Supplementary Figures, Tables and Data

Figure S1

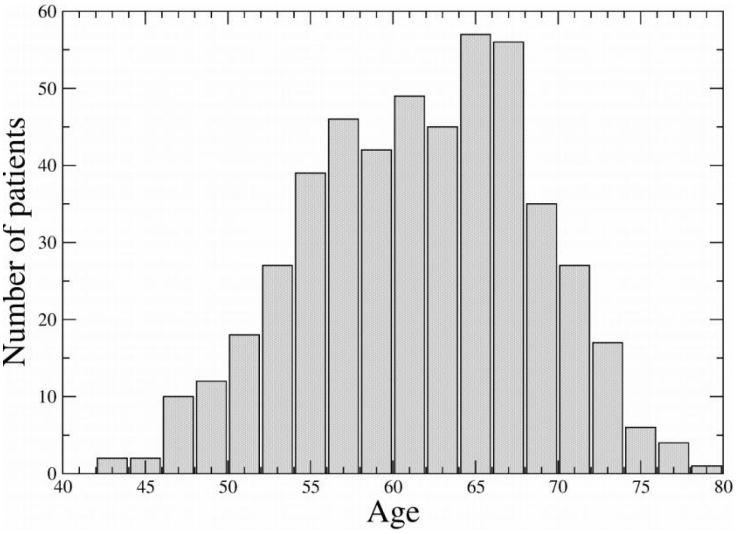


Figure S1: Histogram showing the age range for patients included in the PRAD-TCGA Firehose Legacy cohort used for PCA of RNA-seq expression data.

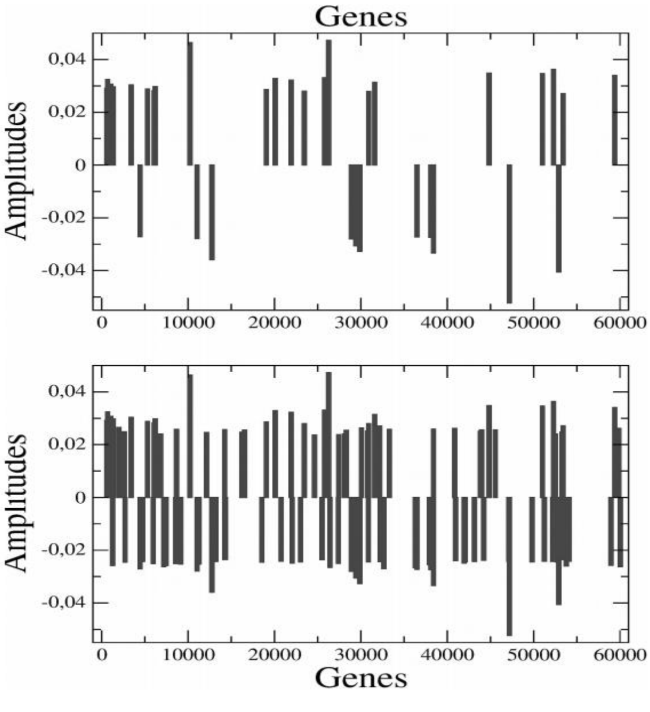
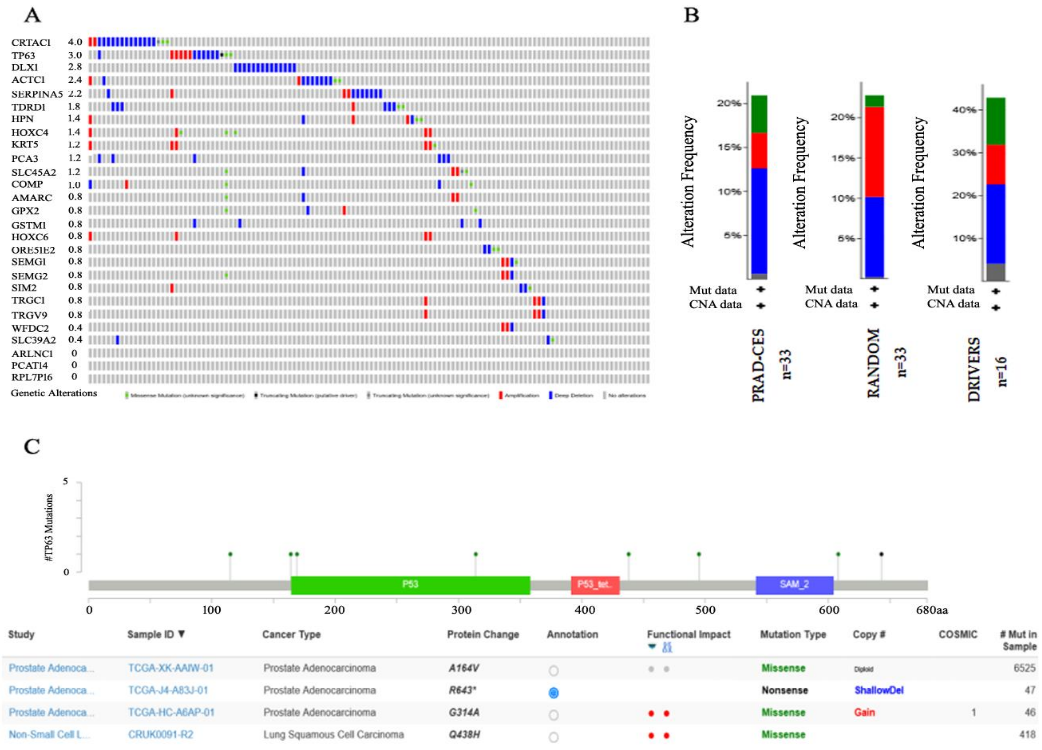


Figure S2: A Barcode-like representation of PRAD genes comprising the unitary vectors along PC1. Top panel, contains 33 genes identified for a delta=0.027; Lower panel representing 100 genes for a delta=0.0235. Within the barcode the major value (i.e., over-expression) corresponds to PCA3, whereas the lower value (i.e., under-expression) belongs to SEMG1.

Figure S3



Study	Sample ID ▼	Cancer Type	Protein Change	Annotation	Functional Impact	Mutation Type	Copy #	COSMIC	# Mut in Sample
Prostate Adenoca...	TCGA-XK-AAIW-01	Prostate Adenocarcinoma	A164V	○	● ●	Missense	Diploid		6525
Prostate Adenoca...	TCGA-J4-A83J-01	Prostate Adenocarcinoma	R643*	●		Nonsense	ShallowDel		47
Prostate Adenoca...	TCGA-HC-A6AP-01	Prostate Adenocarcinoma	G314A	○	● ●	Missense	Gain	1	46
Non-Small Cell L...	CRUK0091-R2	Lung Squamous Cell Carcinoma	Q438H	○	● ●	Missense			418

Figure S3: Differential expression of PRAD-CES genes in the MSKCC, Cancer Cell 2010 cohort. (A) The oncoprint representation tool from Cbioportal is used. Z scores>2, normal vs tumor expression values. (B) Frequency of genomic alterations observed in PRAD for PRAD-CES33 genes, a random selected gene list and Pca driver genes. (C) Recurrent somatic and germline mutations for the protein-coding Tumor Protein P63 (TP63) in NSCLC and PRAD. Non-Small Cell Lung Cancer mutations from TRACERx, NEJM & Nature 2017 dataset (n= 447).

Figure S4

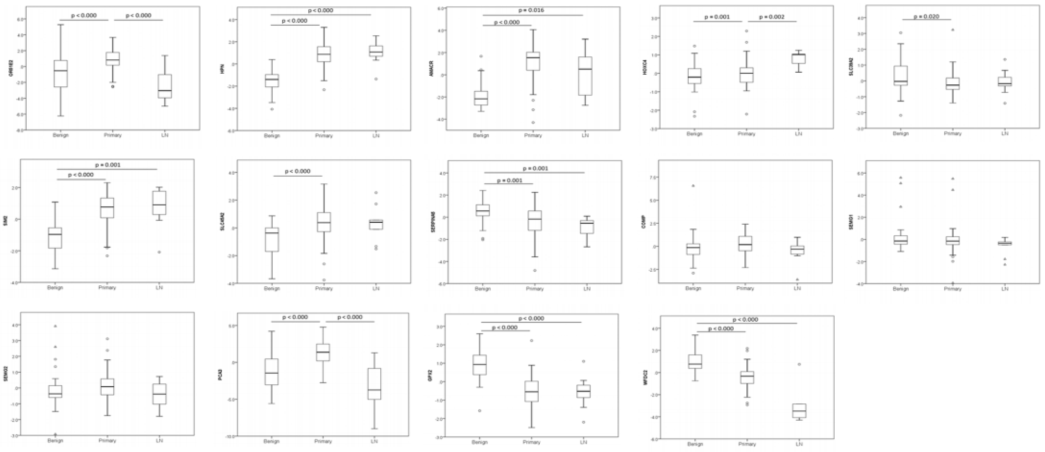


Figure S4: Expression analysis of genes from the PRAD-CES using the data cohort of Lapointe et al., 2004.

