0	0	0	4.17E-05	5	4.57E-06	Both
FGFR4	0	5	0	0	2	0	2.23E-05	4	1.21E-05	Both
LRP1B	0	17	0	0	0	0	1.15E-05	6	5.61E-05	Both
NTRK3	2	7	0	0	0	0	3.10E-05	4	2.32E-04	Both
ERBB4	2	9	0	0	0	0	1.38E-05	6	2.53E-04	Both
EPHA7	0	4	1	0	1	0	2.35E-04	5	4.25E-04	Both
KDR	1	6	1	0	0	1	7.46E-05	5	4.41E-04	Both
NTRK1	0	6	1	0	0	0	2.56E-05	6	4.47E-04	Both
ZMYND10	1	4	0	0	0	0	1.16E-04	2	5.33E-04	Both
PTEN	1	3	1	0	0	0	1.54E-04	4	6.52E-04	Both
LTK	0	3	2	1	0	0	1.65E-04	5	1.73E-03	Both
MYO3B	1	7	0	0	0	0	2.47E-05	5	2.15E-03	Both
PDGFRA	2	6	1	0	0	0	1.90E-05	6	3.16E-03	Both
DOCK3	7	5	0	1	0	0	8.09E-06	6	3.30E-03	DrGaP
PAK4	0	2	1	0	0	0	2.66E-03	2	4.07E-03	DrGaP
PIK3C3	0	6	0	0	0	0	1.04E-05	3	4.09E-03	DrGaP
FLT4	0	5	0	0	0	0	1.02E-05	4	4.23E-03	DrGaP
PAK7	0	4	0	0	0	0	6.03E-05	3	4.23E-03	DrGaP
NRAS	0	3	0	0	0	0	6.19E-05	1	4.38E-03	Both
LMTK2	0	4	0	0	1	0	4.40E-05	2	4.87E-03	DrGaP
TEC	0	3	0	0	0	0	1.13E-04	3	5.07E-03	DrGaP
PRKCG	0	4	0	0	0	0	8.90E-06	3	5.56E-03	DrGaP
INHBA	0	3	1	0	1	0	3.30E-05	3	7.03E-03	Both
CDC42BPA	1	5	0	0	0	0	4.44E-06	3	8.00E-03	DrGaP
PAK3	0	5	0	0	0	0	1.73E-05	2	8.46E-03	Both
SLC38A3	1	3	0	0	0	0	5.39E-05	2	8.57E-03	DrGaP
JAK2	2	4	0	0	1	0	2.74E-05	3	8.78E-03	DrGaP
BAP1	0	0	2	0	0	0	1.36E-03	2	9.49E-03	DrGaP
PIK3CG	0	4	1	0	0	0	2.04E-05	4	9.52E-03	DrGaP
ROR2	0	5	0	0	0	0	1.02E-05	4	9.56E-03	DrGaP
CDH11	0	5	0	1	0	0	3.08E-05	4	9.69E-03	Both
EPHA5	0	6	0	1	0	0	3.50E-05	4	9.90E-03	Both
MSH6	0	3	1	0	0	0	3.24E-05	4	1.28E-02	DrGaP
ERAS	0	1	1	0	0	0	2.13E-04	2	1.63E-02	DrGaP
ROBO1	0	3	0	0	1	0	8.18E-06	1	1.66E-02	DrGaP
MKNK2	0	1	1	0	0	0	9.19E-05	2	2.03E-02	DrGaP
CDK17	0	2	0	0	0	0	6.85E-05	2	2.24E-02	DrGaP
ACVR1B	0	0	1	0	1	0	6.92E-05	2	2.79E-02	DrGaP
LMTK3	1	3	1	0	0	0	4.36E-05	2	2.80E-02	DrGaP
NTRK2	1	6	0	0	0	0	7.83E-06	3	2.83E-02	Both
MKNK1	0	2	0	0	0	0	2.20E-05	1	2.88E-02	DrGaP
RET	0	2	1	0	0	0	2.19E-05	3	3.03E-02	DrGaP
SMAD4	0	2	1	0	0	0	3.12E-05	3	3.22E-02	DrGaP
IRAK2	0	1	0	1	1	0	5.35E-05	3	3.45E-02	DrGaP
GNAS	0	6	0	0	1	0	7.69E-06	6	3.55E-02	DrGaP
TP63	0	3	1	0	0	0	3.92E-05	2	4.02E-02	DrGaP

FOS	0	1	0	0	1	0	9.91E-06	2	4.04E-02	DrGaP
GATA1	0	1	1	0	0	0	6.34E-05	2	4.17E-02	DrGaP
TFDP1	0	3	0	1	0	0	4.34E-05	4	7.05E-02	Ding/Youn

Note: #_pa is the number of positive alpha. Both refers the genes that are identified by both DrGaP and Ding/Youn's methods.

Table S6 Comparison of significance of pathway analysis in the study of Ding *et al.*

