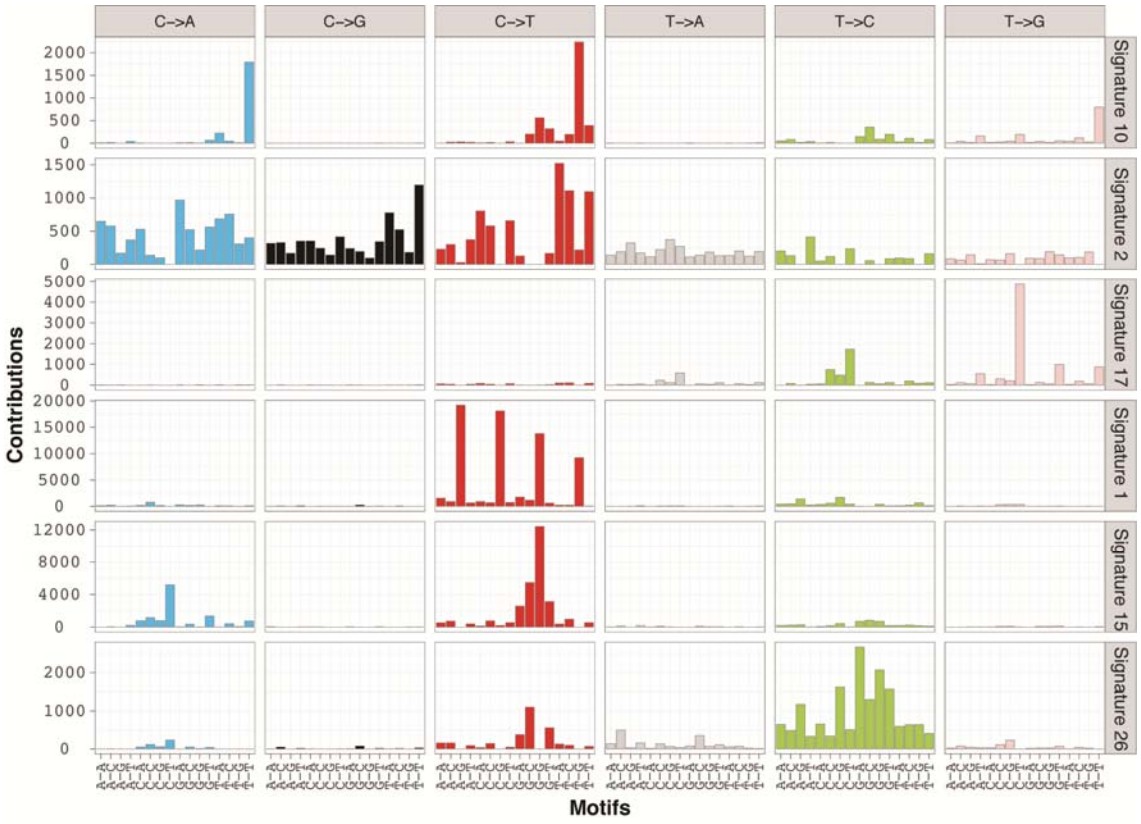
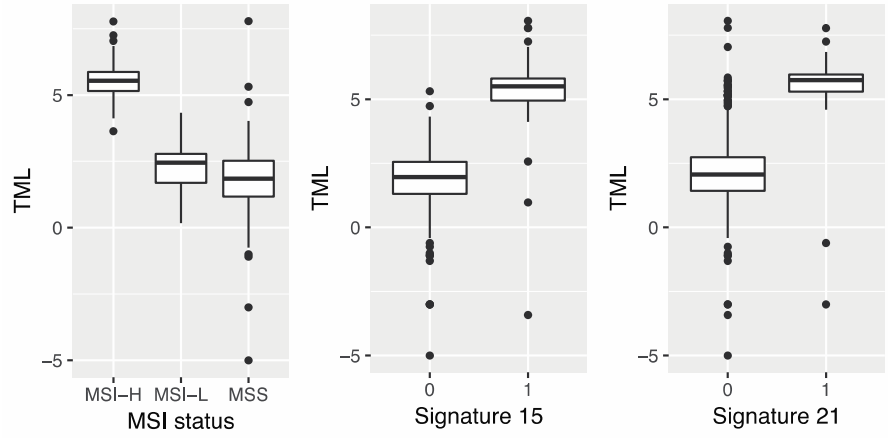
Supplementary Online Content

Li X, Pasche B, Zhang W, Chen K. Association of *MUC16* mutation with tumor mutation load and outcomes in patients with gastric cancer. *JAMA Oncol*. Published online August 9, 2018. doi:10.1001/jamaoncol.2018.2805

