

Supplementary Table 1. Missense mutated residues in each cancer gene grouped according to structural location (core or interface) in the encoded protein. Some proteins have co-crystallization structures for multiple distinct interaction interfaces. Since our model does not distinguish between residues at the same structural location, a representative position was selected arbitrarily to represent each group.

Gene	Location	Representative Residue	Other Residues at Same Location
PPP2R1A	core	220	298
PPP2R1A	interface	257	256 179 217
PPP2R1A	interface	183	
PPP2R1A	interface	41	221
PPP2R1A	interface	219	
PPP2R1A	interface	258	
RB1	interface	857	
RB1	core	550	703 488 449 688 654 755
RB1	interface	876	
RB1	interface	873	
SMAD4	core	504	437 499 324 386
SMAD4	interface	337	355 357 356 353 361 382
MSH2	core	356	217
MSH2	interface	83	758
MSH2	interface	543	
EGFR	core	843	85 742 351 839 789 148 101
EGFR	interface	934	937
EGFR	interface	38	
EGFR	interface	377	373 114 441
EGFR	interface	149	
EGFR	interface	652	
MEN1	core	242	442
MEN1	interface	337	335 159 88
MEN1	interface	96	
SMAD2	core	335	
SMAD2	interface	398	
SMAD2	interface	450	446
CTNNB1	interface	582	623
CTNNB1	core	421	517
CTNNB1	interface	170	166 162
CTNNB1	interface	35	34 31 32
CTNNB1	interface	390	429 426 515
CTNNB1	interface	619	
CTNNB1	interface	415	
CTNNB1	interface	383	
CTNNB1	interface	339	342
CTNNB1	interface	257	425 292
CTNNB1	interface	387	
VHL	interface	169	
VHL	interface	109	105 107 88 112 110 115 78
VHL	interface	184	165 162 82 153 158
VHL	interface	79	
VHL	core	151	74
B2M	core	100	47
B2M	interface	51	76 30
B2M	interface	83	
B2M	interface	54	
CDKN2A	core	52	97 94 20 118 114 81 83 86
CDKN2A	interface	53	74 110 44 42 84 87 88
CBL	core	98	186 877
CBL	interface	322	
CBL	interface	418	417 384
ABL1	core	1060	365 348 111 472
ABL1	interface	72	

CASP8	core	236	325 241
CASP8	interface	463	441 444
FLT3	interface	311	
FLT3	core	814	939
DAXX	interface	371	
DAXX	interface	738	
DAXX	interface	127	87
DAXX	interface	280	
DAXX	interface	315	263 250
AXIN1	core	149	
AXIN1	interface	385	
AXIN1	interface	146	139
PIK3CA	core	359	
PIK3CA	interface	545	546 542 453 454 365 345 79 11 449 1029 357
CSF1R	core	613	
CSF1R	interface	192	250 144
KDM6A	interface	1087	1191
KDM6A	core	1119	
PIK3R1	interface	669	
PIK3R1	core	646	129
PIK3R1	interface	560	564 567 568 464 379 376 574 572
CDH1	core	212	260 316
CDH1	interface	159	
HRAS	interface	13	61
HRAS	interface	59	
HRAS	interface	12	
FBXW7	core	396	398 476 301 558 516 517 437
FBXW7	interface	280	
BRCA1	core	1722	1665
BRCA1	interface	96	
BRCA1	interface	1813	1699
DNMT3A	core	737	
DNMT3A	interface	729	771 736
DNMT3A	interface	48	
H3F3A	interface	50	130
H3F3A	interface	3	9
H3F3A	interface	56	99
SPOP	core	277	
SPOP	interface	102	87 117 131 133
SPOP	interface	281	
MSH6	core	781	175 480 457 868
MSH6	interface	1299	
BCOR	interface	1649	
BCOR	interface	509	
ATRX	core	220	
ATRX	interface	263	
FGFR2	core	690	634 632 617 611 563 253
FGFR2	interface	165	254
FGFR2	interface	311	
FGFR2	interface	252	251
FGFR2	interface	163	
FGFR3	core	677	
FGFR3	interface	248	
MLL3	core	359	385
MLL3	interface	4714	
TP53	core	141	255 278 279 135 134 266 127
TP53	interface	178	179 280 241
TP53	interface	171	177 244
TP53	interface	181	248 243 247 249
TP53	interface	11	
TP53	interface	27	

ERBB2	core	797	466	87
ERBB2	interface	663		
PTPN11	core	308	472	136
PTPN11	interface	181	55	52
NOTCH1	core	2064	1936	2101
NOTCH1	interface	1937	2036	
NOTCH1	interface	2038		
KIT	core	292	432	
KIT	interface	72	261	
MET	core	1251	63	225
MET	interface	221	263	
RUNX1	core	91		
RUNX1	interface	114	157	108
APC	core	568		
APC	interface	640		
APC	interface	546		
APC	interface	2046		
APC	interface	1527		
APC	interface	593	550	
APC	interface	1583		
CREBBP	core	1782		
CREBBP	interface	1122		

Supplementary Table2. A summary of the spatial distribution (core & interface) of missense mutations hosted on 125 known cancer genes. Distinct Muts describes the number of mutated residue groups that affect different structural locations, PPIs details the number of high confidence interactions for each gene, and 3D PPIs describes the number of structurally resolved complexes in the PDB.