KEGG_ID	Pathway	TSP Fisher p-value	TSP Fisher FDR	TSP binomial p-value	TSP binomial FDR	PathScan p-value	PathScan FDR	DrGaP p-value	DrGaP FDR
hsa04540	Gap junction	3.60E-37	2.50E-36	4.10E-44	2.90E-43	4.00E-34	3.50E-38	2.66E-78	2.50E-77
hsa04320	Dorso-ventral	1.50E-28	8.40E-28	1.70E-34	8.80E-34	1.80E-23	1.00E-22	9.09E-63	5.84E-62
hsa04115	p53 signaling	8.00E-25	4.00E-24	1.10E-31	4.80E-31	4.90E-22	2.20E-21	1.22E-56	6.46E-56
hsa04530	Tight junction	1.10E-23	5.50E-23	3.90E-30	1.50E-29	4.80E-24	3.00E-23	1.80E-52	8.43E-52
hsa04912	GnRH signaling	5.00E-23	2.20E-22	3.90E-33	2.00E-32	1.50E-22	6.90E-22	5.88E-62	3.58E-61
hsa04010	MAPK signaling	2.10E-20	8.80E-20	2.10E-43	1.30E-42	6.40E-44	6.90E-43	4.57E-92	4.64E-91
hsa04310	Wnt signaling	2.20E-20	8.80E-20	1.10E-28	3.90E-28	3.90E-22	1.80E-21	6.61E-47	2.60E-46
hsa04150	mTOR signaling	3.50E-20	1.30E-19	1.60E-32	7.80E-32	4.80E-05	1.20E-04	3.65E-18	8.40E-18
hsa04210	Apoptosis	1.20E-16	4.40E-16	5.90E-27	2.10E-26	3.20E-23	1.70E-22	8.59E-51	3.74E-50
hsa04662	B cell receptor	1.30E-15	4.50E-15	9.80E-24	3.00E-23	7.80E-13	2.70E-12	8.90E-35	2.52E-34
hsa04810	actin cytoskel.	2.30E-15	7.70E-15	7.10E-32	3.20E-31	9.60E-29	6.50E-28	4.67E-76	3.80E-75
hsa04360	Axon guidance	1.20E-11	3.80E-11	3.40E-25	1.20E-24	2.10E-23	1.10E-22	1.33E-50	5.61E-50
hsa04370	VEGF signaling	3.40E-11	1.00E-10	7.70E-21	2.30E-20	1.60E-16	6.10E-16	3.02E-44	1.08E-43
hsa04020	Calcium signal.	3.90E-10	1.20E-09	2.80E-18	7.40E-18	9.00E-14	3.20E-13	1.80E-39	5.78E-39
hsa04012	ErbB signaling	9.20E-10	2.60E-09	4.80E-25	1.60E-24	4.80E-19	1.90E-18	4.17E-64	2.83E-63
hsa04110	Cell cycle	1.80E-08	4.90E-08	1.50E-20	4.20E-20	4.70E-17	1.80E-16	8.74E-45	3.23E-44
hsa04660	T cell receptor	1.90E-07	5.00E-07	3.20E-18	8.40E-18	9.40E-12	3.10E-11	1.81E-36	5.38E-36
hsa04650	Killer cell tox.	5.50E-06	1.40E-05	4.10E-16	1.00E-15	2.80E-13	9.80E-13	2.03E-37	6.36E-37
hsa04620	Toll-like recep.	1.20E-05	3.00E-05	0.981	1	0.926	0.948	0.070	0.101
hsa04920	Adipocytokine	6.80E-05	1.60E-04	7.40E-11	1.60E-10	4.40E-09	1.20E-08	3.23E-26	7.57E-26
hsa04060	Cytokine recep.	9.00E-05	2.10E-04	9.30E-13	2.20E-12	6.00E-10	1.70E-09	2.33E-37	7.10E-37
hsa04664	Fc epsilon RI	1.50E-04	3.40E-04	3.80E-13	9.00E-13	1.80E-10	5.60E-10	2.55E-31	6.34E-31
hsa04630	Jak-STAT sig.	2.60E-04	5.60E-04	0.785	1	0.654	0.767	0.00162	0.00299
hsa04914	Progesterone oocyte	9.30E-04	2.00E-03	2.60E-12	5.90E-12	2.10E-10	6.10E-10	9.23E-35	2.56E-34
hsa04670	Leukocyte migration	1.30E-03	2.70E-03	0.634	0.874	0.464	0.739	0.0334	0.04969
hsa04520	Adherens junction	3.90E-03	7.90E-03	2.20E-09	4.60E-09	2.60E-06	6.70E-06	1.03E-31	2.62E-31
hsa04930	Type 2 diabetes mel.	7.30E-03	0.014	0.767	1	0.565	0.721	0.00419	0.0072
hsa04330	Notch signaling	7.60E-03	0.015	0.817	1	0.68	0.79	0.58163	0.64508
hsa04120	Ubiquitin proteolys.	0.01	0.02	0.965	1	0.9	0.929	0.58943	0.64784
hsa04350	TGF-beta signaling	0.014	0.026	0.409	0.664	0.496	0.703	0.02351	0.03586
hsa04910	Insulin signaling	0.025	0.045	3.10E-11	6.90E-11	2.70E-10	7.70E-10	1.06E-32	2.89E-32
hsa04742	Taste transduction	0.051	0.091	1.10E-03	2.20E-03	0.01	0.025	0.01262	0.0204
hsa04340	Hedgehog signaling	0.104	0.181	0.574	0.804	0.144	0.282	0.14363	0.19047
hsa04640	Hematopo. cell lin.	0.106	0.181	0.881	1	0.704	0.804	0.88474	0.91473
hsa05010	Alzheimers disease	0.188	0.317	1.50E-03	2.80E-03	0.526	0.692	0.82769	0.8705
hsa04070	Phosphatidyl. sig.	0.195	0.317	0.089	0.165	0.081	0.171	0.00036	0.00076
hsa05120	Epith. sig. H. pylori	0.21	0.335	3.30E-05	6.60E-05	1.70E-03	4.30E-03	2.63E-27	6.29E-27
hsa04510	Focal adhesion	0.738	1	3.60E-08	7.40E-08	2.00E-09	5.50E-09	6.70E-36	1.94E-35
hsa04740	Olfactory transduc.	0.803	1	0.297	0.501	0.33	0.617	0.44741	0.54043
hsa00562	Inositol phos. metab.	0.95	1	0.04	0.075	0.082	0.171	0.00289	0.0051
hsa04080	Neuroactive interac.	1	1	0.148	0.27	0.15	0.288	0.06789	0.09979
hsa00450	Selenoamino. met.	1	1	1	1	0.415	0.704	NA	NA

Note:

TSP Fisher's and binomial tests for significantly mutated KEGG pathways were originally performed by Ding et al. (Nature 455: 1069-1075, 2008). PathScan tests for KEGG pathways were originally performed by Wendl et al. (Bioinformatics 27:1595-1602, 2011).

Table S7 Driver genes in LUAD

gene	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	avg_alpha	#_pa	p_adj
TP53	0	19	4	2	3	0	3.22E-04	13	2.21E-29
KRAS	0	18	0	0	0	0	1.95E-04	4	8.59E-24
GPRIN2	0	4	0	0	0	4	4.71E-05	2	1.26E-12
RYR2	5	39	3	0	1	0	1.57E-05	9	6.19E-09
PABPC1	2	9	0	0	0	0	7.34E-05	4	2.61E-08
KRTAP5-1	0	0	0	0	0	4	4.15E-05	1	2.94E-08
PRR21	0	4	0	0	3	0	3.19E-05	3	2.04E-06
IGSF3	0	1	0	0	0	3	6.06E-06	2	6.38E-06
KEAP1	0	9	2	0	1	0	5.65E-05	10	8.00E-06
TMPRSS13	0	0	0	0	0	3	1.53E-05	1	9.34E-06
COL11A1	2	16	1	3	0	0	1.64E-04	7	2.14E-05
CCT8L2	1	10	0	0	0	0	7.02E-05	4	3.83E-05
CDH10	1	11	1	0	0	0	1.45E-04	4	4.12E-05
NAV3	1	13	0	0	1	0	1.03E-05	4	4.37E-05
LRP1B	6	26	3	0	1	0	2.60E-05	8	1.99E-04
REG1B	0	5	0	0	0	0	3.24E-04	3	2.07E-04
CSMD3	7	29	1	0	0	0	1.11E-05	5	2.50E-04
EGFR	0	5	0	0	0	1	1.65E-05	4	3.76E-04
THSD7A	0	13	0	0	0	0	5.34E-05	4	3.93E-04
ZAN	4	2	0	0	4	0	2.87E-06	2	6.23E-04
NMUR2	2	7	0	0	0	0	1.66E-04	4	6.39E-04
NLGN4X	3	11	0	0	1	0	3.77E-05	5	6.89E-04
FAM5C	3	7	0	1	0	0	9.03E-05	6	7.73E-04
RP1L1	5	16	1	0	0	0	3.95E-05	7	7.81E-04
GRM1	1	10	1	0	0	0	2.29E-04	7	9.04E-04
KRTAP5-5	1	1	0	0	0	3	4.07E-05	2	1.16E-03
KRTAP4-5	0	0	0	0	0	3	4.76E-05	1	1.52E-03
QRICH2	0	0	0	0	0	4	6.90E-06	1	1.56E-03
ZFHX4	7	21	2	0	0	0	1.23E-05	8	1.74E-03
NTRK1	1	1	0	4	0	0	4.14E-04	1	1.92E-03
SPTA1	3	10	5	0	0	0	8.73E-05	6	1.97E-03
MUC17	4	17	2	0	0	0	2.76E-05	9	2.13E-03
SMPD1	0	1	0	0	0	2	9.17E-06	1	2.97E-03
ZNF804A	1	11	1	0	0	0	7.55E-05	3	3.21E-03
C17orf97	0	0	0	0	0	3	2.04E-05	1	3.37E-03
ADAMTS12	4	7	1	0	0	0	2.94E-05	4	3.39E-03
PRDM9	3	6	3	1	0	0	7.53E-05	6	3.93E-03
RIMS2	0	9	0	0	0	0	5.74E-05	3	3.99E-03
CDH9	4	6	0	0	0	0	1.16E-04	3	4.01E-03
NEFH	6	0	0	0	0	2	5.67E-06	1	4.26E-03
ZNF492	0	0	0	2	0	0	8.69E-03	1	4.31E-03