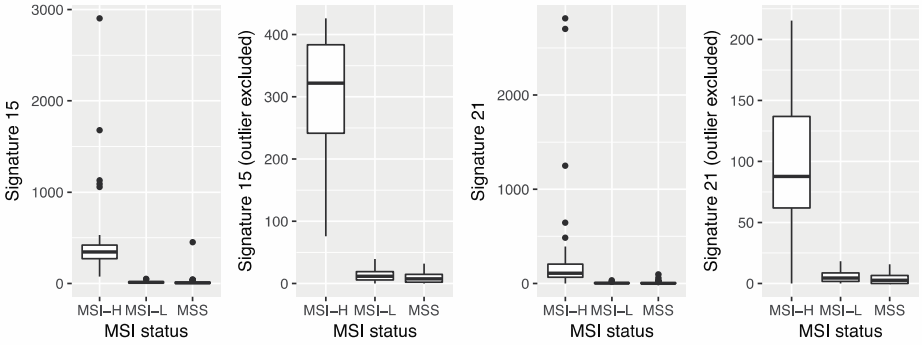
This supplementary material has been provided by the authors to give readers additional information about their work



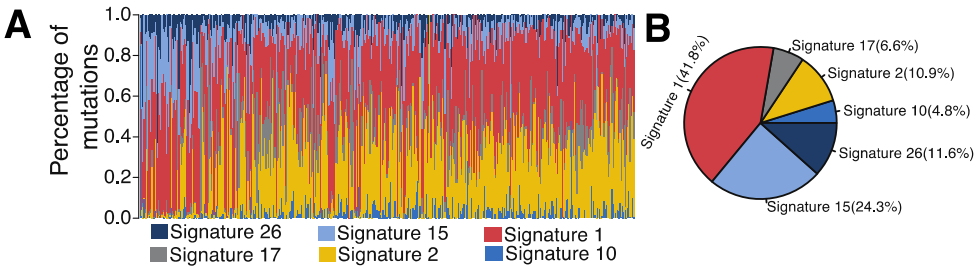
eFigure 1. Mutational signatures extracted from gastric cancer.



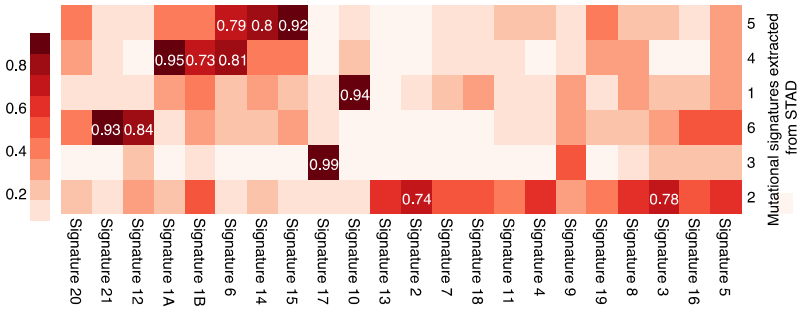
eFigure 2. Tumor mutation load stratified by MSI status, Signatures 15 and 21.