Gene	PPIs	3D PPIs	Core	Interface	Distinct Muts	Gene	PPIs	3D PPIs	Core	Interface	Distinct Muts
ABL1	293	1	5	1	2	KDM5C	12	0	0	0	0
ACVR1B	19	0	0	0	0	KDM6A	26	1	1	2	2
AKT1	188	1	0	1	1	KIT	60	2	2	2	2
ALK	50	1	1	0	1	KLF4	15	0	0	0	0
APC	132	6	1	7	7	KRAS	24	0	1	0	1
AR	49	4	0	0	0	MAP2K1	46	0	0	0	0
ARID1A	27	0	0	0	0	MAP3K1	37	0	0	0	0
ARID1B	2	0	0	0	0	MED12	33	0	0	0	0
ARID2	14	0	0	0	0	MEN1	50	3	2	5	3
ASXL1	14	0	0	0	0	MET	54	3	4	2	2
ATM	92	0	0	0	0	MLH1	29	0	1	0	1
ATRX	25	2	1	1	2	MLL2	30	1	0	0	0
AXIN1	69	2	1	3	3	MLL3	18	1	2	1	2
B2M	19	15	2	5	4	MPL	8	0	0	0	0
BAP1	44	0	0	0	0	MSH2	44	2	2	3	3
BCL2	101	0	0	0	0	MSH6	30	1	5	1	2
BCOR	22	2	0	2	2	MYD88	36	0	1	0	1
BRAF	48	0	5	0	1	NCOR1	131	4	0	0	0
BRCA1	228	5	2	3	3	NF1	12	0	1	0	1
BRCA2	51	2	0	1	1	NF2	37	0	1	0	1
CARD11	16	0	0	0	0	NFE2L2	34	1	0	4	1
CASP8	112	1	3	3	2	NOTCH1	66	2	4	2	3
CBL	170	8	3	4	3	NOTCH2	19	0	1	0	1
CDC73	58	0	0	0	0	NPM1	107	0	0	0	0
CDH1	103	2	3	1	2	NRAS	23	0	0	0	0
CDKN2A	103	1	9	9	2	PAX5	15	0	0	0	0
CEBPA	12	0	0	0	0	PBRM1	22	0	5	0	1
CIC	13	1	0	0	0	PDGFRA	27	0	0	0	0
CREBBP	306	7	1	1	2	PHF6	1	0	0	0	0
CRLF2	0	0	0	0	0	PIK3CA	50	1	1	12	2
CSF1R	20	1	1	3	2	PIK3R1	253	3	2	10	3
CTNNB1	242	6	2	22	11	PPP2R1A	78	4	2	9	6
CYLD	30	0	0	0	0	PRDM1	13	0	0	0	0
DAXX	86	4	0	8	5	PTCH1	6	0	0	0	0
DNMT1	64	0	6	0	1	PTEN	47	1	18	0	1
DNMT3A	35	2	1	4	3	PTPN11	132	1	3	4	2
EGFR	237	7	8	9	6	RB1	194	5	7	3	4
EP300	352	4	0	0	0	RET	42	0	0	0	0
ERBB2	150	4	3	1	2	RNF43	17	2	0	4	1
EZH2	89	0	0	0	0	RUNX1	61	1	1	3	2
FAM123B	5	0	0	0	0	SETD2	7	0	0	0	0
FBXW7	40	1	8	1	2	SETBP1	2	0	0	0	0
FGFR2	34	4	7	7	5	SF3B1	39	2	0	0	0
FGFR3	47	1	1	1	2	SMAD2	233	3	1	3	3
FLT3	17	1	2	1	2	SMAD4	180	3	5	7	2
FOXL2	4	0	0	0	0	SMARCA4	18	0	0	0	0
FUBP1	14	1	0	0	0	SMARCB1	74	0	0	0	0
GATA1	51	0	0	0	0	SMO	3	0	2	0	1
GATA2	28	0	0	0	0	SOCS1	40	0	0	0	0
GATA3	19	0	0	0	0	SOX9	16	0	0	0	0
GNA11	17	0	0	0	0	SPOP	18	2	1	6	3
GNAQ	42	0	0	0	0	SRSF2	4	0	0	0	0
GNAS	31	0	0	0	0	STAG2	11	0	0	0	0
H3F3A	11	9	0	6	3	STK11	40	2	3	0	1
HIST1H3B	0	0	0	0	0	TET2	2	0	0	0	0

HNF1A	3	0	0	0	0	TNFAIP3	50	1	1	0	1
HRAS	86	6	0	4	3	TRAF7	8	0	0	0	0
IDH1	3	0	2	0	1	TP53	565	13	8	14	6
IDH2	1	0	3	0	1	TSC1	46	0	0	0	0
JAK1	74	0	2	0	1	TSHR	21	0	0	0	0
JAK2	107	0	1	0	1	U2AF1	29	1	2	0	1
JAK3	43	0	2	0	1	VHL	107	3	2	16	5
						WT1	5	0	0	0	0

Supplementary Table 3. Tissue specificity of cancer gene mutations at core and interface residues. Core or interface regions are identified by the selected representative residue (see Supplementary Table 1). Each core or interface region was assessed for tissue specificity of mutations occurring using a Fisher's Exact test. This table lists results for each of 137 core and interface sites tested. 21% of sites showed a deviation from expected mutation count for one or more cancer types.

Gene	Representative Residue	Cancer Tissue
PPP2R1A	257	Uterine Carcinosarcoma
SMAD4	337	Colon adenocarcinoma
MEN1	337	Brain Lower Grade Glioma, Pancreatic adenocarcinoma
MEN1	242	Lung squamous cell carcinoma
SMAD2	450	Bladder Urothelial Carcinoma
CTNNB1	619	Rectum adenocarcinoma
CTNNB1	35	Adrenocortical carcinoma, Uterine Corpus Endometrial Carcinoma, Prostate adenocarcinoma
CTNNB1	421	Rectum adenocarcinoma
CTNNB1	339	Prostate adenocarcinoma
CTNNB1	257	Cervical squamous cell carcinoma and endocervical adenocarcinoma
B2M	51	Rectum adenocarcinoma
DNMT3A	729	Acute Myeloid Leukemia
CASP8	236	Cervical squamous cell carcinoma and endocervical adenocarcinoma
PIK3CA	545	Breast invasive carcinoma
PIK3R1	560	Glioblastoma multiforme, Brain Lower Grade Glioma
PIK3R1	646	Glioblastoma multiforme
HRAS	13	Thyroid carcinoma
FBXW7	396	Uterine Carcinosarcoma
CDKN2A	53	Head and Neck squamous cell carcinoma
CDKN2A	52	Head and Neck squamous cell carcinoma
H3F3A	3	Cervical squamous cell carcinoma and endocervical adenocarcinoma
SPOP	102	Prostate adenocarcinoma
FGFR2	252	Uterine Corpus Endometrial Carcinoma, Uterine Carcinosarcoma
FGFR3	248	Bladder Urothelial Carcinoma
		Glioblastoma multiforme, UC,S Head and Neck
TP53	181	squamous cell carcinoma, Brain Lower Grade Glioma, Ovarian serous cystadenocarcinoma
TP53	141	Brain Lower Grade Glioma, Breast invasive carcinoma , Ovarian serous cystadenocarcinoma
TP53	178	Uterine Carcinosarcoma, Brain Lower Grade Glioma, Ovarian serous cystadenocarcinoma
TP53	171	Ovarian serous cystadenocarcinoma
RUNX1	114	Acute Myeloid Leukemia

Supplementary Table 4. Count of the altered sub-networks and number of proteins in the altered sub-networks recovered for each representative mutation.