ARSF	1	3	1	2	1	0	9.24E-05	7	4.33E-03
TCERG1	0	0	0	0	0	2	5.27E-06	1	4.45E-03
TNR	6	6	1	1	0	0	6.79E-05	4	4.67E-03
PXDNL	3	7	1	1	0	0	1.20E-04	5	4.91E-03
FAM120B	0	4	0	0	0	1	4.12E-05	4	4.97E-03
EPHA6	0	9	0	0	0	0	4.96E-05	3	5.46E-03
FAM47B	0	6	2	0	0	0	8.55E-05	5	6.16E-03
HAVCR1	2	5	0	0	0	0	3.70E-05	3	6.17E-03
ZNF536	5	9	2	1	1	0	8.41E-05	7	8.56E-03
ZW10	0	3	0	2	0	0	2.90E-03	3	9.00E-03
FAT3	6	17	1	1	0	0	1.59E-04	8	9.06E-03
C15orf2	1	8	0	0	0	0	4.44E-05	3	9.07E-03
KCNJ12	3	5	0	0	1	0	3.57E-05	5	9.18E-03
CD33	1	3	1	0	0	0	1.72E-04	4	9.21E-03
LGMN	0	2	0	0	1	0	8.12E-06	3	9.24E-03
ATP8A2	1	3	1	2	0	0	5.69E-05	5	9.31E-03
KIAA0748	0	2	1	0	1	0	7.32E-04	4	9.91E-03
LILRB1	3	6	1	0	0	0	1.59E-04	5	1.01E-02
FMN2	3	6	0	0	0	2	2.99E-06	4	1.01E-02
SLIT3	3	4	2	1	1	0	6.78E-05	5	1.11E-02
NALCN	0	10	2	2	0	0	3.18E-05	7	1.19E-02
GRID2	2	6	1	0	1	0	1.62E-04	5	1.21E-02
FCRL1	1	4	0	1	0	0	1.46E-03	3	1.26E-02
TMEM117	2	1	2	0	1	0	8.68E-05	3	1.30E-02
MMP1	1	5	0	0	0	0	1.77E-05	4	1.30E-02
ADAMTS16	1	8	1	1	0	0	3.67E-05	5	1.32E-02
NETO1	2	4	0	1	0	0	2.80E-04	4	1.45E-02
ENOX1	0	2	1	0	1	0	9.18E-05	4	1.46E-02
HDAC9	0	6	0	2	0	0	4.00E-05	6	1.46E-02
GPRC6A	0	6	0	0	0	0	1.53E-05	3	1.50E-02
ZP4	1	1	0	2	2	0	4.25E-04	3	1.51E-02
SF3B4	0	2	0	0	1	0	6.25E-05	3	1.62E-02
CSMD1	4	10	1	1	0	0	5.12E-05	7	1.80E-02
TRPM1	1	5	1	1	0	0	2.80E-05	6	1.81E-02
TMEM132E	1	3	0	0	1	0	1.81E-05	3	2.04E-02
NF1	0	4	1	1	2	0	1.80E-05	5	2.08E-02
KLHL25	0	4	0	0	0	0	1.62E-05	3	2.10E-02
MARK3	0	1	1	0	0	0	2.12E-04	2	2.10E-02
OVGP1	0	0	0	0	0	3	1.23E-05	1	2.22E-02
KCNS2	0	3	1	0	0	0	1.51E-04	4	2.48E-02
PPP3R2	1	1	1	0	0	0	5.63E-04	2	2.48E-02
RBMX	0	2	0	0	0	0	2.71E-04	1	2.50E-02
BNC2	0	1	0	1	0	0	2.20E-04	2	2.59E-02
KCNK2	1	2	1	0	0	0	6.27E-05	3	2.66E-02

GCN1L1	0	1	0	1	2	0	1.69E-05	3	2.67E-02
ACTN2	2	5	1	0	0	0	1.20E-04	4	2.70E-02
DYDC2	0	2	1	0	0	0	1.08E-04	3	2.98E-02
BANP	0	1	1	0	0	0	1.44E-04	2	3.00E-02
SEMA3A	1	3	1	1	0	0	8.95E-05	4	3.07E-02
ADAMTS5	1	7	1	1	0	0	7.64E-05	6	3.59E-02
PTPRG	0	1	0	0	1	0	3.81E-06	2	3.70E-02
INHBA	0	4	0	0	0	0	7.11E-05	3	3.74E-02
PCDH17	3	13	0	0	0	0	2.27E-05	5	3.87E-02
PCDH11X	2	13	1	0	0	0	4.79E-05	4	3.87E-02
BCLAF1	1	3	0	1	0	0	6.67E-05	3	3.96E-02
ATN1	2	0	0	0	0	2	4.85E-06	1	3.98E-02
EMR2	0	2	0	0	1	0	7.73E-06	3	4.02E-02
UNC5B	1	3	0	1	1	1	4.50E-05	5	4.02E-02
OGT	0	1	1	0	0	0	2.95E-04	2	4.03E-02
MYL10	0	2	1	0	0	0	1.96E-04	2	4.19E-02
COL6A6	0	4	0	2	2	0	2.08E-05	4	4.34E-02
TIFAB	0	4	0	0	0	0	6.29E-04	2	4.35E-02
DCAF4L2	2	6	0	0	0	0	7.52E-05	3	4.41E-02
DCAF8L1	0	9	0	0	0	0	6.71E-05	3	4.61E-02
ARHGAP27	0	1	1	2	0	0	9.91E-05	4	4.64E-02
PREPL	0	3	0	0	0	0	9.72E-05	2	4.65E-02
CDC42BPA	0	1	1	2	0	0	5.08E-05	3	4.68E-02
PAPPA2	5	12	0	0	0	0	2.22E-05	3	4.98E-02
ZC3H12C	1	1	1	0	0	0	7.86E-05	2	4.99E-02

Note: #_pa is the number of positive alpha.