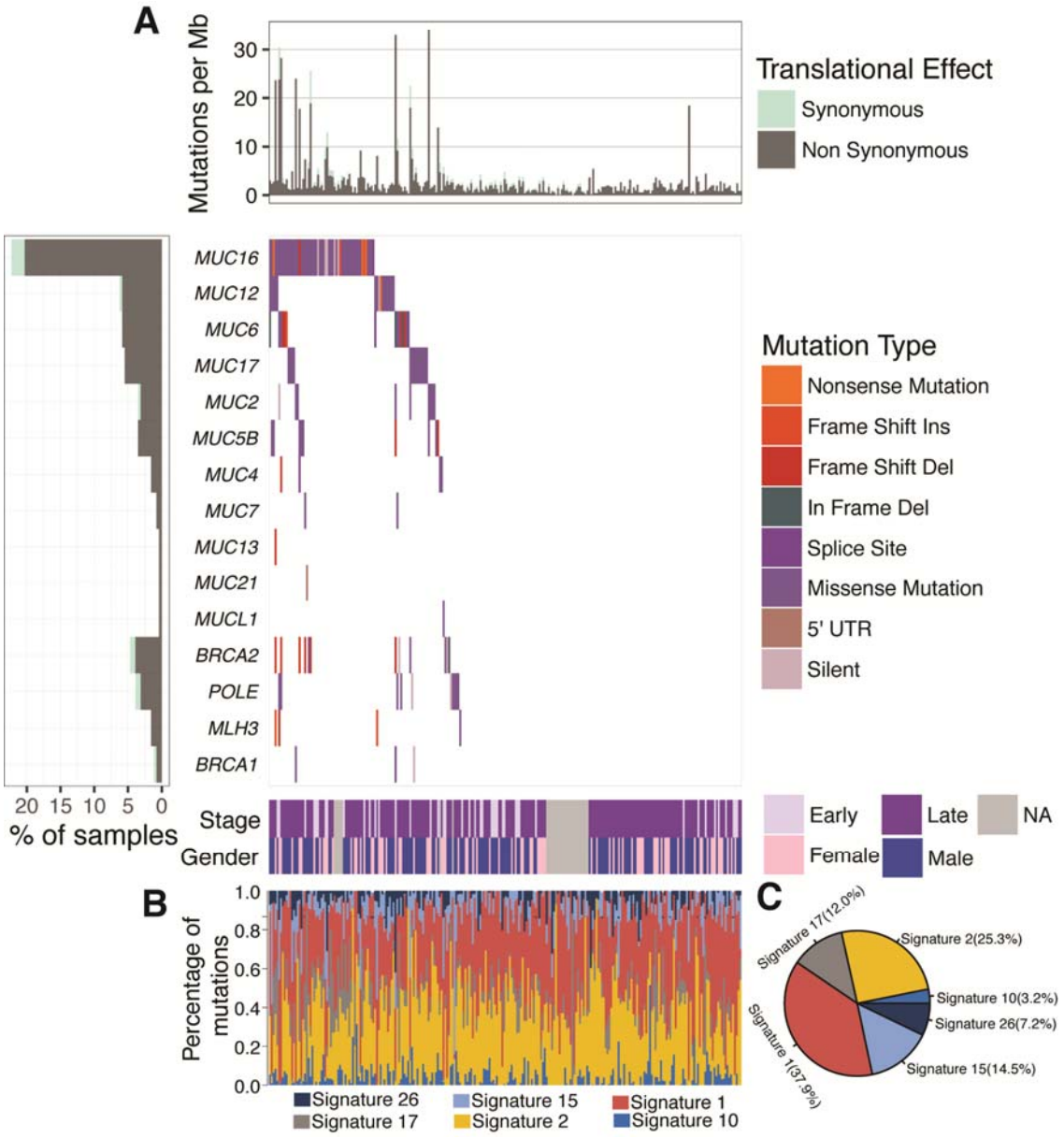
eFigure 3. Mutational activities of Signatures 15 and 21 stratified by MSI status.