Gene	Residues (# of sub-networks, # of proteins)
ABL1	res1060(73,706); res72(77, 809)
APC	res1527(55,792); res1583(37,668); res2046(54,788); res546(42,877); res568(43,726); res593(51,806); res640(53,787)
ATRX	res220(49,544); res263(55,619)
AXIN1	res146(60,764); res149(46,574); res385(58,770)
B2M	res100(35,601); res51(38,669); res54(38,686); res83(60,1037)
BCOR	res1649(77,529); res509(49,662)
BRCA1	res1722(57,565); res1813(54,625); res96(69,735)
CASP8	res236(42,674); res463(50,770)
CBL	res322(71,819); res418(78,753); res98(47,638)
CDH1	res159(41,657); res212(41,653)
CDKN2A	res52(62,576); res53(75,715)
CREBBP	res1122(62,712); res1782(42,647)
CSF1R	res192(77,508); res613(60,541)
	res170(46,746); res257(55,828); res339(46,700); res35(62,808);
CTNNB1	res383(67,804); res387(53,818); res390(60,805); res415(51,696); res421(43,643); res582(53,685); res619(56,752)
DAXX	res127(56,849); res280(69,662); res315(64,587); res371(53,632); res738(102,580)
DNMT3A	res48(68,610); res729(66,634); res737(72,534)
EGFR	res149(51,825); res377(63,766); res38(56,770); res652(55,862); res843(56,724); res934(64,771)
ERBB2	res663(66,846); res797(40,692)
FBXW7	res280(59,798); res396(68,575)
FGFR2	res163(60,711); res165(46,572); res252(44,619); res311(46,575); res690(42,541)
FGFR3	res248(72,637); res677(49,585)
FLT3	res311(74,496); res814(71,445)
H3F3A	res3(43,659); res50(66,661); res56(76,695)
HRAS	res12(39,791); res61(38,795); res59(28,754)
KDM6A	res1087(59,630); res1119(46,544)
KIT	res292(48,699); res72(38,628)
MEN1	res242(66,547); res337(86,603); res96(69,606);
MET	res1251(45,618); res221(40,714)
MLL3	res359(64,566); res4714(73,669)
MSH2	res356(50,528); res543(59,536); res83(58,577)
MSH6	res1299(79,626); res781(67,455)
NOTCH1	res1937(48,648); res2038(54,639); res2064(57,593)
PIK3CA9	res359(46,575); res545(83,712)
PIK3R1	res560(70,797); res646(71,695); res669(84,830)
PPP2R1A	res183(40,747); res219(45,695); res220(40,660); res257(40,739); res258(47,737); res41(40,713)
PTPN11	res181(46,924); res308(32,720)
RB1	res550(63,658); res857(69,768); res873(76,740); res876(80,748)
RUNX1	res114(40,611); res91(32,575)
SMAD2	res335(63,625); res398(63,857); res450(73,838)
SMAD4	res337(89,843); res504(54,693)
SPOP	res102(34,685); res281(32,723); res277(21,656)
TP53	res11(77,591); res141(59,538); res171(72,672); res178(69,586); res181(72,627); res27(89,705)
VHL	res109(40,742); res151(38,647); res169(44,876); res184(36,741); res79(36,775)

Supplementary Table 5. Validation of functional predictions for mutated residues at distinct locations on the same gene. Via our structural analysis we mapped mutated residues to structural features including the core and different interfaces for a given gene. Structural locations were selected for analysis with our pipeline based on observed missense mutations in the TCGA cohort. The observed mutated residue is reported in the “Residue(s) Mutated in TCGA” column. Residues that were evaluated in unrelated works but that occur in the same structural location (core or interface) as the observed TCGA mutated residue are listed in the “Tested Residues at the Same Structural Location” column. In this work, we assume that all residues within a common structural feature most likely have a similar functional consequence, thus we expect that annotations for other mutated residues within the same protein core, or at the same interface will have the same functional consequences. We list the subset of functional annotations that were specific to the structural location and that coincided with findings of the unrelated works in the “Functional Annotations Specific to Location” column, and the reported consequences found via literature search in the “Validation” column.

Gene	Tested Residue(s) at the Same Structural Location	Residue(s) Mutated in TCGA	Structural Location	Functional Annotations Specific to Location	Validation
APC	640	640	KHDRBS1 interaction	GO:0006376~mRNA splice site selection GO:0000245~spliceosome assembly ASF/SF2 in the effected protein set	R640G causes exon 14 skipping by disruption of ASF/SF2 binding. ¹ Observed in familial adenomatous polyposis (FAP) ¹
APC	1495	1527	CTNNB1 interaction	GO:0019226~transmission of nerve impulse GO:0048168~regulation of neuronal synaptic plasticity GO:0001505~regulation of neurotransmitter levels GO:0051402~neuron apoptosis GO:0006836~neurotransmitter transport GO:0007411~axon guidance GO:0007413~axonal fasciculation GO:0007268~synaptic transmission GO:0045665~negative regulation of neuron differentiation	1495 mutation is observed in Medulloblastomas ²
ATRX	220	220	Core Mutation	GO:0051567~histone H3-K9 methylation	H3 tails bearing trimethylated Lys9 are required for ATRX localization to pericentric heterochromatin. ³

ATRX	218	263	H3F3A and HIST1H3A interactions	GO:0034983~peptidyl-lysine deacetylation GO:0043984~histone H4-K16 acetylation GO:0043982~histone H4-K8 acetylation GO:0043967~histone H4 acetylation GO:0043983~histone H4-K12 acetylation GO:0043981~histone H4-K5 acetylation	ATRX ADD domain and HP1 are needed for the localization of ATRX protein to heterochromatin.
					The E218A mutation impairs interaction with histone H3 peptides unmethylated at 'Lys-5' (H3K4me0) but does not reduce the stability of the ADD domain. It does reduce pericentromeric localization.
					The Acetylation of Lys 4 in H3 histones regulates the interplay between HP1 and ATRX during localization. ⁴
BRCA1	1700, 1699	1813, 1699	BRIP1 interaction	GO:0000731~DNA synthesis during DNA repair GO:0045005~maintenance of fidelity during DNA-dependent DNA replication GO:0000076~DNA replication checkpoint GO:0048478~replication fork protection	The BRCA1–BRIP1–TOPBP1 complex is associated with DNA repair during replication. This complex is necessary for the S-phase checkpoint in response to stalled or collapsed replication forks. ⁵
BRCA1	22,10	96	BARD1 interaction	GO:0006978~DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator	The BRCA1–BARD1 complex is involved in the activation of G1/S, S-phase and G2/M checkpoints. BRCA1–BARD1 depletion compromises the induction of p21 and activation of the G1/S checkpoint in response to ionizing radiation. ⁶
CBL	420	418, 417, 384	UBE2D2 interaction	GO:0042787~protein ubiquitination during ubiquitin-dependent protein catabolic process GO:0043161~proteasomal ubiquitin-dependent protein catabolic process GO:0000209~protein polyubiquitination GO:0031145~anaphase-promoting complex-dependent proteasomal ubiquitin-dependent protein catabolic process GO:0051439~regulation of ubiquitin-protein ligase activity during mitotic cell cycle GO:0051438~regulation of ubiquitin-protein ligase activity GO:0051865~protein autoubiquitination GO:0051437~positive regulation of ubiquitin-protein ligase activity during mitotic cell cycle GO:0051443~positive regulation of ubiquitin-protein ligase activity GO:0051444~negative regulation of ubiquitin-protein ligase activity GO:0032434~regulation of proteasomal ubiquitin-dependent protein catabolic process GO:0016574~histone ubiquitination GO:0031398~positive regulation of protein ubiquitination	R420 is a key site for ubiquitination and degradation of RTKs and loss of function events are frequently observed in myeloid malignancies. ⁷