Figure S5

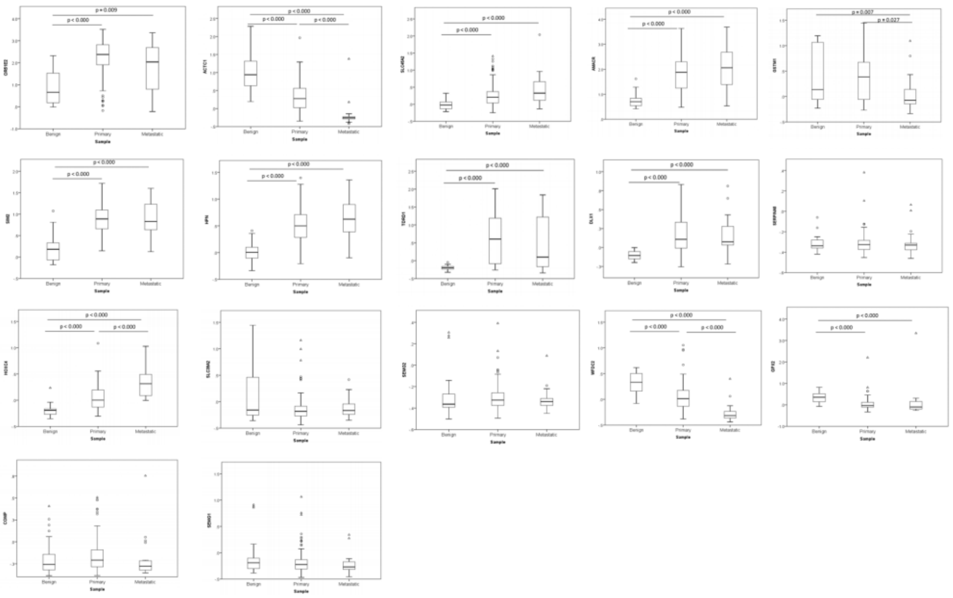


Figure S5: Expression analysis of genes from the PRAD-CES using the data cohort of Taylor.

Figure S6

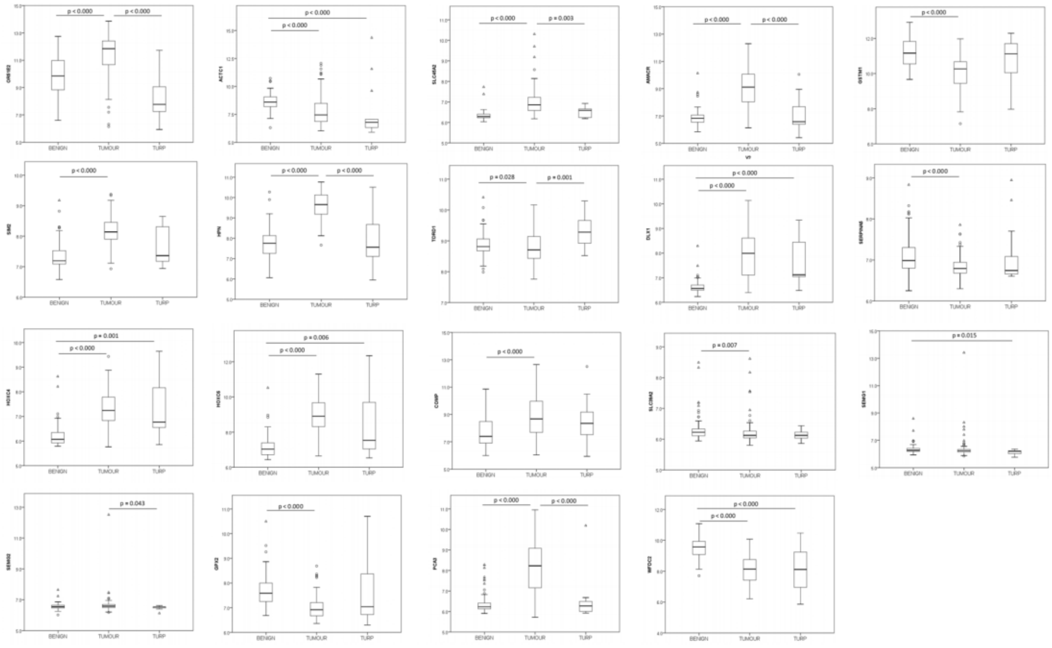


Figure S6: Expression analysis of genes from the PRAD-CES using the data cohort of Ross-Adams Expression analysis of genes from the PRAD-CES using the data cohort of Ross-Adams.

Table S1

RNAseq-ID'	**Ensembl hit**	**PCA 1**	**Gene Name**	**Description°**	**Gene type`**	**Genomic location` (Hurnan,G RCh38.p12)**
597	ENSG00000167332	0.029	OR5182	olfactory receptor family 51 subfamily E member 2	Protein coding	Chromosome 11: 4,680,171-4,697,854 reverse strand
679	ENSG00000232806	0.032	AP001610.2	novel transcript	lincRNA	Chromosome 21:41,559,125-41,562,958 reverse strand.
1070	ENSG00000159263	nom	sIM2	SIM bHLH transcription factor 2	Protein coding	Chromosome 21: 36,699,133-36,749,917 forward strand.
12766	ENSG00000159251	-0.036	ACTC1	actin	Protein coding	Chromosome 15: 34,788,095-34,795,726 reverse strand.
1346	ENSG00000254988	0.03	AP002498.1	novel transcript	antisense	Chromosome 11: 76,955A17-76,978,619 reverse strand.
3409	ENSG00000273179	0.03	AC092535.4	novel transcript	antisense to SPON2	Chromosome 4: 1,167,778-1,168,174 forward strand.
5302	ENSG00000105707	0.029	HPN	hepsin	Protein coding	Chromosome 19: 35,040,506-35,066,571 forward strand.
6083	ENSG00000164175	0.028	SLC45A2	solute carrier family 45 member 2	Protein coding	Chromosome 5: 33,944,623-33,984,693 reverse strand.
6202	ENSG00000095627	0.03	TDRD1	tudor domain containing 1	Protein coding	Chromosome 10:114,179,270-114,232,304 forward strand.

10230	ENSG00000225937	0.046	PCA3	prostate cancer associated 3	Antisense	Chromosome 9: 76,691,980-76,863,307 forward strand.
19073	ENSG00000211689	0.029	TRGC1	T cell receptor gamma constant 1	TR C gene	Chromosome 7: 38,257,879-38,265,678 reverse strand.
20094	ENSG00000280623	0.033	PCAT14	prostate cancer associated transcript 14	lincRNA	Chromosome 22: 23,536,881-23,547,797 forward strand.
21927	ENSG00000242110	0.032	AMACR	alpha-methylacyl-CoA racemase androgen receptor regulated long noncoding RNA	Protein coding	Chromoso me 5: 33,986,165-34,008,104 reverse strand.
25811	ENSG00000260896	0.033	ARLNC1	1	lincRNA	Chromosome 16: 80,826,074-80,892,682 reverse strand.
26265	ENSG00000144355	0.047	DLX1	distal-less homeobox 1	Protein coding	Chromosome 2: 172,084,740-172,089,677 forward strand.
29441	ENSG00000134184	-0.031	GSTM1	glutathione S-transferase mu 1	protein coding	Chromosome 1: 109,687,814-109,709,039 forward strand.
29880	ENSG00000188488	-0.033	SERPINA5	serpin family A member 5	protein coding	Chromosome 14:94,561,442-94,593,118forward strand.
30916	ENSG00000198353	0.028	HOXC4	homeobox C4	protein coding	Chromosome 12: 54,016,931-54,056,030 forward strand.