Table S8 Driver genes in LUSC

gene	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	avg_alpha	#_pa	p_adj
ACTRT1	1	6	0	0	0	0	1.63E-04	4	2.48E-02
ADAM18	0	6	0	4	0	0	7.03E-05	5	3.57E-02
ADAMTS12	7	15	0	1	2	0	3.55E-05	8	1.67E-04
ADCY8	1	10	1	1	0	0	5.71E-05	6	4.58E-02
AGAP3	1	3	0	1	0	0	7.78E-05	2	3.81E-02
AGAP6	0	6	0	0	0	0	1.46E-05	3	1.20E-02
ANKRD30A	2	8	3	2	1	0	3.58E-05	8	4.26E-04
ANO5	2	10	1	0	0	0	3.31E-04	4	3.09E-03
ARID1A	1	4	1	1	2	0	2.29E-05	5	4.27E-02
ARSD	1	3	0	0	0	1	1.31E-05	3	1.23E-02
ASB17	1	5	0	0	0	0	3.73E-05	3	1.23E-02
ASB5	0	6	0	1	0	0	1.10E-04	6	6.30E-03
ATP10B	4	12	1	0	0	0	2.39E-05	7	3.55E-02
BMP5	1	3	2	0	0	0	6.99E-04	5	9.37E-03
C1orf173	6	18	1	0	1	0	1.09E-05	8	1.06E-05
C1QB	1	4	0	0	1	0	3.13E-05	2	4.34E-03
C6	2	9	3	1	0	0	5.49E-05	7	2.11E-03
C8orf22	0	3	1	0	0	0	2.62E-03	3	1.46E-02
CALN1	0	6	1	0	0	0	9.81E-05	4	7.09E-04
CCDC158	0	3	1	2	0	0	7.35E-05	3	4.94E-03
CCT8L2	1	8	0	0	1	0	1.71E-05	5	4.11E-02
CDH10	4	15	3	5	0	0	2.23E-04	12	2.65E-18
CDH18	1	12	0	1	0	0	5.22E-05	7	1.64E-04
CDKN2A	0	6	2	2	1	0	3.68E-04	9	1.01E-10
CLEC4C	0	2	1	0	0	0	1.91E-03	2	1.25E-02
CLRN2	1	5	0	0	0	0	9.85E-05	3	3.92E-02
CLSTN2	2	4	2	1	0	0	5.85E-05	6	9.65E-04
CNGB3	2	11	1	0	1	0	4.48E-05	7	1.47E-05
CNTN5	0	8	0	1	1	0	3.17E-04	7	3.06E-03
CNTNAP5	7	12	1	0	1	0	4.41E-05	9	2.56E-04
COL11A1	2	19	1	1	3	0	9.35E-05	6	1.24E-05
COL22A1	2	13	1	3	1	0	1.68E-05	9	7.95E-04
CPS1	2	14	0	2	0	0	5.21E-05	6	2.03E-04
CR2	1	2	1	0	2	0	1.61E-05	4	2.62E-02
CRB1	1	19	0	0	0	0	6.61E-05	5	4.25E-06
CREBBP	0	10	1	0	1	0	1.66E-05	6	1.09E-03
CRISP1	1	2	1	1	0	0	2.34E-04	4	1.63E-02
CSMD2	2	18	4	1	1	0	7.84E-05	11	5.16E-04
CSMD3	15	44	7	0	4	0	4.14E-05	12	1.04E-18
CTBS	0	1	0	0	0	2	1.40E-05	2	6.14E-03
CXorf59	0	4	0	2	0	0	1.83E-04	5	1.47E-02

DAND5	0	2	1	0	0	0	7.23E-04	3	1.19E-02
DCAF12L1	1	12	2	0	1	0	1.37E-04	8	7.46E-08
DCAF4L2	3	8	0	0	0	0	6.68E-05	5	7.53E-03
DCAF8L2	2	6	0	0	0	0	3.01E-05	5	1.57E-02
DCP1B	0	5	0	0	0	1	3.50E-05	5	4.02E-02
DENND2A	0	4	0	0	1	0	3.38E-05	4	1.31E-02
DGKK	2	4	0	3	0	0	6.79E-05	5	4.25E-02
DLGAP2	0	4	0	0	2	0	1.32E-05	4	1.05E-02
DOLK	1	1	0	0	1	0	4.97E-05	2	3.80E-02
DPP10	2	9	1	2	0	0	3.90E-05	6	1.29E-02
DUSP27	4	10	0	0	0	0	2.68E-05	5	2.26E-02
ENPEP	0	6	1	0	1	0	2.03E-05	5	3.18E-02
EPHA3	3	6	3	1	1	0	7.92E-05	8	4.96E-06
EXO1	1	2	1	3	0	1	5.92E-05	7	2.13E-02
FAM114A1	0	2	0	2	0	0	1.33E-04	4	4.12E-02
FAM135B	7	18	0	0	1	0	1.67E-05	8	3.61E-04
FAM47A	3	6	1	0	2	0	3.34E-05	6	4.66E-04
FAM47C	2	10	2	0	0	0	3.06E-05	8	1.23E-02
FAM50A	0	1	0	2	0	0	1.37E-04	3	1.60E-02
FAM5C	2	14	1	0	0	0	4.25E-05	7	1.11E-06
FAT1	3	8	4	1	0	0	2.84E-05	6	1.41E-02
FBXW7	1	5	2	0	0	0	1.82E-04	5	1.51E-04
FLRT2	3	9	0	0	0	0	7.20E-05	5	3.82E-02
FMN2	4	11	0	0	0	2	1.05E-05	7	1.18E-02
GABRA6	0	2	1	0	2	0	3.28E-04	4	1.79E-02
GIMAP8	1	4	0	1	0	0	1.46E-04	4	3.59E-02
GLT1D1	1	2	2	0	0	0	1.61E-04	3	3.88E-02
GPR17	1	3	0	0	0	0	1.16E-04	2	4.58E-02
GRIA4	0	7	1	0	0	0	1.13E-04	6	2.01E-02
GRM1	2	5	3	1	0	0	2.67E-04	7	6.15E-04
GUCY1A2	2	4	0	1	1	0	8.89E-05	4	1.18E-02
GYPE	0	1	0	2	0	0	1.44E-03	2	2.69E-03
HAVCR1	3	1	0	0	1	0	1.21E-05	2	3.05E-02
HBD	0	4	0	0	0	0	1.03E-03	3	1.91E-02
HCN1	8	11	3	1	1	0	1.32E-04	11	1.12E-06
HEATR7B2	5	12	3	0	2	0	1.78E-04	7	6.75E-04
HLA-A	0	9	2	0	0	0	2.00E-04	7	7.76E-10
HLA-DRB5	1	3	4	0	0	0	3.44E-03	3	4.00E-09
HLTF	1	5	1	1	0	0	5.39E-05	4	3.89E-02
HNRNPH3	0	0	0	2	0	0	3.84E-04	1	2.71E-02
HRC	0	0	0	1	0	2	1.77E-04	2	1.51E-02
HSPD1	1	1	0	3	0	0	2.88E-04	2	2.37E-04
IGSF1	0	4	1	1	1	0	3.97E-05	4	4.98E-02
IGSF3	0	0	0	0	0	2	4.19E-06	1	2.69E-02