				GO:0031396~regulation of protein ubiquitination GO:0051436~negative regulation of ubiquitin-protein ligase activity during mitotic cell cycle	
CBL	298	322	EGFR interaction	GO:0050868~negative regulation of T cell activation GO:0002758~innate immune response-activating signal transduction GO:0002218~activation of innate immune response GO:0031347~regulation of defense response NFAM1 (NFAT activation molecule 1) present in the protein set	The G298E mutation abolishes NFAT activation. ⁸

Supplementary Table 6. The list of GO annotations for the protein sets affected by H-RAS 12 perturbation.

HRAS G12 provoked GO functions	
Cytokine Production	positive regulation of interleukin-12 biosynthetic process negative regulation of interleukin-12 production negative regulation of cytokine production cytokinesis <u>regulation of cytokine production during immune response</u>
GTPase activity	activation of Ras GTPase activity positive regulation of Rac GTPase activity regulation of Ras GTPase activity activation of Rho GTPase activity regulation of Rho GTPase activity positive regulation of Rho GTPase activity <u>negative regulation of small GTPase mediated signal transduction</u>
Endothelial cells	regulation of endothelial cell proliferation endothelial cell differentiation <u>negative regulation of endothelial cell proliferation</u>
Blood	vasculogenesis positive regulation of blood coagulation vascular process in circulatory system
Proliferation	regulation of mesenchymal cell proliferation positive regulation of smooth muscle cell proliferation positive regulation of mesenchymal cell proliferation
Apoptosis	positive regulation of cell killing positive regulation of anti-apoptosis induction of apoptosis by oxidative stress induction of apoptosis by intracellular signals <u>regulation of cell killing</u>
Response to Stimulus	response to nutrient response to hypoxia response to hydroperoxide response to lipid response to ethanol acute-phase response learning or memory learning response to oxygen levels <u>response to protein stimulus</u>
Sexual Reproduction	oogenesis spermatid differentiation ovulation cycle process gamete generation ovulation cycle sperm motility organelle fission sexual reproduction female gamete generation oocyte differentiation
Cell Cycle	cell cycle phase regulation of mitosis negative regulation of mitotic cell cycle <u>regulation of mitotic cell cycle</u>

	M phase of mitotic cell cycle interphase of mitotic cell cycle interphase nuclear division mitosis
Cell Growth	regulation of epidermal growth factor receptor activity positive regulation of cell growth regulation of developmental growth response to growth hormone stimulus transforming growth factor beta receptor signaling pathway regulation of growth regulation of cell growth growth hormone receptor signaling pathway positive regulation of developmental growth <u>positive regulation of epidermal growth factor receptor activity</u>
Regulatory Processes	regulation of behavior regulation of protein maturation by peptide bond cleavage negative regulation of cell-matrix adhesion regulation of isotype switching positive regulation of isotype switching regulation of glycoprotein biosynthetic process regulation of focal adhesion formation regulation of metabolic process regulation of smooth muscle cell proliferation regulation of microtubule-based process regulation of receptor-mediated endocytosis regulation of microtubule-based movement regulation of protein kinase B signaling cascade regulation of nuclear division regulation of cilium beat frequency involved in ciliary motility positive regulation of macromolecule biosynthetic process regulation of protein processing positive regulation of cell-substrate adhesion positive regulation of behavior positive regulation of nitric-oxide synthase 2 biosynthetic process regulation of vasoconstriction positive regulation of cellular biosynthetic process regulation of cell cycle process regulation of nitric-oxide synthase 2 biosynthetic process regulation of interferon-alpha production positive regulation of tyrosine phosphorylation of STAT protein <u>positive regulation of DNA recombination</u>
Signaling	inactivation of MAPK activity positive regulation of NF-kappaB import into nucleus positive regulation of JAK-STAT cascade JAK-STAT cascade transmembrane receptor protein serine/threonine kinase signaling pathway positive regulation of protein kinase B signaling cascade regulation of receptor activity negative regulation of Ras protein signal transduction
Component Assembly	actin filament bundle formation sensory cilium assembly membrane raft formation negative regulation of actin filament bundle formation

Mitochondrion Localization	mitochondrion localization, microtubule-mediated mitochondrion transport along microtubule establishment of mitochondrion localization
Homeostasis and Transport	cellular homeostasis cation homeostasis ion homeostasis calcium ion homeostasis cellular metal ion homeostasis cellular di-, tri-valent inorganic cation homeostasis monovalent inorganic cation homeostasis metal ion homeostasis cellular ion homeostasis cellular cation homeostasis calcium ion transport into cytosol cytosolic calcium ion transport regulation of protein import into nucleus regulation of intracellular transport regulation of intracellular protein transport regulation of nucleocytoplasmic transport cytosolic calcium ion homeostasis cellular chemical homeostasis surfactant homeostasis phagocytosis, engulfment regulation of cilium movement involved in ciliary motility chemical homeostasis within a tissue cellular calcium ion homeostasis di-, tri-valent inorganic cation homeostasis
Cell Migration	cell chemotaxis neutrophil chemotaxis regulation of positive chemotaxis positive regulation of positive chemotaxis regulation of chemotaxis positive regulation of chemotaxis regulation of smooth muscle cell migration
Immune System	regulation of T-helper 2 type immune response negative regulation of leukocyte activation negative regulation of lymphocyte activation negative regulation of alpha-beta T cell activation regulation of T cell receptor signaling pathway positive regulation of T cell mediated immunity regulation of alpha-beta T cell activation negative regulation of T cell activation positive regulation of humoral immune response mediated by circulating immunoglobulin immune effector process regulation of humoral immune response mediated by circulating immunoglobulin positive regulation of immunoglobulin mediated immune response regulation of immunoglobulin production acute inflammatory response positive regulation of adaptive immune response positive regulation of humoral immune response positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains leukocyte mediated immunity regulation of immunoglobulin mediated immune response