31604	ENSG00000105664	0.031	COMP	cartilage oligomeric matrix protein	protein coding	Chromosome 19: 18,782,773-18,791,305 reverse strand.
38412	ENSG00000165794	-0.033	SLC39A2	solute carrier family 39 member 2	protein coding	Chromosome 14: 20,999,255-21,001,871 forward strand.
44850	ENSG00000274326	0.035	AL359314.1	RNA gene	mist RNA	Chromosome 9: 76,779,657-76,779,917 forward strand.
47198	ENSG00000124233	-0.052	SEMG1	semenogelin 1	protein coding	Chromosome 20: 45,207,033-45,209,768 forward strand.
51014	ENSG00000242899	0.035	RPL7P16	ribosomal protein L7 pseudogene 16	Processed pseudogene	Chromosome 3: 132,243,528-132,244,265 reverse strand.
52309	ENSG00000223400	0.036	AP006748.1	novel transcript	lincRNA	Chromosome 21:41,576,135-41,581,319 reverse strand.
52910	ENSG00000124157	-0.041	SEMG2	semenogelin 2	Protein coding	Chromosome 20: 45,221,300-45,224,458 forward strand.
59397	ENSG00000197757	0.034	HOXC6	homeobox C6	Protein coding	Chromosome 12:53,990,624-54,030,823forward strand
11041	ENSG00000176153.11	-0.028	GPX2	Glutathione Peroxidase 2	Protein coding	Chromosome 14: 64,939,152-64,942,905 reverse strand.

23459	ENSG00000250767.1	0.028	AC139783.1	Fumarate Hydratase (FH) Pseudogene	IncRNA	Chromosome 5: 33,997,044-33,997,724 reverse strand.
28911	ENSG00000101443.16	-0_028	W1IDC2	WAP Four-Disulfide Core Domain 2	Protein coding	Chromosome 20: 45,469,753-45,481,532 forward strand
36502	ENSG00000095713	-0_027	CRTAC1	cartilage acidic protein 1	protein coding	Chromosome 10: 97,865,000-98,030,828 reverse strand.
38100	ENSG00000186081	-11027	KRT5	Keratin 5	Protein coding	Chromosome 12: 52,514,575-52,520,530 reverse strand
4450	ENSG00000073282	-0_027	TP63	Tumor Protein P63	Protein coding	Chromosome 3: 189,631,389-189,897,276 forward strand.
53412	ENSG00000211695	0.027	TRGV9	T cell receptor gamma variable 9	TR V gene	Chromosome 7: 38,317,017-38,318,861 reverse strand.
Legend: a PRAD-TCGA; b Genecards; c Ensembl						

Table SI: Detailed information about the 33 genes included in the PRAD core signature (PRAD-CES33).

[PRAD-TCGA]	**Genecards**	**Ensembl**		**Text-mining**			**Genecards**	**Gene Product Expression'**		
RNAseq-1D	**Gene Name**	**Biotype**	**Pca Association**	**Association**	**Driver; Biomarker;Other**	**Disease Association**	**URL**	**Prostate**	**Other tissues**	**Localization**
597	OR51E2	Protein coding	YES	over-expression	D;B;ND	MalaCards: No disord	bin/carddisp.pl?gene=OR51E2&keywords=ORmn...//www.ye.	ND	ND	PM

						ers were found for OR51E2 Gene				
679	AP001610.2	lincRNA	ND	ND	ND;ND;ND	MalaCards: No data available.	bin/carddisp.pl?gene=ENSG00000232806&keywords=AP001610	YES	>10	ND
1070	SIM2	Protein coding	YES	over-expression	D?; NO:ND	MalaCards: down syndrome.	bin/carddisp.pl?gene=SIM26keywords=SIM2	ND	2	IC, nucleus
12766	ACTC1	Protein coding	ND	ND	ND;ND;ND	MalaCards: 94 diseases, no prostate cancer, 2 other tumors.	bin/carddisp.pl?gene=ACTC1&keywords=ACTC1	ND	5	IC, cytoplasm
1346	AP002498.1	antisense	ND	ND	ND;ND;ND	MalaCards: No data available.	bin/carddisp.pl?gene=ENSG000002731796keywords=AC092535	YES	>10	ND
3409	AC092535.4	antisense to SPON2	ND	ND	ND;ND;ND	MalaCards: No data available.	https://www.genecards.org/cgi-	ND	ND	ND
5302	HPN	Protein coding	YES	over-expression	D;B;ND	Male cards: prostate cancer 1.	bin/carddisp.pl?gene=1-1PN&keywords=HPN	YES	>10	EC

6083	SLC45A2	Protein coding	YES	ND	D?;B; ND	(melanome).	bin/carddisp.pl?gene=SLC45A2&keywords=S https://www.genecards.org/cgi-	NO	3	PM
6202	TDRD1	Protein coding	YES	over-expression	D?;B; ND	MalaCards: No disorders were found for TDRD1 Gene.	bin/carddisp.pl?gene=TDRD1&keywords=TD	ND	5	IC, nucleus
10230	PCA3	Antisense	YES	over-expression	D;B;ND	MalaCards: 7 diseases, none cancer.	bin/carddisp.pl?gene=PCA3&keywords=PCA3	YES	>10	EC (low confidence)
19073	TRGC1	TR C gene	YES	over-expression	ND;ND;ND	TRGC1 Gene.	bin/carddisp.pl?gene=TRGC16keywords=TR	ND	ND	ND
20094	PCAT14	linc RNA	YES	down regulation over-expression,	D;B;ND	MalaCards: No data available.	https://www.genecards.org/cgi-	ND	ND	ND
21927	AMACR	Protein coding	YES	polymorphism	D;B;ND	cancer,	bin/carddisp.pl?gene=PCAT14&keywords=PC	YES	>10	IC, cytoplasm
25811	ARLNC1	linc RNA	YES	over-expression	D;ND; ND	MalaCards: No data available.	napswwww.genecaros.orwcgi-	ND	ND	ND
26265	DLX1	Protein coding	YES	over-expression down regulation,	D;B;ND	MalaCards: 4 diseases, none cancer.	bin/carddisp.pl?gene=AMACR&keywords=AM	ND	4	IC, nucleus
29441	GSTM1	protein coding	YES	polymorphism	ND:ND:Risk factor	cancer.	hdps://www.genecards.org/egi-	YES	>10	EC, IC

29880	SERPINA5	protein coding	YES	downregulation	0?;ND:ND	MalaCards: No data available.	bin/carddisp.pl?gene=ARLNCI &keywords=ARLNC1	YES	>10	EC
30916	HOXC4	protein coding	YES	over-evmssion	D?;NID:ND	MalaCards: 36 diseases, none cancer.	https://www.genecards.org/cgi-	ND	ND	IC, nucleus
31604	COMP	protein coding	ND	over-expression	D?;B;ND	MalaCards: No data available.	bin/carddispfl?gene=DLX18keywords=DLX1	YES	>10	EC
38412	SLC39A2	protein coding	YES	downregulation	D?;ND;ND	MalaCards: No data available.	bin/carddisp.pl?gene=GSTM1&keywords=GSTM1	ND	ND	PM
44850	AL359314.1	mistRNA	Putative	ND	ND;ND;ND	MalaCards: No data available.	bin/carddisp.pl?gene=SEBPrNA5&keywords=SERPINA5	ND	ND	ND
47198	SEMG1	protein coding	YES	ND	ND;B;ND	MalaCards: No data available.	rrepe.wwww.yerrecerUb.-7,1,1,1-	YES	>10	EC
51014	RPL7P16	Processed pseudogene	ND	ND	ND;ND;ND	MalaCards: No data available.	bin/carddisp.pl?gene=HOXC4&keywords=HO	YES	ND	IC
52309	AP006748.1	lincRNA	?	ND	ND;ND;ND	MalaCards: No data available.	irrye.wwww.yer mud: ue.urytLyr-	YES	ND	IC, EC