IL1RAPL1	3	6	2	0	0	0	1.75E-04	6	2.30E-02
IMPG1	1	8	0	0	1	0	3.66E-05	6	4.66E-03
ITGA8	1	9	0	3	0	0	3.47E-05	7	2.16E-03
ITGAD	0	6	2	1	0	0	4.82E-05	8	2.36E-02
KCND2	1	7	0	0	0	0	2.14E-05	5	3.28E-02
KCNIP4	1	4	1	1	0	0	4.08E-04	5	3.76E-04
KCNJ12	10	9	0	0	0	0	9.40E-05	4	2.31E-06
KCNT2	2	2	0	1	2	0	4.65E-05	4	2.71E-02
KDM6A	0	2	2	4	0	0	5.96E-04	6	1.07E-04
KDR	3	4	1	1	0	0	1.20E-03	4	1.20E-02
KEAP1	0	15	0	0	2	0	7.31E-05	7	4.09E-11
KIAA2022	1	11	1	0	0	0	2.40E-05	4	3.08E-03
KIF16B	1	5	0	0	2	0	2.34E-05	6	6.55E-03
KIF2B	4	9	0	0	1	0	1.57E-05	5	4.80E-02
KLHL1	2	9	1	0	0	0	1.09E-04	6	5.89E-04
KLHL4	0	6	1	1	0	0	5.87E-05	5	4.54E-02
KLK15	0	1	0	1	1	0	2.16E-04	3	4.13E-02
KRTAP21-1	0	4	0	0	0	0	1.18E-04	3	3.41E-02
KRTAP4-5	0	0	0	0	0	2	2.81E-05	1	4.33E-03
KRTAP5-1	0	0	0	0	0	10	9.18E-05	1	8.38E-21
KRTAP5-5	0	2	0	0	0	9	4.88E-05	3	5.89E-18
KRTAP5-8	0	1	0	0	0	2	2.78E-05	2	2.65E-02
LILRA2	4	4	0	1	1	0	8.09E-04	5	4.60E-04
LPHN3	3	11	0	1	0	0	2.95E-05	6	4.24E-02
LPPR4	1	4	1	1	0	0	6.61E-04	4	8.03E-03
LRFN5	3	11	2	0	0	0	7.16E-05	5	7.89E-07
LRP1B	5	41	2	0	2	0	1.36E-05	9	1.42E-08
LRP2	7	17	1	1	0	0	4.49E-05	9	1.71E-02
LRRC7	5	10	0	1	0	0	4.59E-05	7	3.28E-02
LRRTM1	5	4	0	0	3	0	1.45E-05	5	7.07E-04
MAGEB6	3	8	1	0	0	0	7.54E-05	7	3.08E-02
MAGEC1	1	11	0	0	2	1	1.12E-05	5	7.69E-06
MAGEE2	0	3	1	0	1	0	5.46E-05	3	2.36E-02
MARCO	1	4	0	3	0	0	1.35E-04	5	4.95E-05
MCCC1	0	1	0	3	0	0	2.26E-04	2	3.20E-02
MCF2	2	4	0	2	2	0	3.95E-05	4	7.57E-03
MCHR2	1	4	1	1	1	0	2.35E-04	5	3.09E-04
MLL2	3	9	4	6	6	1	3.16E-05	11	1.55E-08
MMP16	2	6	2	0	0	0	7.17E-05	6	6.85E-05
MS4A14	1	7	0	0	1	0	1.46E-05	5	1.31E-02
MSLNL	2	1	1	0	1	0	6.44E-04	3	4.06E-02
MTNR1B	0	4	1	0	0	0	8.82E-05	4	3.55E-02
MUC16	29	73	4	2	1	0	1.32E-05	9	1.16E-05
MUC17	9	17	1	1	0	0	9.94E-05	7	1.16E-02

MUC6	4	13	0	0	0	0	6.84E-06	7	2.24E-02
MYH1	4	16	0	0	0	0	1.88E-05	6	1.76E-02
MYH13	1	13	0	0	0	0	1.52E-05	6	2.63E-02
MYH2	3	16	1	0	0	0	3.76E-05	7	4.18E-05
MYH8	1	12	0	0	0	0	3.07E-05	4	2.15E-03
NAALAD2	2	4	1	1	0	0	5.17E-05	4	3.15E-02
NAV3	4	17	2	1	0	0	2.62E-05	11	8.59E-04
NEFH	2	2	0	0	0	3	7.43E-06	1	3.25E-02
NF1	1	9	2	2	0	0	2.20E-05	7	4.55E-02
NFE2L2	0	11	0	0	0	1	6.92E-05	8	1.21E-06
NLGN4X	3	9	0	0	1	0	3.58E-05	5	1.86E-03
NLRP3	5	10	3	0	0	0	6.45E-05	7	4.91E-05
NRK	3	7	0	1	0	0	3.03E-05	3	3.16E-02
NTM	4	3	2	0	0	0	1.26E-04	4	4.67E-03
NUP205	0	5	2	0	0	0	1.12E-04	5	3.63E-02
NUPL2	0	1	0	0	0	2	1.30E-05	2	4.58E-02
OLFM4	1	5	0	1	0	0	2.34E-04	4	1.70E-02
OPN1SW	2	3	0	1	0	0	2.01E-04	3	1.05E-02
OVGP1	0	3	1	0	0	3	2.95E-05	5	3.54E-04
PABPC1	3	8	0	0	0	0	2.91E-05	5	4.62E-03
PABPC3	8	7	3	0	0	0	4.69E-04	5	3.35E-05
PANK3	0	5	0	0	0	0	4.98E-05	2	1.33E-02
PAPPA2	7	26	1	0	0	0	1.71E-05	8	5.15E-06
PCDH11X	3	17	1	0	0	0	2.56E-04	6	1.68E-07
PCLO	15	20	0	3	0	0	6.70E-04	6	3.58E-04
PEG3	1	9	3	0	1	0	1.86E-05	8	9.36E-03
PIK3CA	0	10	0	0	0	0	2.87E-05	3	2.78E-05
PIK3CG	0	11	1	1	0	0	6.13E-05	8	5.83E-05
PKHD1	5	15	2	1	0	0	1.97E-05	6	1.81E-03
PKHD1L1	5	22	0	0	2	0	4.38E-06	5	2.98E-02
PLD5	2	7	0	1	0	0	9.41E-05	6	1.25E-03
PLXNA4	3	9	2	1	1	0	9.36E-05	8	9.78E-03
PNLIPRP3	1	6	0	1	0	0	7.07E-05	4	2.26E-02
POTEA	1	6	0	1	0	0	5.41E-05	4	4.65E-03
POTEC	2	7	0	1	1	0	5.31E-05	7	2.88E-02
POU6F2	1	3	0	2	0	0	1.06E-04	3	4.77E-02
PRAME	2	5	1	0	0	0	4.32E-04	5	2.77E-02
PRDM9	4	11	3	1	0	0	1.00E-04	8	5.11E-06
PRG4	9	3	0	0	0	4	3.25E-06	3	7.46E-05
PRIM2	1	4	1	1	0	0	7.15E-05	4	1.64E-02
PTEN	0	3	3	1	1	0	1.82E-04	8	2.82E-05
PTPN11	0	1	3	0	0	0	5.80E-04	2	2.98E-05
PYHIN1	1	5	0	0	0	0	2.56E-04	2	3.57E-02
RAG2	0	6	0	0	0	0	3.88E-05	2	4.28E-02