	positive regulation of B cell mediated immunity
	regulation of B cell mediated immunity
Development	regulation of cell development
	striated muscle tissue development
	skeletal muscle tissue development
	lung alveolus development
	neural tube development
	limbic system development
	olfactory lobe development
	oocyte development
	embryonic development
	epithelium development
	skeletal muscle organ development
	branching morphogenesis of a tube
	myeloid cell differentiation
	myeloid leukocyte differentiation
	negative regulation of T-helper cell differentiation
	alpha-beta T cell differentiation
	positive regulation of T cell differentiation
	regulation of T-helper 2 cell differentiation
	negative regulation of cell development
	positive regulation of alpha-beta T cell differentiation
	regulation of alpha-beta T cell differentiation
	regulation of T-helper cell differentiation
	regulation of T cell differentiation
	negative regulation of CD4-positive, alpha beta T cell differentiation
	negative regulation of alpha-beta T cell differentiation
	positive regulation of muscle cell differentiation
	mammary gland morphogenesis
	mammary gland involution
	tissue morphogenesis
	morphogenesis of a branching structure
	brain morphogenesis
	cell maturation
	neuromuscular junction development
	convergent extension
	convergent extension involved in gastrulation
	heart development
	subpallium development
Metabolic Process	triglyceride metabolic process
	regulation of cellular metabolic process
	negative regulation of macromolecule metabolic process
	organic ether metabolic process
	receptor metabolic process
	acylglycerol metabolic process
	regulation of cAMP metabolic process
	regulation of cAMP biosynthetic process
Neurological System	neutral lipid metabolic process
	glycerol ether metabolic process
	axon ensheathment
	negative regulation of axonogenesis
	response to axon injury
	retinal ganglion cell axon guidance
	regulation of axon extension

regulation of membrane potential
positive regulation of axon extension
regulation of neuron differentiation
ensheathment of neurons
central nervous system neuron differentiation
negative regulation of neurogenesis

Other establishment or maintenance of epithelial cell apical/basal polarity

Supplementary Table7. The list of protein sets (in Entrez Gene Ids) affected by H-RAS G12 perturbation.

HRAS G12 mutation disturbed protein sets	
	65095 134728 55614 4301 6721 83937 10454 10513 9777 27289 3556 3554 7305 4145 1943 11261 1946 4140 1944 1945 55763
	54915 3993 817 165918 11186 1621 123920 85406 7128 7126 7049 10209 5267 4733 2318 81539 1063 5269 55227 154796
	56241 5911 5910 5912 145957 596 1122 4656 6383 493856 2549 91754 114609 6478 81622 2260 200894 10332 4214 115207
	115209 445 7866 1949 51507 23541 23095 5774 5777 6271 85021 2045 2041 163033 2049 9411 644 9551 1937 434 2160
	54496 10411 10146 11266 11346 11340 1901 8195 7265 100820829 7266 266747 847 23433 6610 10567 2633 10241 9021
	57142 10841 5229 6753 4076 84941 5818 5819 5790 8835 22882 8831 29889 2912 2065 4619 238 4615 23263 2342 79009
	5457 5924 5921 5923 157310 27342 9118 5788 613 4254 54106 3703 4916 4915 91662 29109 7189 64127 1476 8649 81609
	8427 10067 9369 9363 3416 23613 51479 5074 27 9833 1839 6477 7694 1373 91057 25945 409 7441 462 84632 1956 50855
	7342 6714 3562 3563 3249 3566 84331 3565 93145 51277 3845 54514 54922 7529 6655 6850 2905 2909 84446 393 392 390
	10235 394 7039 58491 3303 6780 5256 5257 2069 6789 6788 2064 51196 5315 10879 64848 84206 585 583 64112 3156 11083
	1437 971 924 1438 1439 8729 2066 149428 1003 1002 8503 8502 3595 64284 9240 283349 23558 23559 79577 23463 178
	4926 6921 6923 53916 11156 2886 2057 6285 2888 6281 3697 23011 183 57106 2 185 7988 26036 1509 3083 5868 2622 53343
	2769 22800 5894 10395 11336 11339 5899 23233 387755 1915 5104 19 92609 867 84181 6386 5863 55288 3082 155061 2690
	84643 10276 3903 55201 83593 889 3909 4763 6628 10576 10572 407 1969 8764 11244 1613 24148 55704 50628 5803 51497
	2876 81793 204851 7108 1501 84313 166379 1047 5364 5365 2339 7064 6134 5934 1942 150084 3717 1268 23511 57521 663
Set 1	9475 104 5898 22808 3654 11059 3656 29984 6002 2487 85463 117178 8651 11311 8655 1460 2242 995 994 5345 9278 5147
	9372 998 5140 4887 7535 22920 51562 8531 8533 4233 4232 27071 56886 5590 1400 5595 5597 5596 79874 170685 55644
	2147 929 6259 91608 259173 921 923 1380 925 23286 79665 91404 10333 150372 221527 9093 23265 9657 9655 9712 10125
	3579 54933 8887 3570 55423 369 80351 6440 27143 64759 28956 382 5585 23411 387 388 389 6678 5328 84067 5871 5877
	5879 4359 604 60485 576 8741 56997 56288 27429 7096 7097 2202 64581 81607 2208 2560 57679 102723859 7098 7099
	10912 115352 51135 115727 2046 30000 23643 10640 203259 3689 3688 4682 11140 80176 11060 5578 56896 166824 57176
	1514 26128 9616 5294 54476 5293 5290 54472 8408 5880 246330 5055 9223 6553 51555 2036 6224 3183 4843 26959 27106
	285971 389015 326624 114790 23450 9046 10507 10469 84251 26469 84256 4155 4012 55770 80305 54908 51096 83452 9922
	342371 55914 10718 9429 5270 6640 6641 27165 5900 939 5906 84552 5908 5909 23071 6990 673 55824 575 5510 95 6014
	6016 6018 6390 79738 29907 63928 2778 10049 8036 23677 4893 4892 2773 2775 2776 5605 5604 6453 10072 8522 22913
	7879 8525 4800 59307 353376 26015 9463 421 23179 9542 6303 26019 309 3959 3958 3816 3817 3815 3818 3956 11213
	10781 3265 10038 4110 3266 3268 11218 23258 9311 284996 826 4294 22866 54437 51028 80342 4609 387119 131890 84662
	117583 5331 6604 5336 7016 10253 399687 10256 27241 84951 81488 4067 6768 1730 2770 84612 5780 5781 5783 54386
	51735 55319 140691 8772 60493 56704 29899 225689 6885 6881 79370 149371 7082 7163 1184 7161 80270 6693 10313
	10928 23533 23109 9101 3739 59349 3730 9135 85444 951 11178 9770 57162 399664 1445 57161 1114 23037 81848 1448
	5289 9138 9649 57003 22827 8412 57002 84164 22821 377630 6549 84767 1364 3192 6237 9519 9693 4582
Set 2	221150 202 7813 6790 3619 83903 332 9793 5347 51560 9212 10112 55139 9903
Set 3	3611 57118 9459 993 1850 90462 6660 54540 5599 29780 1033 8260
Set 4	5029 2277 9368 2324 3693 3791 2321 7424 7422
Set 5	5159 5155 5154 1845 11333 417 80310
Set 6	857 2319 858 7851 2804 3301
Set 7	151295 3480 9365 342574 6876 3643
Set 8	4716 967 26056 10806 7248
Set 9	7706 50852 7051 5920 28998
Set 10	3084 5867 7448 57732 1950
Set 11	4512 8834 2232 1327 3329
Set 12	1762 23564 27037 3659 481
Set 13	7074 4830 9479 286
Set 14	4055 26173 10522 2273
Set 15	10006 916 79574 952
Set 16	1436 146433 8563 27258
Set 17	55506 2146 480
Set 18	221178 10657 117153
Set 19	9367 2664 6009
Set 20	25804 2922 6635
Set 21	84174 1435 919
Set 22	9722 8224 6853
Set 23	10044 84433
Set 24	5869 9610
Set 25	2077 2048
Set 26	26228 7006
Set 27	25763 3064
Set 28	2533 280636
Set 29	8543 10461
Set 30	5997 7905
Set 31	23371 3695
Set 32	345757 3932