52910	SEMG2	Protein coding	YES	ND	NOB; ND	esophagus.	binicarddisp.pl?gene=COMP&keywords=COMP	YES	EC	ND
59397	HOXC6	Protein coding	YES	over-mpression	D;B;ND	MalaCards: No data available.	hdps://www.genecards.org/cg,	ND	1	EC
11041	GPX2	Protein coding	YES	over-expression	D?:13: NOA?	MalaCards: No data available	bin/carddisp.pl?gene=SLC39A2&keywords=SLC39A2	YES	>10	EC, PM
23459	ACL39783 I	IncRNA	ND	ND	ND;ND;ND	including prostate.	bin/carddisp.pl?gene=ENSG000002743268Eeg="1=-„,	YES	>10	ND
28911	WFDC2	Protein coding	NO	over-expression	D?;B; ND	MalaCards: 97 diseases cervical cancer, hem	bin/carddisp.pl?gene=SEMG16keywords=SE	NO	>10	
36502	CRTAC1	protein coding	ND	ND	ND;ND;ND	MalaCards:No disorders were found for TRG'	https://www.genecards.org/cgi-	YES	>10	
38100	KRT5	Protein coding	YES	ND	ND;ND;ND	MalaCards: colon cancer, barren	bin/carddisp.pl?gene=RPL7P16&keywords=R https://www.genecards.org/cgi-	5	IC, PM, EC	
4450	TP63	Protein coding	YES	down regulation	D?;B; ND	MalaCards:Ovarian cancer.	bin/carddisp.pl?gene=ENSG000002234008Ee	> 5	IC, cytoplasm, nucleus	

									, EC	
53412	TRGV9	TR V gene	NO	ND	ND;ND;ND	MalaCards:181 diseases, some cancer	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SEMG2&keywords=SE	ND	ND	ND
Legend: D, Driver; D?, Putative driver; B, Biomarker; NOA, Non-Oncogen Addiction; ND, No Data ; aIntegrated Proteomics or The Human Protein Atlas or RNA-gene expression; EC, Extracellular; IC, Intracellular; PM, Plasma Membrane; ?, Ambiguos info.										

Table SII: Gene Classification, Disease Association and Gene Product Expression

Table S3

Dataset				
Gene Name	**Lapointe**	**Ross-Adams**	**Taylor**	**Up *vs.* Down***
ORE51E2	√	√	√	Up
SIM2	√	√	√	Up
ACTC1	0	√	√	Down
HPN	√	√	√	Up
SLC45A2	√	√	√	Up
TDRD1	0	√	√	Up
AMARC	√	√	√	Up
DLX1	0	√	√	Up
GSTM1	0	√	X	Down
SERPINA5	√	√	X	Down
HOXC4	√	√	√	Up
HOXC6	0	√	0	Up
COMP	X	√	X	Up
SLC39A2	√	√	X	Down
SEMG1	X	X	X	n.s
SEMG2	X	X	X	n.s
GPX2	√	√	√	Down
PCA3	√	√	0	Up
WFDC2	√	√	√	Down
Legend: "√": Significant difference in expression between bening and primary tumors at P<0.05; "X": no significant difference: "0": not available; * Consistent Up vs. Down-regulation in primary tumors vs.benign.				

Table SIII: Summary of the expression of PRAD-CES genes in three independent data cohorts.

Data S1

Data S1	Enrichment analysis for Biological Process using the tool Enrich
GO_Biological_Process_2018	
Tab Content:	
Tab 1	PC1
Tab 2	PC2
Tab 3	PC3

Term	Overlap	P-value	Adjusted P-value	Old P-value	Old Adjusted P-value	Odds Ratio	Combined Score	Genes
regulation of serine-type endopeptidase activity (GO:1900003)	11-Feb	1.44E-04	0.734104	0	0	110.1928	974.8417	SEMG2; SEMG1
positive regulation of endopeptidase activity (GO:0010950)	24-Feb	7.12E-04	1	0	0	50.50505	366.0117	SEMG2; SEMG1
antibacterial humoral response (GO:0019731)	Feb-35	0.00152	1	0	0	34.63203	224.76923	SEMG2; SEMG1
spermatogenesis (GO:0007283)	3/153	0.00202	1	0	0	11.88354	73.709714	TDRD1; WFDC2; SERPINA5
male gamete generation (GO:0048232)	3/154	0.00206	1	0	0	11.80638	73.012031	TDRD1; WFDC2; SERPINA5
protein heterooligomerization (GO:0051291)	Feb-49	0.00296	1	0	0	24.73717	144.05238	SEMG2; SEMG1
positive regulation of blood pressure (GO:0045777)	06-Jan	0.00986	1	0	0	101.0101	466.58897	OR51E2
positive regulation of fibroblast apoptotic process (GO:2000271)	06-Jan	0.00986	1	0	0	101.0101	466.58897	TP63

positive regulation of hormone metabolic process (GO:0032352)	06-Jan	0.00986	1	0	0	101.0101	466.58897	HPN
negative regulation of calcium ion import (GO:0090281)	07-Jan	0.01149	1	0	0	86.58009	386.65618	SEMG1
xenobiotic catabolic process (GO:0042178)	07-Jan	0.01149	1	0	0	86.58009	386.65618	GSTM1
basement membrane organization (GO:0071711)	08-Jan	0.01313	1	0	0	75.75758	328.26865	HPN
regulation of fibroblast apoptotic process (GO:2000269)	08-Jan	0.01313	1	0	0	75.75758	328.26865	TP63
detection of mechanical stimulus involved in sensory perception (GO:0050974)	09-Jan	0.01476	1	0	0	67.34007	283.91662	HPN
regulation of flagellated sperm motility (GO:1901317)	09-Jan	0.01476	1	0	0	67.34007	283.91662	SEMG1
positive regulation of developmental process (GO:0051094)	2/113	0.0149	1	0	0	10.72674	45.118067	DLX1;HPN
mitotic G1/S transition checkpoint (GO:0044819)	10-Jan	0.01638	1	0	0	60.60606	249.18786	TP63
skeletal muscle thin filament assembly (GO:0030240)	10-Jan	0.01638	1	0	0	60.60606	249.18786	ACTC1
mitotic G1 DNA damage checkpoint (GO:0031571)	10-Jan	0.01638	1	0	0	60.60606	249.18786	TP63
G1 DNA damage checkpoint (GO:0044783)	10-Jan	0.01638	1	0	0	60.60606	249.18786	TP63

regulation of plasminogen activation (GO:0010755)	10-Jan	0.01638	1	0	0	60.60606	249.18786	HPN
heart process (GO:0003015)	11-Jan	0.01801	1	0	0	55.09642	221.32716	ACTC1
cochlea morphogenesis (GO:0090103)	11-Jan	0.01801	1	0	0	55.09642	221.32716	HPN
hemidesmosome assembly (GO:0031581)	11-Jan	0.01801	1	0	0	55.09642	221.32716	KRT5
hepatocyte growth factor receptor signaling pathway (GO:0048012)	11-Jan	0.01801	1	0	0	55.09642	221.32716	HPN
cell-substrate junction assembly (GO:0007044)	11-Jan	0.01801	1	0	0	55.09642	221.32716	KRT5
response to thyroid hormone (GO:0097066)	11-Jan	0.01801	1	0	0	55.09642	221.32716	HPN
skeletal myofibril assembly (GO:0014866)	12-Jan	0.01963	1	0	0	50.50505	198.52902	ACTC1
cellular response to fatty acid (GO:0071398)	12-Jan	0.01963	1	0	0	50.50505	198.52902	OR51E2
response to fatty acid (GO:0070542)	13-Jan	0.02125	1	0	0	46.62005	179.56317	OR51E2
DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator (GO:0006978)	13-Jan	0.02125	1	0	0	46.62005	179.56317	TP63
DNA damage response, signal transduction resulting in transcription (GO:0042772)	14-Jan	0.02286	1	0	0	43.29004	163.56363	TP63
response to X-ray (GO:0010165)	15-Jan	0.02447	1	0	0	40.40404	149.90403	TP63
regulation of water loss via skin (GO:0033561)	16-Jan	0.02609	1	0	0	37.87879	138.12059	TP63