RALY	0	1	0	0	0	2	7.05E-05	2	7.82E-04
RANBP17	1	2	1	1	1	0	5.39E-05	5	1.86E-02
RASA1	0	0	2	3	0	1	1.08E-04	6	7.09E-04
RASSF9	0	5	1	0	0	0	5.05E-05	4	1.42E-02
RB1	0	2	3	2	1	0	1.42E-04	7	7.68E-05
REG1A	0	4	0	1	1	0	1.77E-04	5	4.67E-03
REG1B	0	4	0	2	0	0	4.12E-04	2	2.51E-04
REG3A	0	6	0	0	0	0	1.15E-04	2	4.94E-04
RELN	10	18	3	4	0	0	3.31E-05	11	1.79E-03
RIMS2	3	10	0	0	0	0	3.23E-05	5	1.12E-02
RPL10L	1	7	0	0	0	0	1.42E-04	5	1.74E-02
RXFP1	0	7	0	0	0	0	3.37E-05	2	1.85E-02
RXRG	1	3	2	0	0	0	4.81E-04	5	9.38E-03
RYR2	9	55	2	2	2	0	2.42E-05	11	1.64E-14
SALL1	3	13	1	0	2	1	1.97E-05	9	3.91E-03
SCN1A	3	18	1	1	0	0	2.57E-05	6	4.85E-05
SCN2A	2	7	0	2	1	0	2.85E-05	6	2.36E-02
SEMA3E	2	3	1	2	0	0	7.89E-05	5	1.19E-02
SEMG2	0	2	2	0	1	0	1.61E-04	4	2.25E-02
SEPT14	1	2	1	2	0	0	1.59E-04	5	1.84E-02
SERPINB12	1	3	1	1	0	0	9.43E-04	5	3.17E-02
SI	3	14	1	1	0	0	3.56E-05	7	2.10E-03
SKA3	0	1	0	4	0	0	2.48E-04	4	7.21E-04
SLC17A6	1	5	2	0	0	0	7.27E-05	5	1.51E-03
SLC25A10	1	5	0	0	1	0	3.86E-05	5	2.68E-03
SLC26A7	1	4	2	0	0	0	5.20E-05	6	1.20E-02
SLC6A11	1	1	0	2	0	1	1.22E-04	2	7.37E-03
SLC8A1	3	6	2	0	0	0	1.48E-04	7	3.09E-02
SLCO1B1	2	5	2	0	0	0	1.34E-04	6	3.84E-02
SLCO1C1	1	10	0	2	0	0	2.02E-04	7	1.35E-05
SLIT2	4	9	2	1	0	0	4.74E-05	8	3.52E-02
SLITRK2	2	7	0	0	1	0	7.24E-05	6	1.78E-02
SLITRK3	6	8	0	0	1	0	6.56E-05	6	2.81E-02
SLITRK4	0	3	3	0	0	0	9.88E-05	3	2.81E-02
SORCS1	3	9	1	1	0	0	1.32E-04	7	8.20E-03
SPANXN1	0	1	1	2	0	0	1.08E-03	4	1.05E-02
SPHKAP	3	20	1	0	0	0	2.47E-05	7	5.44E-03
SPRYD5	2	5	0	1	0	0	2.10E-04	5	2.25E-02
SPTA1	9	20	1	0	1	0	1.17E-05	10	7.55E-03
SRPK1	0	2	0	0	2	0	6.55E-05	3	2.76E-02
SYMPK	1	1	0	4	0	0	5.10E-04	4	3.24E-02
SYNE2	5	7	2	1	0	0	2.41E-05	3	4.56E-02
TDRD5	1	7	1	0	1	0	3.62E-05	6	9.37E-03
TECRL	2	5	0	0	0	0	4.03E-05	3	4.60E-02

TFAP2D	2	7	1	0	0	0	1.21E-04	5	7.49E-03
THEMIS	0	8	0	1	0	0	7.62E-05	5	9.73E-03
THSD7B	2	10	0	0	1	0	8.16E-06	4	3.80E-02
TLR4	2	5	1	0	1	0	1.74E-05	6	6.59E-03
TMEM132D	2	14	0	0	0	0	4.28E-05	5	1.41E-03
TMEM35	1	4	0	0	0	0	6.61E-05	3	2.94E-02
TNKS1BP1	1	3	0	0	3	0	2.76E-06	4	2.83E-02
TNN	4	15	0	0	2	0	2.60E-05	8	1.52E-04
TNR	5	12	0	2	1	0	3.28E-05	9	4.91E-05
TP53	1	63	12	6	11	3	1.32E-03	18	1.8E-151
TRIM42	0	7	2	0	0	0	5.77E-05	5	9.11E-03
TRIM58	3	10	1	1	0	0	1.18E-04	6	1.27E-05
TRPS1	0	9	1	0	0	1	1.18E-05	7	5.02E-03
TRPV5	1	4	0	1	1	0	5.69E-05	5	1.17E-02
UGT3A1	0	7	0	0	0	0	8.26E-05	5	3.84E-02
UNC5D	5	7	0	0	0	0	3.08E-05	4	2.71E-02
USH1C	0	6	0	0	1	0	3.75E-05	4	3.54E-02
USH2A	12	38	3	3	0	0	2.15E-05	9	8.84E-08
USP29	1	7	1	0	0	0	2.75E-05	3	2.96E-02
VAMP3	1	2	1	0	0	0	6.84E-04	3	9.70E-03
VEGFC	0	7	0	0	0	0	5.09E-05	5	2.50E-03
VGLL1	0	4	0	1	0	0	3.73E-04	3	1.74E-02
VMO1	0	0	0	6	0	0	3.29E-03	1	2.02E-09
VN1R5	0	3	2	0	0	0	1.19E-04	3	1.46E-03
VWA3B	3	8	0	1	0	0	8.03E-05	4	1.73E-02
WDR72	0	6	1	0	1	0	1.29E-05	6	2.95E-02
XIRP2	14	33	2	0	0	0	9.77E-06	7	7.85E-04
ZC4H2	1	6	0	0	0	0	2.81E-04	2	3.19E-02
ZCCHC12	1	4	0	0	1	0	5.75E-05	4	2.44E-02
ZFHX4	4	38	4	0	2	0	3.43E-05	11	1.41E-12
ZFP42	0	3	0	0	1	0	2.41E-05	3	2.75E-02
ZNF208	4	10	2	0	0	0	3.54E-05	6	3.23E-02
ZNF479	3	5	5	0	0	0	2.07E-03	4	9.14E-08
ZNF516	0	4	0	0	3	0	1.31E-05	4	3.17E-02
ZNF536	7	14	0	0	1	0	1.11E-05	7	9.04E-04
ZNF645	1	4	0	0	1	0	4.98E-05	5	3.95E-02
ZNF679	0	4	0	2	0	0	2.20E-04	6	2.85E-02
ZNF716	1	6	0	0	0	0	4.83E-05	2	1.33E-02
ZNF787	0	0	1	1	1	0	3.50E-04	3	4.98E-02
ZNF804A	2	11	2	0	1	0	2.53E-05	6	2.76E-05
ZNF804B	8	12	3	0	0	0	3.03E-04	7	3.41E-05
ZNF835	1	5	0	0	0	0	3.80E-05	2	1.84E-02
ZNF99	3	4	2	1	1	0	7.72E-05	6	2.16E-03