Set 33	6048 7922
Set 34	4068 114836
Set 35	55740 6195
Set 36	51256 7249
Set 37	83394 2185
Set 38	283455 1326
Set 39	6645 23139
Set 40	950 7057

Supplementary Table8. The list of GO annotations for the protein sets affected by H-RAS G13, Q61 perturbation.

HRAS G13, Q61 provoked GO functions	
Response to UV	response to UV
	protein tetramerization
	positive regulation of actin filament polymerization
Protein Polymerization	regulation of actin polymerization or depolymerization
	regulation of actin filament polymerization
	regulation of protein polymerization
Metabolic Processes	nitric oxide metabolic process
	arginine metabolic process
	activation-induced cell death of T cells
T cell apoptosis/homeostasis	T cell homeostasis
	T cell apoptosis
Regulatory Processes	regulation of telomere maintenance
	regulation of survival gene product expression
	positive regulation of multicellular organism growth
Others	response to hydrogen peroxide
	neuron maturation
	immunoglobulin biosynthetic process
	microspike assembly
	response to food
	mitochondrion organization

Supplementary Table 9. The list of protein sets (in Entrez Gene ID) affected by H-RAS G 13, Q61 perturbation.

HRAS G13/Q61 mutation disturbed protein sets

Gene Set 1	65095 134728 123920 6721 83937 10513 9777 10458 27289 3556 3554 7305 95 11261 11260 1946 4140 26015 3998 54915 3993 2912 11186 85406 7128 6093 10209 5267 916 2318 81539 51168 1063 5303 5269 55227 154796 4830 56241 5911 5910 5912 57118 1937 4656 274 3145 6383 6382 2547 2549 91754 114609 6478 1527 81622 2263 2260 200894 529 79665 10333 115207 8667 445 8519 1949 51507 103 23541 23095 5774 5777 2046 85021 11006 1843 2049 9411 26128 9649 434 7161 2160 54496 54540 10411 10146 11266 11340 23242 7265 100820829 7266 266747 847 3635 23433 6610 10567 2633 6614 9021 10841 5229 84941 5818 5819 5792 22882 23184 56302 55971 90864 3064 3069 4615 23263 2342 7074 230 6103 5457 5924 9278 6881 5921 1759 5923 29765 157310 29760 29763 5788 613 4254 54106 10879 3703 644 85377 4916 91662 29109 7189 64127 1476 8649 90462 81609 8427 6440 9368 9369 54453 9363 22931 23564 23613 22837 56896 9833 340205 7694 1373 403 402 23643 930 25945 7441 84632 84631 79574 3265 50855 6714 3562 3563 3249 3566 51374 84331 3565 93145 51277 3845 54514 54922 54518 7529 6655 8976 6654 6850 285971 2909 84446 393 392 88 390 10235 394 928 5257 2146 6789 6788 6660 51196 6259 5315 27143 5585 64848 84206 3665 585 583 64112 117248 152831 924 79695 1438 1439 8729 10900 291 1003 8503 8502 2590 64284 9240 57403 283349 23559 23559 79577 8291 971 178 6921 6923 53916 975 11156 2886 2057 2885 2059 6285 2888 6281 3697 183 57106 2 23015 185 5869 26036 1509 3083 5868 2622 53343 2769 57085 22800 5894 10395 11336 11339 5899 23233 9093 5104 19 92609 27037 867 84181 6386 5863 28956 9138 3082 84067 2690 3146 3903 55201 83593 889 203259 4763 6628 10430 10572 356 1613 342371 55704 50628 5803 51497 8844 2876 207 81793 204851 7108 9922 166379 1047 5364 5365 2339 7064 5934 55568 150084 4301 9479 57521 23043 23040 5781 5898 22808 3654 11059 3656 2099 29984 6002 2487 85463 117178 64979 8658 8651 57142 2242 995 994 993 5345 23767 5147 9372 998 5140 4887 7535 22920 51562 8531 4233 4232 56886 3416 1400 5595 7444 5597 5596 5599 170685 55644 2147 929 4609 91608 259173 921 923 1380 925 23286 10332 23463 4214 9094 55323 150372 221527 387755 6709 23265 9657 23301 9712 10434 10125 833 3579 51365 5090 4289 3570 369 80351 64759 382 27 387 388 5270 5328 3818 5872 9965 54622 5871 5876 5877 5879 50618 51225 6477 60485 576 575 56997 56288 7096 7097 2202 64581 81607 2560 5900 7098 7099 10912 115352 51135 115727 6271 7294 30000 10313 10640 57002 8260 11069 5909 4682 11140 80176 3683 11060 1454 163033 166824 219790 57176 1514 80270 9616 10006 9610 5294 54476 5293 5290 54472 5880 51411 59349 246330 5055 27185 9223 9818 51555 2036 6224 3183 4843 54994 55603 326624 9550 114790 23450 9047 9046 10469 26469 4155 4012 11252 55770 80305 84313 952 64787 7111 24148 80739 55914 4703 114132 6641 1070 81488 5906 84552 54756 5908 10818 286 7802 23071 673 29993 6011 29124 6014 6016 6018 6390 25890 401409 79738 29907 63928 2778 10049 8036 23677 4893 983 2773 2775 2776 5605 5604 10072 5601 5602 8522 22913 7879 8525 4800 1850 5565 59307 89797 353376 9467 534 9463 421 829 23179 6300 6303 26019 309 3959 3958 3816 3817 3815 3953 302 3956 11213 10781 10787 10038 4110 3266 9644 11218 284996 51429 80817 4294 22866 54437 51028 80342 131890 84665 10048 71 84662 117583 5331 5336 7016 5338 10253 399687 10256 27241 2905 6768 1730 84612 5780 481 5783 54386 51735 5563 55319 140691 60493 29899 229 1033 226 149371 7163 1184 91404 388228 6693 10928 23533 23109 54869 9459 9101 6549 3739 5528 634 3732 3730 4926 951 953 11178 9770 57162 1445 57161 1114 23037 81848 1448 5289 5163 2589 22827 8411 5739 6237 22821 377630 51606 1809 84767 84164 9519 9693 4582
Gene Set 2	10718 84951 420 84256 400745 57489 2064 3937 115209 100124696 2069 1956 2066 116449 8412 9542 2065 27071
Gene Set 3	5159 5155 5154 1845 11333 417
Gene Set 4	165918 3688 9135 23011 83452 27342
Gene Set 5	1364 1945 1969 1944 2041
Gene Set 6	220164 5979 4902 2674 2668
Gene Set 7	3301 7851 858 2804 2319
Gene Set 8	7706 50852 7051 5920 28998
Gene Set 9	4055 26173 10522 2273
Gene Set 10	1436 146433 8563 27258
Gene Set 11	399664 493856 596
Gene Set 12	3084 1950 7448
Gene Set 13	9365 3480 151295
Gene Set 14	27352 399823 4771
Gene Set 15	9367 2664 6009
Gene Set 16	7454 257364 8751
Gene Set 17	7424 3791 2324
Gene Set 18	25804 2922 6635
Gene Set 19	8772 826 85444
Gene Set 20	84643 6780 91057
Gene Set 21	84174 1435 919
Gene Set 22	27165 55824 6640
Gene Set 23	10044 84433
Gene Set 24	10806 7248
Gene Set 25	26228 7006
Gene Set 26	558 23371
Gene Set 27	2533 280636
Gene Set 28	8543 10461
Gene Set 29	5590 23258