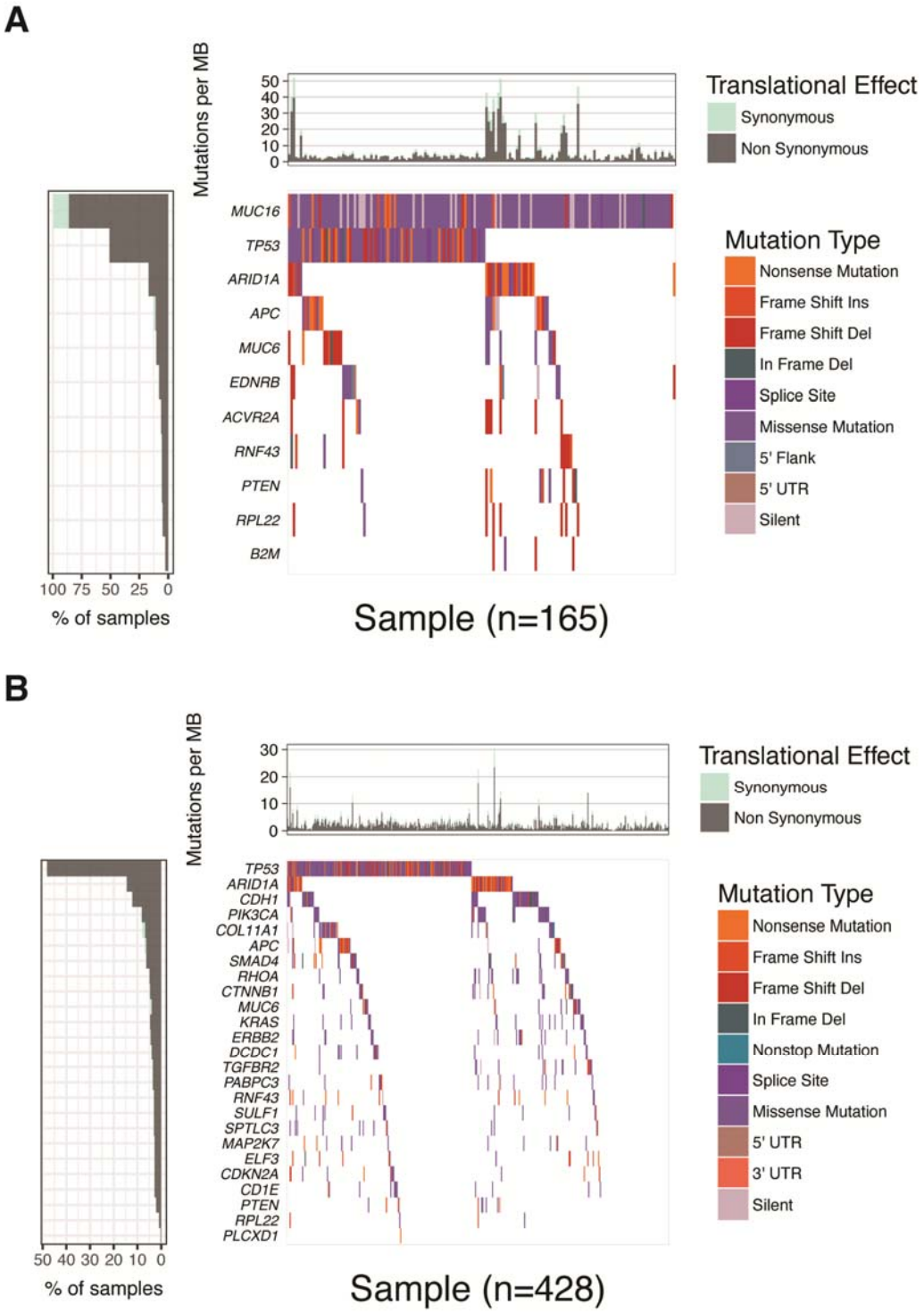
eFigure 4. Mutational activity of each signature in each TCGA sample (A) and total contribution of each signature (B).