establishment of skin barrier (GO:0061436)	16-Jan	0.02609	1	0	0	37.87879	138.12059	TP63
positive regulation of protein processing (GO:0010954)	17-Jan	0.02769	1	0	0	35.65062	127.86297	HPN
cardiac myofibril assembly (GO:0055003)	17-Jan	0.02769	1	0	0	35.65062	127.86297	ACTC1
positive regulation by host of viral transcription (GO:0043923)	17-Jan	0.02769	1	0	0	35.65062	127.86297	HPN
positive regulation of nitrogen compound metabolic process (GO:0051173)	17-Jan	0.02769	1	0	0	35.65062	127.86297	HPN
negative regulation of programmed cell death (GO:0043069)	3/408	0.02925	1	0	0	4.456328	15.738604	COMP;HPN;TP63
piRNA metabolic process (GO:0034587)	18-Jan	0.0293	1	0	0	33.67003	118.86179	TDRD1
regulation of cellular response to transforming growth factor beta stimulus (GO:1903844)	18-Jan	0.0293	1	0	0	33.67003	118.86179	DLX1
muscle tissue morphogenesis (GO:0060415)	19-Jan	0.0309	1	0	0	31.89793	110.9067	ACTC1
negative regulation of calcium ion transport (GO:0051926)	19-Jan	0.0309	1	0	0	31.89793	110.9067	SEMG1
steroid hormone mediated signaling pathway (GO:0043401)	20-Jan	0.0325	1	0	0	30.30303	103.83117	OR51E2

intrinsic apoptotic signaling pathway in response to DNA damage by p53 class mediator (GO:0042771)	20-Jan	0.0325	1	0	0	30.30303	103.83117	TP63
cellular response to steroid hormone stimulus (GO:0071383)	20-Jan	0.0325	1	0	0	30.30303	103.83117	OR51E2
zinc II ion transport (GO:0006829)	21-Jan	0.0341	1	0	0	28.86003	97.501733	SLC39A2
glutathione derivative metabolic process (GO:1901685)	22-Jan	0.0357	1	0	0	27.54821	91.810234	GSTM1
glutathione derivative biosynthetic process (GO:1901687)	22-Jan	0.0357	1	0	0	27.54821	91.810234	GSTM1
regulation of calcium ion import (GO:0090279)	22-Jan	0.0357	1	0	0	27.54821	91.810234	SEMG1
inner ear morphogenesis (GO:0042472)	22-Jan	0.0357	1	0	0	27.54821	91.810234	HPN
zinc II ion transmembrane transport (GO:0071577)	23-Jan	0.03729	1	0	0	26.35046	86.668143	SLC39A2
positive regulation of blood circulation (GO:1903524)	23-Jan	0.03729	1	0	0	26.35046	86.668143	OR51E2
limb development (GO:0060173)	24-Jan	0.03888	1	0	0	25.25253	82.002337	COMP
negative regulation of epithelial to mesenchymal transition (GO:0010719)	25-Jan	0.04047	1	0	0	24.24242	77.751915	HPN
positive regulation of cell differentiation (GO:0045597)	2/194	0.0406	1	0	0	6.248047	20.018813	DLX1;TP63

response to gamma radiation (GO:0010332)	26-Jan	0.04205	1	0	0	23.31002	73.86577	TP63
negative regulation of catalytic activity (GO:0043086)	26-Jan	0.04205	1	0	0	23.31002	73.86577	SERPINA5
cardiac muscle cell development (GO:0055013)	27-Jan	0.04363	1	0	0	22.44669	70.300713	ACTC1
transition metal ion transport (GO:0000041)	27-Jan	0.04363	1	0	0	22.44669	70.300713	SLC39A2
modulation by host of viral transcription (GO:0043921)	27-Jan	0.04363	1	0	0	22.44669	70.300713	HPN
negative regulation of apoptotic process (GO:0043066)	3/485	0.04518	1	0	0	3.748828	11.610092	COMP;HPN;TP63
regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900739)	30-Jan	0.04837	1	0	0	20.20202	61.190341	TP63
positive regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900740)	30-Jan	0.04837	1	0	0	20.20202	61.190341	TP63
positive regulation of transcription from RNA polymerase II promoter (GO:0045944)	4/848	0.04956	1	0	0	2.858776	8.5891434	DLX1;HOXC4;SIM2;TP63
protein oligomerization (GO:0051259)	2/217	0.04965	1	0	0	5.585812	16.772506	SEMG2;SEMG1

negative regulation of BMP signaling pathway (GO:0030514)	Jan-32	0.05151	1	0	0	18.93939	56.173728	DLX1
positive regulation of Notch signaling pathway (GO:0045747)	Jan-33	0.05308	1	0	0	18.36547	53.920949	TP63
ncRNA metabolic process (GO:0034660)	Jan-34	0.05464	1	0	0	17.82531	51.817059	TDRD1
positive regulation of osteoblast differentiation (GO:0045669)	Jan-35	0.05621	1	0	0	17.31602	49.848373	TP63
cardiac muscle tissue development (GO:0048738)	Jan-36	0.05777	1	0	0	16.83502	48.002805	ACTC1
cardiac muscle tissue morphogenesis (GO:0055008)	Jan-36	0.05777	1	0	0	16.83502	48.002805	ACTC1
positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway (GO:1901030)	Jan-37	0.05932	1	0	0	16.38002	46.269637	TP63
defense response to bacterium (GO:0042742)	2/241	0.0598	1	0	0	5.029549	14.166762	SEMG2; SEMG1
actin-myosin filament sliding (GO:0033275)	Jan-38	0.06088	1	0	0	15.94896	44.639341	ACTC1
muscle filament sliding (GO:0030049)	Jan-38	0.06088	1	0	0	15.94896	44.639341	ACTC1
mitotic DNA damage checkpoint (GO:0044773)	Jan-39	0.06243	1	0	0	15.54002	43.103412	TP63
positive regulation of viral transcription (GO:0050434)	Jan-41	0.06553	1	0	0	14.78197	40.285	HPN

intrinsic apoptotic signaling pathway by p53 class mediator (GO:0072332)	Jan-43	0.06862	1	0	0	14.09443	37.762335	TP63
heart contraction (GO:0060047)	Jan-44	0.07016	1	0	0	13.7741	36.598355	ACTC1
myofibril assembly (GO:0030239)	Jan-47	0.07476	1	0	0	12.89491	33.442408	ACTC1
positive regulation of macromolecule metabolic process (GO:0010604)	2/276	0.07575	1	0	0	4.391744	11.331806	ACTC1; HPN
intrinsic apoptotic signaling pathway in response to DNA damage (GO:0008630)	Jan-48	0.07629	1	0	0	12.62626	32.489861	TP63
glutathione metabolic process (GO:0006749)	Jan-49	0.07782	1	0	0	12.36858	31.581561	GSTM1
antimicrobial humoral immune response mediated by antimicrobial peptide (GO:0061844)	Jan-49	0.07782	1	0	0	12.36858	31.581561	SEMG1
blood circulation (GO:0008015)	Jan-50	0.07934	1	0	0	12.12121	30.71464	ACTC1
heart morphogenesis (GO:0003007)	Jan-50	0.07934	1	0	0	12.12121	30.71464	ACTC1
positive regulation of ossification (GO:0045778)	Jan-52	0.08239	1	0	0	11.65501	29.094629	TP63
proteolysis (GO:0006508)	2/291	0.08297	1	0	0	4.165365	10.368844	HPN;WFDC2
negative regulation of cellular response to transforming growth factor beta stimulus (GO:1903845)	Jan-53	0.08391	1	0	0	11.43511	28.336898	DLX1

negative regulation of cellular response to growth factor stimulus (GO:0090288)	Jan-55	0.08693	1	0	0	11.01928	26.915718	DLX1
regulation of BMP signaling pathway (GO:0030510)	Jan-56	0.08845	1	0	0	10.82251	26.248626	DLX1
protein homotetramerization (GO:0051289)	Jan-57	0.08995	1	0	0	10.63264	25.608331	TP63
regulation of transcription from RNA polymerase II promoter (GO:0006357)	5/1478	0.09278	1	0	0	2.050273	4.8746678	DLX1;HOXC4;SIM2;TP63;HOXC6
negative regulation of peptidase activity (GO:0010466)	Jan-62	0.09746	1	0	0	9.775171	22.7598	SERPINA5
negative regulation of neuron differentiation (GO:0045665)	Jan-64	0.10044	1	0	0	9.469697	21.762845	DLX1
regulation of cell division (GO:0051302)	Jan-65	0.10193	1	0	0	9.324009	21.290822	TP63
cellular response to light stimulus (GO:0071482)	Jan-66	0.10342	1	0	0	9.182736	20.835276	TP63
negative regulation of epithelial cell proliferation (GO:0050680)	Jan-66	0.10342	1	0	0	9.182736	20.835276	HPN
cellular response to UV (GO:0034644)	Jan-67	0.1049	1	0	0	9.045681	20.395403	TP63
regulation of endopeptidase activity (GO:0052548)	Jan-68	0.10639	1	0	0	8.912656	19.970451	SERPINA5
regulation of epithelial to mesenchymal transition (GO:0010717)	Jan-68	0.10639	1	0	0	8.912656	19.970451	HPN