Table S9 Driver pathways in LUAD

pathway_id	pathway_name	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	p_adj
hsa04510	Focal adhesion	95	251	21	31	7	2	7.9E-33
hsa04010	MAPK signaling pathway	60	184	15	18	7	1	3.8E-27
hsa04020	Calcium signaling pathway	87	236	18	12	8	2	4.7E-22
hsa04512	ECM-receptor interaction	61	155	14	20	5	0	1.8E-18
hsa04514	Cell adhesion molecules (CAMs)	44	137	8	5	4	0	6.0E-18
hsa04530	Tight junction	37	122	8	7	3	2	9.1E-17
hsa04210	Apoptosis	15	48	10	6	4	0	1.2E-16
hsa04540	Gap junction	35	91	13	8	2	1	1.9E-16
hsa04810	Regulation of actin cytoskeleton	51	159	17	12	4	1	2.2E-15
hsa04110	Cell cycle	15	70	11	9	5	1	2.2E-15
hsa04144	Endocytosis	35	125	2	16	2	1	1.9E-14
hsa04310	Wnt signaling pathway	20	92	14	9	5	0	4.0E-14
hsa04060	Cytokine-cytokine receptor interaction	44	107	12	9	1	1	5.0E-13
hsa04012	ErbB signaling pathway	24	73	1	5	0	2	2.8E-12
hsa04115	p53 signaling pathway	9	47	6	4	4	0	1.4E-11
hsa04145	Phagosome	30	66	10	3	4	0	1.9E-11
hsa04520	Adherens junction	12	53	11	5	2	2	4.6E-11
hsa04370	VEGF signaling pathway	16	67	3	6	1	0	6.6E-09
hsa04120	Ubiquitin mediated proteolysis	21	95	10	4	1	1	9.7E-08
u0002	HMTs histone methylation reader	23	60	5	5	5	0	2.6E-07
u0001	Ch remodeling gene	18	51	8	4	1	2	1.4E-06
hsa04350	TGF-beta signaling pathway	18	42	4	2	0	0	5.1E-06
hsa02010	ABC transporters	23	59	6	7	3	0	6.7E-06
hsa04150	mTOR signaling pathway	11	28	4	2	1	0	8.4E-06
hsa04114	Oocyte meiosis	27	46	8	7	3	0	1.1E-05
hsa04142	Lysosome	12	34	2	3	3	3	2.2E-05
hsa04630	Jak-STAT signaling pathway	30	63	7	3	2	0	3.1E-05
hsa03018	RNA degradation	7	36	1	2	1	0	6.1E-05
u0004	DNMTs and Methyl-CpG binding	1	12	2	1	0	0	2.1E-04
hsa04141	Protein processing in endoplasmic reticulum	26	59	7	3	2	1	3.0E-04
hsa04070	Phosphatidylinositol signaling system	21	68	4	5	2	0	3.4E-04
hsa04146	Peroxisome	7	26	1	1	1	0	1.3E-03
u0003	HATs HDACs	9	16	3	4	1	1	1.8E-03

Table S10 Driver pathways in LUSC

pathway_id	pathway_name	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	p_adj
hsa04350	TGF-beta signaling pathway	15	116	20	16	15	3	6.4E-60
hsa04141	Protein processing in endoplasmic reticulum	169	400	36	17	15	1	2.3E-58
hsa04070	Phosphatidylinositol signaling system	52	218	23	15	19	3	2.3E-54
hsa04340	Hedgehog signaling pathway	27	142	17	11	12	3	6.0E-50
hsa04060	Cytokine-cytokine receptor interaction	121	329	28	33	22	6	3.5E-48
hsa04122	Sulfur relay system	144	397	28	27	18	1	3.1E-43
hsa04145	Phagosome	94	217	18	8	6	0	8.1E-32
hsa04144	Endocytosis	100	282	19	25	14	1	4.8E-25
hsa04150	mTOR signaling pathway	77	174	17	12	6	0	7.8E-24
hsa04630	Jak-STAT signaling pathway	56	151	9	6	9	0	4.0E-22
hsa04310	Wnt signaling pathway	92	271	15	17	11	1	1.5E-20
hsa04510	Focal adhesion	63	150	12	13	6	0	9.8E-20
hsa04120	Ubiquitin mediated proteolysis	58	149	11	12	8	0	7.8E-18
hsa04146	Peroxisome	67	206	21	9	6	0	1.4E-17
u0002	HMTs histone methylation reader	37	132	20	16	9	1	2.8E-17
hsa04114	Oocyte meiosis	29	79	14	5	6	0	1.5E-16
hsa04142	Lysosome	78	177	15	17	10	0	7.9E-15
hsa03410	Base excision repair	25	69	5	6	4	2	2.4E-13
hsa04130	SNARE interactions in vesicular transport	39	141	14	10	7	0	1.4E-12
hsa04370	VEGF signaling pathway	46	108	9	9	8	0	1.9E-12
hsa04115	p53 signaling pathway	36	84	6	7	3	2	2.2E-12
hsa04512	ECM-receptor interaction	39	90	7	10	4	0	4.1E-12
hsa03050	Proteasome	59	153	14	8	6	0	1.5E-10
hsa03030	DNA replication	39	136	8	5	3	1	4.3E-10
hsa04140	Regulation of autophagy	17	60	5	5	2	0	2.9E-09
hsa04520	Adherens junction	28	83	3	4	3	1	1.2E-08
hsa03018	RNA degradation	32	87	12	5	4	0	1.3E-08
u0003	HATs HDACs	14	45	3	5	3	0	1.7E-08
u0001	Ch remodeling gene	52	104	11	17	7	0	7.4E-08
hsa04514	Cell adhesion molecules (CAMs)	47	110	12	6	5	0	8.4E-08

hsa04020	Calcium signaling pathway	48	121	7	11	5	0	5.6E-06
hsa04080	Neuroactive ligand-receptor interaction	15	51	2	8	3	2	9.1E-06
hsa03020	RNA polymerase	24	64	8	3	4	0	1.7E-05
hsa04330	Notch signaling pathway	47	105	8	9	4	0	3.6E-05
hsa04530	Tight junction	22	51	5	3	0	0	6.4E-05
hsa04810	Regulation of actin cytoskeleton	18	42	3	2	0	0	1.5E-04
hsa04210	Apoptosis	35	78	5	9	3	2	5.4E-04
hsa04012	ErbB signaling pathway	15	61	8	1	0	1	1.7E-03
hsa04110	Cell cycle	22	54	5	4	0	0	9.6E-03