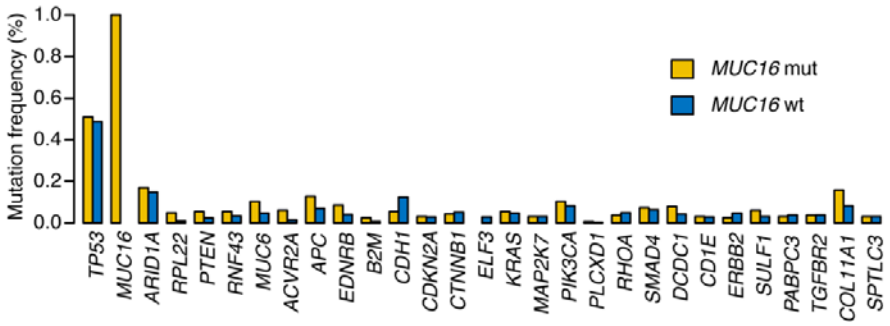
eFigure 5. Cosine similarity between six extracted mutational signatures versus 21 COSMIC signatures.



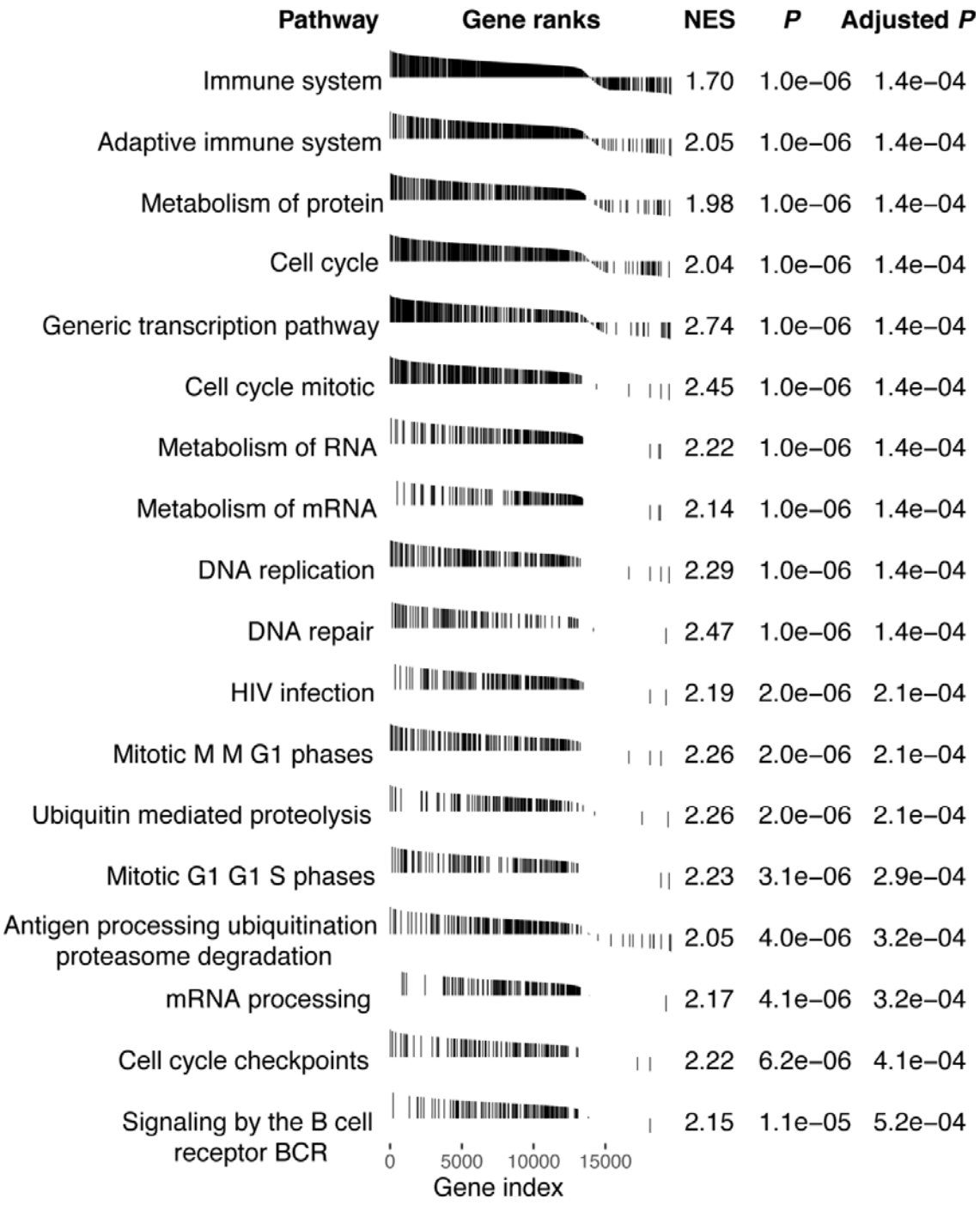
eFigure 6. Mutation patterns of mucin gene family in relation to genes associated with genomic instability (e.g. *BRCA1/2*, *POLE* and *MLH3*) in the Asian cohort. (**A**) The upper panel exhibited mutation loads and left panel gene mutation frequency. The middle panel depicted gene mutation patterns across each sequencing sample. The color code for different mutation types are shown on the right panel. The bottom panel showed tumor TNM stage and sex. (**B**) Mutational activities in each sample. (**C**) Proportion of each mutational signatures.



eFigure 7. SMG mutation landscape stratified by *MUC16* mutation.



eFigure 8. Mutation frequencies of SMGs stratified by *MUC16* mutation.



eFigure 9. Gene set enrichment plots of top up-regulated signaling pathways.

eTable 1. Differential gene expression analysis result (uploaded as excel file).

eTable. *MUC16* mutation frequency among human cancer types downloaded from cBioPortal (http://www.cbioportal.org).

STUDY_ABBREVIATION	STUDY_NAME	NUM_OF_CASES_ALTERED	PERCENT_CASES_ALTERED
SKCM UCLA (Cell 2016)	Whole-exome sequences (WES) of pretreatment melanoma tumors (UCLA, Cell 2016)	31	81.60%
DESM (Broad 2015)	Desmoplastic Melanoma (Broad Institute, Nat Genet 2015)	16	80%
Melanoma (Broad)	Skin Cutaneous Melanoma (Broad, Cell 2012)	88	72.70%
Melanoma (TCGA)	Skin Cutaneous Melanoma (TCGA, Provisional)	252	68.50%
Melanoma (Broad/DFCI)	Melanoma (Broad/Dana Farber, Nature 2012)	17	68%
Lung squ (TCGA)	Lung Squamous Cell Carcinoma (TCGA, Provisional)	80	44.70%
Small Cell Lung (UCOLOGNE)	Small Cell Lung Cancer (U Cologne, Nature 2015)	49	44.50%
Lung squ (TCGA pub)	Lung Squamous Cell Carcinoma (TCGA, Nature 2012)	76	42.70%
NSCLC (TCGA 2016)	Pan-Lung Cancer (TCGA, Nat Genet 2016)	467	40.80%
Lung adeno (TCGA)	Lung Adenocarcinoma (TCGA, Provisional)	92	40%
Lung adeno (TCGA pub)	Lung Adenocarcinoma (TCGA, Nature 2014)	91	39.60%
Lung adeno (Broad)	Lung Adenocarcinoma (Broad, Cell 2012)	72	39.60%
Stomach (TCGA pub)	Stomach Adenocarcinoma (TCGA, Nature 2014)	34	39.10%
Lung adeno (MSKCC)	Lung Adenocarcinoma (MSKCC 2015)	13	38.20%
Bladder	Bladder Urothelial	19	38%