Gene Set 30 345757 3932

Gene Set 31 6048 7922

Gene Set 32 4068 114836

Gene Set 33 8224 6853

Gene Set 34 55740 6195

Gene Set 35 8440 171177

Gene Set 36 283455 1326

Gene Set 37 6645 23139

Gene Set 38 2167 52

Gene Set 39 1674 9212

Supplementary Table 10. The list of GO annotations for the protein sets affected by H-RAS A59 perturbation.

HRAS A59 provoked GO functions	
GPCR signalling	regulation of G-protein coupled receptor protein signaling pathway activation of phospholipase C activity by metabotropic glutamate receptor signaling pathway glutamate signaling pathway metabotropic glutamate receptor signaling pathway
Homeostasis	di-, tri-valent inorganic anion homeostasis anion homeostasis cellular di-, tri-valent inorganic anion homeostasis cellular anion homeostasis phosphate ion homeostasis <u>cellular phosphate ion homeostasis</u>
Differentiation	glial cell differentiation myoblast differentiation
Growth	regulation of organ growth regulation of cardiac muscle growth
Development	tongue development induction of an organ sensory organ development metanephros development developmental induction gut development ureteric bud development cell fate specification cell fate commitment odontogenesis gliogenesis ossification cell-cell signaling involved in cell fate specification regulation of cardiac muscle tissue development
Virus & host	regulation of cAMP-mediated signaling interaction with symbiont virus-host interaction
Response to Stimulus	calcium-mediated signaling regulation of response to biotic stimulus response to exogenous dsRNA
Transport	protein import into nucleus, translocation regulation of ion transport membrane docking energy coupled proton transport, against electrochemical gradient regulation of ion transmembrane transport negative regulation of ryanodine-sensitive calcium-release channel activity vesicle docking ATP hydrolysis coupled proton transport regulation of transmembrane transport regulation of transmembrane transporter activity positive regulation of transporter activity positive regulation of transporter activity regulation of metal ion transport positive regulation of ion transmembrane transporter activity protein targeting substrate-bound cell migration

	<u>regulation of ion transmembrane transporter activity</u>
Catabolic Process	regulation of catabolic process
	negative regulation of catabolic process
	regulation of protein catabolic process
	regulation of cyclin-dependent protein kinase activity
	negative regulation of protein catabolic process
Proliferation	regulation of cardiac muscle cell proliferation <u>positive regulation of cardiac muscle cell proliferation</u>
VEGFR signalling	positive regulation of vascular endothelial growth factor receptor signaling pathway
	regulation of vascular endothelial growth factor receptor signaling pathway
	actin filament polymerization
	male sex determination
	positive regulation of nitric oxide biosynthetic process
	negative regulation of cell-cell adhesion
	zymogen activation
Others	negative regulation of protein modification process
	T cell activation via T cell receptor contact with antigen bound to MHC molecule on antigen presenting cell
	negative regulation of cellular protein metabolic process
	positive regulation of neuron apoptosis

Supplementary Table 11. The list of protein sets (in Entrez Gene ID) affected by H-RAS A59 perturbation.