Table S11 Driver genes in non-hypermutated CRC

gene	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	avg_alpha	#_pa	p_adj
APC	1	10	139	9	42	0	2.40E-03	13	0
TP53	1	78	20	3	15	1	1.46E-03	17	6.1E-208
KRAS	0	85	0	0	0	0	4.92E-04	5	1.2E-200
PIK3CA	0	29	0	0	0	0	4.01E-05	7	1.43E-25
NRAS	0	18	0	0	0	0	9.94E-05	5	1.30E-24
FBXW7	1	22	1	1	0	1	2.08E-04	9	1.53E-23
SMAD4	0	17	1	1	0	1	1.61E-04	9	3.62E-17
AMER1	0	1	12	0	2	0	7.58E-04	4	6.07E-16
SOX9	0	0	3	0	6	0	1.50E-04	2	7.15E-11
SMAD2	0	6	4	1	0	0	4.69E-04	8	6.89E-10
LRP1B	5	21	4	2	0	0	5.48E-05	9	9.18E-10
TCF7L2	0	6	5	1	1	0	2.91E-04	8	3.19E-08
BRAF	0	7	0	0	0	0	4.06E-05	1	3.91E-06
CTNNB1	0	10	0	0	0	0	5.55E-05	5	1.48E-05
ACVR1B	0	8	2	0	0	0	1.07E-04	4	2.12E-05
TNFRSF10C	0	6	0	0	0	0	1.09E-04	1	1.03E-04
ELF3	0	1	1	0	3	0	2.23E-04	2	2.58E-04
NUTM2F	0	5	0	0	1	0	1.32E-05	3	2.73E-04
ARID1A	1	4	6	0	1	0	2.00E-04	6	2.87E-04
GRIK3	2	13	1	1	0	0	1.66E-04	5	2.91E-04
EIF4A2	0	4	0	0	0	1	1.27E-04	4	3.50E-04
LIFR	1	9	2	0	0	0	5.94E-05	7	3.77E-04
PCDH9	4	14	0	0	0	0	2.22E-05	7	3.91E-04
ERBB4	3	8	0	1	0	0	2.23E-05	6	4.95E-04
PCBP1	0	5	0	0	0	0	3.53E-05	2	5.16E-04
KRTAP5-5	1	3	0	0	0	0	1.40E-03	1	8.49E-04
TTN	13	64	7	1	1	0	1.47E-05	8	1.80E-03
FAT4	6	21	0	0	1	0	5.74E-06	8	1.96E-03
DMD	4	11	2	1	0	0	8.27E-05	6	2.41E-03
IL1RAPL2	3	4	2	0	0	0	2.07E-03	2	2.64E-03
ADAM29	1	9	0	0	0	0	1.83E-04	3	4.38E-03
SLITRK1	3	8	0	0	1	0	9.72E-05	4	4.43E-03
CNTN6	1	8	0	0	0	0	1.21E-04	3	0.01
GPC6	0	6	0	1	0	0	9.97E-05	4	0.01
ATM	0	6	3	1	1	1	3.46E-05	10	0.02
TGIF1	0	1	1	0	2	0	7.06E-05	3	0.02
RBM10	0	0	4	0	1	0	5.84E-04	3	0.02
WBSCR17	2	7	1	0	0	0	1.26E-04	3	0.02
OPCML	2	5	1	0	0	0	2.15E-04	3	0.03
TENM1	3	12	1	1	0	0	5.46E-05	3	0.03
PCDHB13	1	5	0	0	0	0	1.00E-05	6	0.03
TLL1	1	9	0	1	0	0	5.62E-05	7	0.03
KLHL4	1	8	0	0	0	0	1.30E-04	4	0.03
CASP14	0	5	1	0	0	0	1.18E-03	2	0.05

Table S12 Driver genes in HGS-OvCa

gene	silent	missense	nonsense	splicing	Fs_indel	nFs_indel	mean_alpha	#_pa	p_adj
TP53	0	187	29	34	43	11	7.55E-04	22	0
BRCA1	0	1	4	0	6	0	1.46E-04	6	3.91E-09
NF1	0	5	3	1	4	0	4.25E-05	8	4.07E-06
CSMD3	3	18	1	0	0	0	7.02E-06	9	1.74E-04
CDK12	0	4	2	0	2	1	1.79E-05	6	9.53E-04
RB1	0	1	2	1	2	0	1.21E-04	4	1.22E-03
BRCA2	0	3	2	0	5	0	1.10E-05	4	2.05E-03
USH2A	3	17	2	1	0	0	2.18E-05	8	7.81E-03
HIST1H1C	0	3	1	0	0	0	5.41E-04	3	0.01
SI	0	8	0	1	0	0	9.37E-06	6	0.02
SNTG1	1	2	3	0	0	0	3.43E-05	5	0.02
NLRP3	0	4	0	1	0	0	2.93E-05	4	0.02
CREBBP	1	3	1	1	2	0	4.31E-05	5	0.02
ZNF706	0	1	1	0	0	0	1.05E-03	2	0.02
TMEM132D	3	5	2	0	0	0	3.15E-05	7	0.02
RB1CC1	1	2	3	0	0	2	9.82E-06	4	0.02
MYH4	1	8	0	1	0	0	1.07E-05	6	0.03
TSPYL1	0	0	2	0	0	1	1.21E-04	3	0.03
BAI3	0	8	0	1	0	0	8.36E-06	5	0.03
TMPRSS3	1	1	0	2	0	0	8.69E-05	2	0.03
LRRC7	1	7	0	0	0	0	1.22E-05	5	0.04
DUSP19	0	4	0	0	0	0	2.58E-05	2	0.04
GNAS	0	1	2	0	0	0	1.26E-03	1	0.04
C1orf95	0	2	1	0	0	0	3.65E-04	3	0.04
CDC27	0	2	0	1	1	0	1.69E-05	3	0.04
GPR149	1	5	0	1	0	0	3.20E-04	5	0.04
KIAA1462	1	2	1	0	2	0	3.68E-05	4	0.04
SLCO1C1	0	6	0	0	0	0	6.37E-06	4	0.05
EFEMP1	0	3	0	1	1	0	3.29E-05	5	0.05