(DFCI/MSKCC 2014)	Carcinoma (Dana Farber & MSKCC, Cancer Discov 2014)		
Stomach/Esophageal (TCGA)	TCGA data for Esophagus-Stomach Cancers (TCGA, Nature 2017)	95	35.80%
Stomach (TCGA)	Stomach Adenocarcinoma (TCGA, Provisional)	140	35.40%
Bladder (TCGA 2014)	Bladder Urothelial Carcinoma (TCGA, Nature 2014)	44	34.60%
Bladder (TCGA)	Bladder Urothelial Carcinoma (TCGA, Provisional)	44	33.80%
Esophagus (TCGA)	Esophageal Carcinoma (TCGA, Provisional)	54	29.20%
TSAM	Paired-exome sequencing of acral melanoma (TGEN, Genome Res 2017)	11	28.90%
Esophagus (Broad)	Esophageal Adenocarcinoma (Broad, Nat Genet 2013)	41	28.10%
Breast (BCCRC Xenograft)	Breast cancer patient xenografts (British Columbia, Nature 2014)	8	27.60%
ACC (TCGA)	Adrenocortical Carcinoma (TCGA, Provisional)	23	26.10%
Colorectal (DFCI 2016)	Colorectal Adenocarcinoma (DFCI, Cell Reports 2016)	149	24.10%
Stomach (Pfizer UHK)	Stomach Adenocarcinoma (Pfizer and UHK, Nat Genet 2014)	24	24%
Uterine (TCGA)	Uterine Corpus Endometrial Carcinoma (TCGA, Provisional)	59	23.80%
Prostate (SU2C)	Metastatic Prostate Cancer, SU2C/PCF Dream Team (Robinson et al., Cell 2015)	35	23.30%
Uterine (TCGA pub)	Uterine Corpus Endometrial Carcinoma (TCGA, Nature 2013)	56	23.30%
DLBC (TCGA)	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma (TCGA, Provisional)	11	22.90%

chRCC (TCGA)	Kidney Chromophobe (TCGA, Provisional)	15	22.70%
Head & neck (TCGA pub)	Head and Neck Squamous Cell Carcinoma (TCGA, Nature 2015)	62	22.20%
Breast (METABRIC)	Breast Cancer (METABRIC, Nature 2012 & Nat Commun 2016)	449	21.90%
NEPC (Trento/Cornell/Broad 2016)	Neuroendocrine Prostate Cancer (Trento/Cornell/Broad 2016)	23	21.50%
Pancreas (UTSW)	Pancreatic Cancer (UTSW, Nat Commun 2015)	23	21.10%
Head & neck (TCGA)	Head and Neck Squamous Cell Carcinoma (TCGA, Provisional)	106	20.70%
The MBC Project	The Metastatic Breast Cancer Project (Provisional, October 2017)	21	20.40%
MPNST (MSKCC)	Malignant Peripheral Nerve Sheath Tumor (MSKCC, Nat Genet 2014)	3	20%
Head & neck (Broad)	Head and Neck Squamous Cell Carcinoma (Broad, Science 2011)	14	18.90%
GBC (Shanghai)	Gallbladder Carcinoma (Shanghai, Nat Genet 2014)	6	18.80%
Colorectal (Genentech)	Colorectal Adenocarcinoma (Genentech, Nature 2012)	13	18.10%
Stomach (TMUCIH 2015)	Gastric Adenocarcinoma (TMUCIH, PNAS 2015)	14	17.90%
Colorectal (TCGA)	Colorectal Adenocarcinoma (TCGA, Provisional)	40	17.90%
Cervical (TCGA)	Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma (TCGA, Provisional)	34	17.80%
Liver (AMC)	Liver Hepatocellular Carcinoma (AMC, Hepatology 2014)	40	17.30%
Colorectal (TCGA pub)	Colorectal Adenocarcinoma (TCGA, Nature	36	17%