regulation of osteoblast differentiation (GO:0045667)	Jan-69	0.10787	1	0	0	8.783487	19.559715	TP63
regulation of Notch signaling pathway (GO:0008593)	Jan-70	0.10934	1	0	0	8.658009	19.162531	TP63
positive regulation of transcription, DNA-templated (GO:0045893)	4/1120	0.11076	1	0	0	2.164502	4.7626504	DLX1;HOXC4;SIM2;TP63
actomyosin structure organization (GO:0031032)	Jan-71	0.11082	1	0	0	8.536065	18.778277	ACTC1
positive regulation of growth (GO:0045927)	Jan-71	0.11082	1	0	0	8.536065	18.778277	HPN
regulation of neuron death (GO:1901214)	Jan-72	0.11229	1	0	0	8.417508	18.406364	TP63
regulation of epithelial cell proliferation (GO:0050678)	Jan-72	0.11229	1	0	0	8.417508	18.406364	HPN
negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0090101)	Jan-77	0.11962	1	0	0	7.870917	16.713654	DLX1
response to ionizing radiation (GO:0010212)	Jan-77	0.11962	1	0	0	7.870917	16.713654	TP63
extracellular matrix disassembly (GO:0022617)	Jan-78	0.12107	1	0	0	7.770008	16.405225	HPN
regulation of hydrolase activity (GO:0051336)	Jan-80	0.12398	1	0	0	7.575758	15.815198	SERPINA5
sensory perception of sound (GO:0007605)	Jan-81	0.12543	1	0	0	7.48223	15.532878	HPN

epidermis development (GO:0008544)	Jan-81	0.12543	1	0	0	7.48223	15.532878	KRT5
positive regulation of protein secretion (GO:0050714)	Jan-82	0.12688	1	0	0	7.390983	15.258568	OR51E2
DNA damage response, signal transduction by p53 class mediator (GO:0030330)	Jan-82	0.12688	1	0	0	7.390983	15.258568	TP63
negative regulation of endopeptidase activity (GO:0010951)	Jan-83	0.12833	1	0	0	7.301935	14.991954	SERPINA5
positive regulation of gene expression (GO:0010628)	3/771	0.13306	1	0	0	2.358212	4.7563433	ACTC1;HPN;TP63
cellular response to BMP stimulus (GO:0071773)	Jan-87	0.13409	1	0	0	6.966214	13.996649	DLX1
divalent metal ion transport (GO:0070838)	Jan-88	0.13553	1	0	0	6.887052	13.764287	SLC39A2
regulation of neuron apoptotic process (GO:0043523)	Jan-89	0.13696	1	0	0	6.80967	13.538025	TP63
protein tetramerization (GO:0051262)	Jan-90	0.13839	1	0	0	6.734007	13.317639	TP63
cellular response to acid chemical (GO:0071229)	Jan-91	0.13982	1	0	0	6.660007	13.102918	OR51E2
positive regulation of cellular metabolic process (GO:0031325)	Jan-92	0.14125	1	0	0	6.587615	12.893659	HPN
skin development (GO:0043588)	Jan-94	0.14409	1	0	0	6.447453	12.490764	TP63
positive regulation of protein localization to membrane (GO:1905477)	Jan-95	0.14551	1	0	0	6.379585	12.296767	TP63

negative regulation of cell motility (GO:2000146)	Jan-97	0.14834	1	0	0	6.248047	11.922832	SEMG1
positive regulation of neuron differentiation (GO:0045666)	Jan-98	0.14975	1	0	0	6.184292	11.742579	DLX1
positive regulation of cell growth (GO:0030307)	Jan-98	0.14975	1	0	0	6.184292	11.742579	HPN
response to UV (GO:0009411)	Jan-98	0.14975	1	0	0	6.184292	11.742579	TP63
regulation of apoptotic process (GO:0042981)	3/815	0.14989	1	0	0	2.230898	4.2339671	COMP;HPN;TP63
cellular response to transforming growth factor beta stimulus (GO:0071560)	1/100	0.15257	1	0	0	6.060606	11.394765	DLX1
peptide metabolic process (GO:0006518)	1/104	0.15818	1	0	0	5.827506	10.746161	GSTM1
positive regulation of epithelial cell proliferation (GO:0050679)	1/107	0.16236	1	0	0	5.664118	10.297057	HPN
negative regulation of hydrolase activity (GO:0051346)	1/108	0.16375	1	0	0	5.611672	10.153891	SERPINA5
positive regulation of establishment of protein localization to mitochondrion (GO:1903749)	1/110	0.16652	1	0	0	5.509642	9.8767739	TP63
cellular response to oxidative stress (GO:0034599)	1/115	0.17341	1	0	0	5.270092	9.2336221	GPX2
actin filament organization (GO:0007015)	1/120	0.18025	1	0	0	5.050505	8.6535986	ACTC1
regulation of cell differentiation (GO:0045595)	1/121	0.18161	1	0	0	5.008765	8.5444109	DLX1

sulfur compound biosynthetic process (GO:0044272)	1/122	0.18297	1	0	0	4.96771	8.4373514	GSTM1
negative regulation of multicellular organismal process (GO:0051241)	1/125	0.18703	1	0	0	4.848485	8.1283788	HPN
muscle contraction (GO:0006936)	1/137	0.20309	1	0	0	4.4238	7.052076	ACTC1
regulation of signal transduction by p53 class mediator (GO:1901796)	1/138	0.20441	1	0	0	4.391744	6.972436	TP63
cellular response to growth factor stimulus (GO:0071363)	1/139	0.20573	1	0	0	4.360148	6.8941701	DLX1
inorganic cation transmembrane transport (GO:0098662)	1/140	0.20705	1	0	0	4.329004	6.8172455	SLC39A2
positive regulation of cellular process (GO:0048522)	2/519	0.21082	1	0	0	2.335494	3.6357543	DLX1;HPN
skeletal system development (GO:0001501)	1/146	0.21493	1	0	0	4.1511	6.3821553	COMP
negative regulation of cell differentiation (GO:0045596)	1/150	0.22013	1	0	0	4.040404	6.1152452	HPN
negative regulation of transcription from RNA polymerase II promoter (GO:0000122)	2/565	0.23892	1	0	0	2.145347	3.0713273	DLX1;TP63
cellular response to lipid (GO:0071396)	1/178	0.25566	1	0	0	3.404835	4.643936	OR51E2
organonitrogen compound biosynthetic process (GO:1901566)	1/181	0.25937	1	0	0	3.348401	4.5187024	GSTM1

protein homooligomerization (GO:0051260)	1/190	0.27039	1	0	0	3.189793	4.1718434	TP63
regulation of cell growth (GO:0001558)	1/201	0.28366	1	0	0	3.015227	3.7991602	HPN
positive regulation of multicellular organismal process (GO:0051240)	1/202	0.28485	1	0	0	3.0003	3.7677501	HPN
positive regulation of signal transduction (GO:0009967)	1/206	0.28961	1	0	0	2.942042	3.6458677	TP63
extracellular matrix organization (GO:0030198)	1/229	0.31637	1	0	0	2.646553	3.0457851	COMP
apoptotic process (GO:0006915)	1/231	0.31865	1	0	0	2.623639	3.0005722	TP63
regulation of programmed cell death (GO:0043067)	1/268	0.35953	1	0	0	2.26142	2.313359	TP63
cellular response to oxygen-containing compound (GO:1901701)	1/274	0.36593	1	0	0	2.2119	2.2236686	OR51E2
negative regulation of transcription, DNA-templated (GO:0045892)	2/813	0.39035	1	0	0	1.490924	1.4025394	DLX1;TP63
positive regulation of apoptotic process (GO:0043065)	1/307	0.40004	1	0	0	1.974139	1.8086973	TP63
negative regulation of cell proliferation (GO:0008285)	1/363	0.45389	1	0	0	1.669588	1.3187992	HPN
transmembrane receptor protein tyrosine kinase signaling pathway (GO:0007169)	1/396	0.4834	1	0	0	1.530456	1.1125026	HPN