HRAS A59 mutation disturbed protein sets
134728 123920 6721 83937 10457 10513 5563 9771 9770 10879 3554 11260 11266 55763 1527 3998 54915 54737 2912 11186 9463 1794 85406 10200 3339 51160 916 2318 81539 51168 1063 6654 2312 5269 55227 56241 5911 5910 291 4656 274 3145 6383 6382 3672 5818 2547 3383 2549 114609 26258 81622 2263 2260 200894 529 2264 10332 10333 115207 25890 8667 4218 445 8751 51507 103 23541 5774 5777 2046 2045 11006 1843 6278 1845 2049 9411 644 3265 2167 2160 54496 114132 51678 11340 5133 23242 7265 51028 7266 266747 23433 6610 10567 5290 6614 95 10841 5229 59349 5819 8936 5792 22882 51411 3635 56302 55971 7171 90864 3069 4615 2915 2342 7074 230 2224 6103 5924 1759 5923 29765 157310 29760 29763 64398 613 9113 4254 54106 3703 4509 85377 947 91662 29109 7189 64127 1476 2533 81609 8427 7128 9368 9369 54453 9363 22931 23613 22837 7456 7454 6478 5582 9833 55052 6477 7694 1373 403 402 25945 56886 84631 79574 5991 1953 6714 183 3562 3563 3249 51375 51374 84331 9901 22843 51277 3845 54514 54922 54518 7529 6655 8976 5303 6850 2905 84446 393 88 10235 3304 928 793 5257 6789 6788 5311 51196 27143 27 64848 84206 3665 79890 585 583 4140 64112 117248 93343 90423 1435 152831 79695 1439 8729 10900 5912 4188 8503 8502 2590 57403 283349 50856 8291 178 53916 11156 2057 2885 2059 7827 2888 6281 3697 9094 57106 2 23015 185 5780 26036 3083 55644 53343 2769 146722 57085 22800 11333 5894 11336 5898 22808 23233 5104 19 92609 4214 84181 51225 28956 84062 9138 3082 84067 23263 79720 3146 3903 55201 83593 889 203259 4763 83692 257364 6628 10430 10572 356 1613 24148 55704 23338 50628 50624 51497 8844 2876 207 80817 204851 7108 57610 9922 1047 5364 2339 7064 5934 55568 4301 9479 57521 23043 23040 5781 11339 5899 3654 3656 29984 6002 695 85461 85463 Set 1 117178 64979 8658 2248 2249 8651 2247 995 994 23607 23767 5147 9372 998 5140 4887 7535 22920 10787 51562 8531 4233 7441 3416 1400 5595 7444 5596 170685 2147 929 417 924 925 23286 23287 23463 339287 3821 3820 23468 55323 150372 221527 387755 6709 23265 9657 23301 9712 10434 10125 833 3579 51365 5090 4289 369 80351 7532 5585 387 388 4703 5328 64859 5872 9965 54622 5876 5877 5878 5879 50619 50618 151888 340205 60485 56997 56288 2803 7096 7097 2202 64581 81607 2560 81488 7098 7099 115352 51135 115727 26230 89848 7294 30000 23643 10640 160 11069 4682 11140 3683 4830 1454 166824 219790 57176 1514 80270 801 10006 9610 4089 5294 54476 5293 2633 54472 170961 5880 5886 23184 246330 5055 27185 8817 9818 92369 51555 6224 3183 84174 54994 55212 55603 9550 114790 9047 10469 4155 4012 3227 11252 55770 80305 84313 952 64787 7111 80739 55914 10636 5270 10411 6641 1070 5900 5906 54756 5908 5909 286 8871 7802 23071 673 29992 29993 26088 6011 29124 6014 6016 302 3035 6390 3565 401409 52 534 29907 2255 2254 2253 2252 2251 2250 10048 10049 988 8036 23677 4893 64284 2773 5155 2775 2776 5605 5604 10072 5601 5602 8522 22913 7879 8525 4800 5565 89790 59307 89797 353376 9467 26015 919 1399 421 829 23179 6300 6303 50807 3959 3958 3953 3818 3956 11213 10781 1937 10038 4110 3266 9644 11218 284996 51429 81793 4294 22866 54437 100820829 131890 84665 2778 71 84662 117583 5331 5336 7016 5338 10253 399687 10256 27245 6768 1730 8822 84612 5869 5868 5783 54386 51735 5863 140691 8773 60493 29899 5154 229 6881 226 149371 91404 388228 9149 6693 10928 23533 54869 9454 9456 8074 9101 3739 5528 634 1808 3732 3730 4926 951 953 11178 57162 57161 1114 23037 8678 26057 1448 5163 10078 9649 2589 22827 8411 5739 6237 22821 377630 6461 51606 1809 84767 84164 9519 9693 4582 Set 2 84951 84256 420 57489 2064 3937 115209 100124696 400745 1956 2066 116449 8412 9542 2065 27071 Set 3 57118 993 1850 983 6660 54540 5599 1033 6093 8260 90462 Set 4 90780 51421 399823 4771 27352 154810 23560 10015 Set 5 7706 50852 7051 5920 28998 Set 6 220164 5979 4902 2674 2668 Set 7 23011 83452 165918 27342 9135 Set 8 7448 273 1950 3084 Set 9 975 930 1820 8519 Set 10 4055 26173 10522 2273 Set 11 1436 146433 8563 27258 Set 12 3993 84552 50855 Set 13 8440 171177 719 Set 14 399664 493856 596 Set 15 23555 8945 338785 Set 16 9367 2664 6009 Set 17 25804 2922 6635 Set 18 3645 3643 5167 Set 19 2622 7161 Set 20 26228 7006 Set 21 558 23371 Set 22 5037 7182 Set 23 22839 60412

Set 24	8543 10461
Set 25	5590 23258
Set 26	345757 3932
Set 27	6048 7922
Set 28	4068 114836
Set 29	5296 114932

References

- 1 Goncalves, V. *et al.* A missense mutation in the APC tumor suppressor gene disrupts an ASF/SF2 splicing enhancer motif and causes pathogenic skipping of exon 14. *Mutation research* **662**, 33-36, doi:10.1016/j.mrfmmm.2008.12.001 (2009).
- 2 Huang, H. *et al.* APC mutations in sporadic medulloblastomas. *The American journal of pathology* **156**, 433-437, doi:10.1016/S0002-9440(10)64747-5 (2000).
- 3 Kourmouli, N., Sun, Y. M., van der Sar, S., Singh, P. B. & Brown, J. P. Epigenetic regulation of mammalian pericentric heterochromatin in vivo by HP1. *Biochemical and biophysical research communications* **337**, 901-907, doi:10.1016/j.bbrc.2005.09.132 (2005).
- 4 Eustermann, S. *et al.* Combinatorial readout of histone H3 modifications specifies localization of ATRX to heterochromatin. *Nature structural & molecular biology* **18**, 777-782, doi:10.1038/nsmb.2070 (2011).
- 5 Levran, O. *et al.* The BRCA1-interacting helicase BRIP1 is deficient in Fanconi anemia. *Nature genetics* **37**, 931-933, doi:10.1038/ng1624 (2005).
- 6 Roy, R., Chun, J. & Powell, S. N. BRCA1 and BRCA2: different roles in a common pathway of genome protection. *Nature reviews. Cancer* **12**, 68-78, doi:10.1038/nrc3181 (2012).
- 7 Makishima, H. *et al.* CBL mutation-related patterns of phosphorylation and sensitivity to tyrosine kinase inhibitors. *Leukemia* **26**, 1547-1554, doi:10.1038/leu.2012.7 (2012).
- 8 Zhang, Z., Elly, C., Qiu, L., Altman, A. & Liu, Y. C. A direct interaction between the adaptor protein Cbl-b and the kinase zap-70 induces a positive signal in T cells. *Current biology : CB* **9**, 203-206 (1999).