	2012)		
Prostate Organoids	Prostate Adenocarcinoma Organoids (MSKCC, Cell 2014)	2	16.70%
GBM (TCGA)	Glioblastoma Multiforme (TCGA, Provisional)	45	16.50%
Sarcoma (TCGA)	Sarcoma (TCGA, Provisional)	38	15%
Liver (TCGA)	Liver Hepatocellular Carcinoma (TCGA, Provisional)	55	14.70%
Prostate (FHCRC, 2016)	Prostate Adenocarcinoma (Fred Hutchinson CRC, Nat Med 2016)	20	14.70%
ESCC (UCLA 2014)	Esophageal Squamous Cell Carcinoma (UCLA, Nat Genet 2014)	20	14.60%
Ewing Sarcoma (Institut Curie)	Ewing Sarcoma (Institut Cuire, Cancer Discov 2014)	20	14.60%
Cholangiocarcinoma (TCGA)	Cholangiocarcinoma (TCGA, Provisional)	5	14.30%
ccRCC (U Tokyo)	Clear Cell Renal Cell Carcinoma (U Tokyo, Nat Genet 2013)	15	14.20%
ccRCC (IRC)	Multiregion Sequencing of Clear Cell Renal Cell Carcinoma (IRC, Nat Genet 2014)	11	14.10%
DLBCL (Broad 2012)	Diffuse Large B-Cell Lymphoma (Broad, PNAS 2012)	8	13.80%
Esophagus sq (ICGC)	Esophageal Squamous Cell Carcinoma (ICGC, Nature 2014)	12	13.60%
ucs (Johns Hopkins 2014)	Uterine Carcinosarcoma (Johns Hopkins University, Nat Commun 2014)	3	13.60%
Stomach (UTokyo)	Stomach Adenocarcinoma (U Tokyo, Nat Genet 2014)	4	13.30%
Ovarian (TCGA)	Ovarian Serous Cystadenocarcinoma (TCGA, Provisional)	42	13.30%
ccRCC (TCGA)	Kidney Renal Clear Cell Carcinoma (TCGA, Provisional)	59	13.20%
GBM (TCGA 2013)	Glioblastoma	37	13.20%

	(TCGA, Cell 2013)		
Glioma (UCSF)	Low-Grade Gliomas (UCSF, Science 2014).	8	13.10%
PAAC (JHU)	Acinar Cell Carcinoma of the Pancreas (Johns Hopkins, J Pathol 2014)	3	13%
Small Cell Lung (JHU)	Small Cell Lung Cancer (Johns Hopkins, Nat Genet 2012)	6	11.80%
HCC (Inserm, 2015)	Hepatocellular Carcinomas (Inserm, Nat Genet 2015)	28	11.50%
Ovarian (TCGA pub)	Ovarian Serous Cystadenocarcinoma (TCGA, Nature 2011)	35	11.10%
MBL (Sickkids 2016)	Medulloblastoma (Sickkids, Nature 2016)	5	10.90%
Prostate (Broad/Cornell 2013)	Prostate Adenocarcinoma (Broad/Cornell, Cell 2013)	6	10.70%
Uterine CS (TCGA)	Uterine Carcinosarcoma (TCGA, Provisional)	6	10.50%
Breast (TCGA 2015)	Breast Invasive Carcinoma (TCGA, Cell 2015)	52	10.30%
ACyC (MSKCC, 2013)	Adenoid Cystic Carcinoma (MSKCC, Nat Genet 2013)	6	10%
Breast (Sanger)	Breast Invasive Carcinoma (Sanger, Nature 2012)	10	10%
LGG-GBM (TCGA 2016)	Merged Cohort of LGG and GBM (TCGA, Cell 2016)	79	9.90%
Prostate (MICH)	Prostate Adenocarcinoma, Metastatic (Michigan, Nature 2012)	6	9.80%
AMPCA (BCM,2016)	Ampullary Carcinoma (Baylor College of Medicine, Cell Reports 2016)	15	9.40%
Breast (TCGA pub)	Breast Invasive Carcinoma (TCGA, Nature 2012)	43	8.90%
Glioma (TCGA)	Brain Lower Grade Glioma (TCGA, Provisional)	25	8.80%
Breast (TCGA)	Breast Invasive Carcinoma (TCGA,	85	8.80%