regulation of transcription, DNA-templated (GO:0006355)	3/1598	0.49746	1	0	0	1.137786	0.7944509	SIM2;TP63;HOXC6
regulation of intracellular signal transduction (GO:1902531)	1/422	0.50555	1	0	0	1.436163	0.9796044	TP63
regulation of gene expression (GO:0010468)	2/1037	0.5162	1	0	0	1.168873	0.7729199	ACTC1;HPN
negative regulation of nucleic acid-templated transcription (GO:1903507)	1/444	0.52358	1	0	0	1.365001	0.8832485	TP63
nervous system development (GO:0007399)	1/455	0.53235	1	0	0	1.332001	0.8397655	SIM2
cellular protein metabolic process (GO:0044267)	1/484	0.55473	1	0	0	1.252191	0.7378823	SEMG1
positive regulation of nucleic acid-templated transcription (GO:1903508)	1/502	0.5681	1	0	0	1.207292	0.6826819	TP63
negative regulation of cellular macromolecule biosynthetic process (GO:2000113)	1/512	0.57535	1	0	0	1.183712	0.6543248	TP63
negative regulation of gene expression (GO:0010629)	1/618	0.64535	1	0	0	0.980681	0.4294996	TP63

Term	**Overlap**	**P-value**	**Adjusted P-value**	**Old P-value**	**Old Adjusted P-**	**Odds Ratio**	**Combined Score**	**Genes**
								IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV

t activation, classical pathway (GO:0006958)	24/123	1.99E-48	1.01E-44	0	0	125.88513	13826.79	3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-39;IGHV3-
humoral immune response mediated by circulating immunoglobulin (GO:0002455)	24/125	3.05E-48	7.78E-45	0	0	123.87097	13552.58	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-39;IGHV3-
regulation of protein activation cascade (GO:2000257)	18/108	6.67E-34	1.13E-30	0	0	107.52688	8214.042	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-

regulation of complement activation (GO:0030449)	18/109	7.98E-34	1.02E-30	0	0	106.5404	8119.519	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
regulation of humoral immune response (GO:0002920)	18/113	1.61E-33	1.64E-30	0	0	102.76906	7759.967	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
regulation of immune effector process (GO:0002697)	18/114	1.91E-33	1.63E-30	0	0	101.86757	7674.453	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
								IGHV3-30;IGHV3-

								11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
regulation of acute inflammatory response (GO:0002673)	18/121	6.06E-33	4.42E-30	0	0	95.974407	7119.651	
regulation of protein processing (GO:0070613)	18/128	1.79E-32	1.14E-29	0	0	90.725806	6631.906	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
Fc-gamma receptor signaling pathway involved in phagocytosis (GO:0038096)	18/133	3.75E-32	2.12E-29	0	0	87.315062	6318.314	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
								IGHV3-30;IGHV3-11;IGHV3-33;IGHV

receptor signaling pathway (GO:0038094)	18/134	4.32E-32	2.21E-29	0	0	86.663457	6258.714	1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
Fc receptor mediated stimulatory signaling pathway (GO:0002431)	18/135	4.99E-32	2.31E-29	0	0	86.021505	6200.096	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
Fc-epsilon receptor signaling pathway (GO:0038095)	18/182	1.44E-29	6.12E-27	0	0	63.807161	4237.495	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
								IGHV3-30;IGHV3-11;IGHV3-33;IGHV

Fc receptor signaling pathway (GO:0038093)	18/183	1.60E-29	6.26E-27	0	0	63.458488	4207.808	1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
receptor-mediated endocytosis (GO:0006898)	18/188	2.65E-29	9.64E-27	0	0	61.770762	4064.65	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
regulation of immune response (GO:0050776)	18/251	5.74E-27	1.95E-24	0	0	46.266547	2795.553	IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
								IGHV3-30;IGHV3-11;IGHV3-33;IGHV1-

endocytosis (GO:0006897)	18/263	1.36E-26	4.33E-24	0	0	44.155526	2629.922	2;IGHV4-34;IGHV3-23;IGKV1-5;IGHV4-59;IGLV3-1;IGHV1-46;IGHV4-
regulation of B cell activation (GO:0050864)	14/95	2.71E-25	8.14E-23	0	0	95.076401	5378.171	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
plasma membrane invagination (GO:0099024)	14/103	9.07E-25	2.57E-22	0	0	87.691826	4854.555	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
positive regulation of lymphocyte activation (GO:0051251)	14/104	1.05E-24	2.81E-22	0	0	86.848635	4795.388	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
								IGHV5-51;IGHV3-30;IGHV

B cell receptor signaling pathway (GO:0050853)	14/104	1.05E-24	2.67E-22	0	0	86.848635	4795.388	3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
phagocytosis, engulfment (GO:0006911)	14/104	1.05E-24	2.55E-22	0	0	86.848635	4795.388	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
positive regulation of B cell activation (GO:0050871)	14/119	7.70E-24	1.79E-21	0	0	75.901328	4039.539	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
phagocytosis (GO:0006909)	14/135	4.90E-23	1.09E-20	0	0	66.905615	3436.931	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
								IGHV5-51;IGHV3-30;IGHV

defense response to bacterium (GO:0042742)	15/241	2.68E-21	5.69E-19	0	0	40.155267	1902.168	3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-59;IGHV
antigen receptor-mediated signaling pathway (GO:0050851)	14/257	5.12E-19	1.04E-16	0	0	35.144973	1480.187	IGHV5-51;IGHV3-30;IGHV3-21;IGHV3-11;IGHV3-33;IGHV1-2;IGHV3-23;IGHV4-
glomerular filtration (GO:000309	10-Jan	0.015396	1	0	0	64.516129	269.2691	IGKV3-20
renal filtration	11-Jan	0.016923	1	0	0	58.651026	239.2439	IGKV3-20
antibacterial humoral response	Jan-35	0.052888	1	0	0	18.43318	54.18574	IGKV3-20
negative regulation of nucleic acid-templated transcriptio	1/444	0.501664	1	0	0	1.453066	1.00236	ZBED6
negative regulation of cellular macromolecule biosynthetic process	1/512	0.552708	1	0	0	1.2600806	0.747133	ZBED6
negative regulation of gene expression	1/618	0.622336	1	0	0	1.0439503	0.495119	ZBED6
negative regulation of transcription, DNA-	1/813	0.724029	1	0	0	0.7935563	0.256258	ZBED6

regulation of transcription from RNA polymerase II promoter	1/1478	0.907616	1	0	0	0.4365097	0.042312	ZBED6
regulation of transcription, DNA-	1/1598	0.924488	1	0	0	0.4037305	0.031699	ZBED6

Term	Overlap	P-value	Adjusted P-value	Old P-value	Old Adjusted P-	Odds Ratio	Combined Score	Genes
regulation of B cell activation (GO:0050864)	Sep-95	7.73E-15	3.94E-11	0	0	65.3358	2123.018	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
plasma membrane invagination (GO:0099024)	9/103	1.64E-14	4.18E-11	0	0	60.2611	1912.826	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
positive regulation of lymphocyte activation (GO:0051251)	9/104	1.79E-14	3.05E-11	0	0	59.6817	1889.085	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
phagocytosis, engulfment (GO:0006911)	9/104	1.79E-14	2.29E-11	0	0	59.6817	1889.085	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
B cell receptor signaling pathway (GO:0050853)	9/104	1.79E-14	1.83E-11	0	0	59.6817	1889.085	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2

positive regulation of B cell activation (GO:0050871)	9/119	6.23E-14	5.29E-11	0	0	52.1588	1586.024	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
complement activation, classical pathway (GO:0006958)	9/123	8.44E-14	6.15E-11	0	0	50.4626	1519.092	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
humoral immune response mediated by circulating immunoglobulin (GO:0002455)	9/125	9.79E-14	6.24E-11	0	0	49.6552	1487.424	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
phagocytosis (GO:0006909)	9/135	1.98E-13	1.12E-10	0	0	45.977	1344.788	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2
defense response to bacterium (GO:0042742)	10/241	8.77E-13	4.48E-10	0	0	28.6164	794.4509	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2;LTF
antigen receptor-mediated signaling pathway (GO:0050851)	9/257	6.64E-11	3.08E-08	0	0	24.1513	565.9778	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;IGLC2;IGHA1;IGHA2