	Provisional)		
pRCC (TCGA)	Kidney Renal Papillary Cell Carcinoma (TCGA, Provisional)	24	8.50%
ccRCC (TCGA pub)	Kidney Renal Clear Cell Carcinoma (TCGA, Nature 2013)	35	8.40%
ACbC (MSKCC/Breast 2015)	Adenoid Cystic Carcinoma of the Breast (MSKCC, J Pathol. 2015)	1	8.30%
Pancreas (TCGA)	Pancreatic Adenocarcinoma (TCGA, Provisional)	12	8%
Prostate (TCGA)	Prostate Adenocarcinoma (TCGA, Provisional)	38	7.60%
MBL (Sickkids 2016)	Mutational profiles of metastatic breast cancer (France, 2016)	16	7.50%
Head & neck (MDA)	Oral Squamous Cell Carcinoma (MD Anderson, Cancer Discov 2013)	3	7.50%
MM (Broad)	Multiple Myeloma (Broad, Cancer Cell 2014)	13	6.30%
Uveal melanoma (TCGA)	Uveal Melanoma (TCGA, Provisional)	5	6.30%
Prostate (TCGA 2015)	Prostate Adenocarcinoma (TCGA, Cell 2015)	20	6%
Breast (Broad 2012)	Breast Invasive Carcinoma (Broad, Nature 2012)	6	5.80%
PCPG (TCGA)	Pheochromocytoma and Paraganglioma (TCGA, Provisional)	10	5.40%
NBL (Cologne 2015)	Neuroblastoma (Broad, Nat Genet 2013)	3	5.40%
Pancreas (QCMG 2016)	Pancreatic Adenocarcinoma (QCMG, Nature 2016)	20	5.20%
Pancreas (ICGC)	Pancreatic Adenocarcinoma (ICGC, Nature 2012)	5	5.10%
Cholangiocarcinoma (JHU)	Intrahepatic Cholangiocarcinoma (Johns Hopkins University, Nat Genet 2013)	2	5%
Thymoma(TCGA)	Thymoma (TCGA, Provisional)	6	4.90%
Mesothelioma	Mesothelioma	4	4.60%

(TCGA)	(TCGA, Provisional)		
Testicular germ cell (TCGA)	Testicular Germ Cell Cancer (TCGA, Provisional)	7	4.50%
ACRNET (Nature, 2017)	Whole-Genome Sequencing of Pancreatic Neuroendocrine Tumors (Nature, 2017)	4	4.10%
CLL(IUOPA 2015)	Chronic Lymphocytic Leukemia (IUOPA, Nature 2015)	20	4%
ACyC (MDA 2015)	Adenoid Cystic Carcinoma (MDA, Clin Cancer Res 2015)	4	3.90%
CLL (Broad 2013)	Chronic Lymphocytic Leukemia (Broad, Cell 2013)	6	3.80%
Prostate (Broad/Cornell 2012)	Prostate Adenocarcinoma (Broad/Cornell, Nat Genet 2012)	4	3.70%
nccRCC (Genentech 2014)	Renal Non-Clear Cell Carcinoma (Genentech, Nat Genet 2014)	5	3.40%
TET (NCI)	Thymic Epithelial Tumors (NCI, Nat Genet 2014)	1	3.10%
CCLE (Novartis/Broad 2012)	Cancer Cell Line Encyclopedia (Novartis/Broad, Nature 2012)	24	2.70%
Thyroid (TCGA)	Thyroid Carcinoma (TCGA, Provisional)	11	2.70%
MBL (PCGP)	Medulloblastoma (PCGP, Nature 2012)	1	2.70%
PRAD Hallmarks (CPCG-GENE, 2017)	Genomic Hallmarks of Prostate Adenocarcinoma (CPC-GENE, Nature 2017)	12	2.70%
Thyroid (TCGA pub)	Papillary Thyroid Carcinoma (TCGA, Cell 2014)	10	2.50%
ALL (St. Jude)	Hypodiploid Acute Lymphoid Leukemia (St Jude, Nat Genet 2013)	1	2.30%
AML (TCGA pub)	Acute Myeloid Leukemia (TCGA, NEJM 2013)	4	2.10%
AML (TCGA)	Acute Myeloid Leukemia (TCGA, Provisional)	4	2.10%
NPC (Singapore)	Nasopharyngeal	1	1.80%

	Carcinoma (Singapore, Nat Genet 2014)		
Breast (BCCRC 2012)	Breast Invasive Carcinoma (British Columbia, Nature 2012)	1	1.50%
chRCC (TCGA)	Kidney Chromophobe (TCGA, Cancer Cell 2014)	1	1.50%
Sarcoma (MSKCC)	Sarcoma (MSKCC/Broad, Nat Genet 2010)	3	1.40%
NBL (AMC)	Neuroblastoma (AMC Amsterdam, Nature 2012)	1	1.10%
Ewing Sarcoma (DFCI)	Pediatric Ewing Sarcoma (DFCI, Cancer Discov 2014)	1	1%
MBL (ICGC)	Medulloblastoma (ICGC, Nature 2012)	1	0.80%