retina homeostasis (GO:0001895)	May-38	2.16E-09	9.20E-07	0	0	90.7441	1810.491	IGHG3;IGKC;IGHA1;IGHA2;LTF
antibacterial humoral response (GO:0019731)	Apr-35	1.81E-07	7.10E-05	0	0	78.8177	1223.681	IGHM;IGHA1;IGHA2;LTF
regulation of protein activation cascade (GO:2000257)	4/108	1.72E-05	0.006273	0	0	25.5428	280.2054	IGHG3;IGHG4;IGHG2;IGKC
regulation of complement activation (GO:0030449)	4/109	1.78E-05	0.006072	0	0	25.3084	276.7138	IGHG3;IGHG4;IGHG2;IGKC
regulation of humoral immune response (GO:0002920)	4/113	2.06E-05	0.006562	0	0	24.4126	263.4484	IGHG3;IGHG4;IGHG2;IGKC
regulation of immune effector process (GO:0002697)	4/114	2.13E-05	0.006394	0	0	24.1984	260.2973	IGHG3;IGHG4;IGHG2;IGKC
regulation of acute inflammatory response (GO:0002673)	4/121	2.69E-05	0.007634	0	0	22.7985	239.8931	IGHG3;IGHG4;IGHG2;IGKC

regulation of protein processing (GO:0070613)	4/128	3.36E-05	0.009019	0	0	21.5517	222.0171	IGHG3;IGHG4;IGHG2;IGKC
Fc-gamma receptor signaling pathway involved in phagocytosis (GO:0038096)	4/133	3.90E-05	0.009955	0	0	20.7415	210.5579	IGHG3;IGHG4;IGHG2;IGKC
Fc-gamma receptor signaling pathway (GO:0038094)	4/134	4.02E-05	0.009763	0	0	20.5867	208.3833	IGHG3;IGHG4;IGHG2;IGKC
Fc receptor mediated stimulatory signaling pathway (GO:0002431)	4/135	4.14E-05	0.009594	0	0	20.4342	206.2455	IGHG3;IGHG4;IGHG2;IGKC
positive regulation of respiratory burst (GO:0060267)	08-Feb	5.65E-05	0.012543	0	0	172.414	1686.322	IGHA1;IGHA2
regulation of respiratory burst (GO:0060263)	10-Feb	9.07E-05	0.019284	0	0	137.931	1283.863	IGHA1;IGHA2

glomerular filtration (GO:0003094)	10-Feb	9.07E-05	0.018513	0	0	137.931	1283.863	IGHA1;IGHA2
renal filtration (GO:0097205)	11-Feb	1.11E-04	0.021737	0	0	125.392	1142.098	IGHA1;IGHA2
receptor-mediated endocytosis (GO:0006898)	4/188	1.49E-04	0.02824	0	0	14.6735	129.2556	IGKC;SAA1;IGHA1;IGHA2
positive regulation of metabolic process (GO:0009893)	18-Feb	3.06E-04	0.055797	0	0	76.6284	620.0321	IGHA1;IGHA2
endocytosis (GO:0006897)	4/263	5.36E-04	0.094284	0	0	10.4891	79.00078	IGKC;SAA1;IGHA1;IGHA2
defense response to Gram-negative bacterium (GO:0050829)	Feb-71	0.004742	0.806543	0	0	19.4269	103.9609	IGHM;LTF
epidermis development (GO:0008544)	Feb-81	0.006127	1	0	0	17.0285	86.76096	KRT17;KRT15
regulation of osteoclast development (GO:2001204)	06-Jan	0.00867	1	0	0	114.943	545.7406	LTF

positive regulation of osteoblast proliferation (GO:0033690)	06-Jan	0.00867	1	0	0	114.943	545.7406	LTF
negative regulation of response to external stimulus (GO:0032102)	2/107	0.010478	1	0	0	12.8908	58.76237	SAA1;LTF
positive regulation of toll-like receptor 4 signaling pathway (GO:0034145)	08-Jan	0.011543	1	0	0	86.2069	384.6258	LTF
regulation of interleukin-1 secretion (GO:0050704)	09-Jan	0.012977	1	0	0	76.6284	332.9176	SAA1
membrane disruption in other organism (GO:0051673)	09-Jan	0.012977	1	0	0	76.6284	332.9176	LTF
macrophage migration (GO:1905517)	10-Jan	0.014409	1	0	0	68.9655	292.4078	SAA1

macrophage chemotaxis (GO:0048246)	10-Jan	0.014409	1	0	0	68.9655	292.4078	SAA1
negative regulation of lipopolysaccharide-mediated signaling pathway (GO:0031665)	10-Jan	0.014409	1	0	0	68.9655	292.4078	LTF
negative regulation by host of viral process (GO:0044793)	10-Jan	0.014409	1	0	0	68.9655	292.4078	LTF
modulation by host of viral process (GO:0044788)	11-Jan	0.015839	1	0	0	62.6959	259.8935	LTF
positive regulation of interleukin-1 production (GO:0032732)	12-Jan	0.017266	1	0	0	57.4713	233.2752	SAA1
negative regulation of ATPase activity (GO:0032780)	12-Jan	0.017266	1	0	0	57.4713	233.2752	LTF

regulation of peptide secretion (GO:0002791)	15-Jan	0.021538	1	0	0	45.977	176.457	SAA1
regulation of toll-like receptor 4 signaling pathway (GO:0034143)	16-Jan	0.022958	1	0	0	43.1034	162.6767	LTF
regulation of osteoblast proliferation (GO:0033688)	16-Jan	0.022958	1	0	0	43.1034	162.6767	LTF
bone morphogenesis (GO:0060349)	16-Jan	0.022958	1	0	0	43.1034	162.6767	LTF
negative regulation of cell development (GO:0010721)	17-Jan	0.024376	1	0	0	40.568	150.6764	LTF
defense response to fungus (GO:0050832)	17-Jan	0.024376	1	0	0	40.568	150.6764	LTF
negative regulation of osteoclast differentiation (GO:0045671)	18-Jan	0.025791	1	0	0	38.3142	140.1422	LTF

regulation of lipopolysaccharide-mediated signaling pathway (GO:0031664)	18-Jan	0.025791	1	0	0	38.3142	140.1422	LTF
regulation of viral process (GO:0050792)	18-Jan	0.025791	1	0	0	38.3142	140.1422	LTF
acute-phase response (GO:0006953)	18-Jan	0.025791	1	0	0	38.3142	140.1422	SAA1
positive regulation of toll-like receptor signaling pathway (GO:0034123)	19-Jan	0.027205	1	0	0	36.2976	130.8291	LTF
innate immune response in mucosa (GO:0002227)	19-Jan	0.027205	1	0	0	36.2976	130.8291	LTF
negative regulation of response to biotic stimulus (GO:0002832)	19-Jan	0.027205	1	0	0	36.2976	130.8291	LTF

negative regulation of viral process (GO:0048525)	21-Jan	0.030027	1	0	0	32.8407	115.1282	LTF
mucosal immune response (GO:0002385)	24-Jan	0.034245	1	0	0	28.7356	96.96019	LTF
regulation of protein transport (GO:0051223)	27-Jan	0.038445	1	0	0	25.5428	83.23172	SAA1
acute inflammatory response (GO:0002526)	28-Jan	0.039841	1	0	0	24.6305	79.38056	SAA1
positive regulation of interleukin-1 secretion (GO:0050716)	29-Jan	0.041235	1	0	0	23.7812	75.82535	SAA1
negative regulation of tumor necrosis factor superfamily cytokine production (GO:1903556)	31-Jan	0.044018	1	0	0	22.2469	69.48069	LTF

regulation of cytokine secretion (GO:0050707)	31-Jan	0.044018	1	0	0	22.2469	69.48069	SAA1
positive regulation of bone mineralization (GO:0030501)	31-Jan	0.044018	1	0	0	22.2469	69.48069	LTF
skeletal system morphogenesis (GO:0048705)	31-Jan	0.044018	1	0	0	22.2469	69.48069	LTF
negative regulation of multi-organism process (GO:0043901)	Jan-33	0.046793	1	0	0	20.8986	63.99223	LTF
bone development (GO:0060348)	Jan-34	0.048177	1	0	0	20.284	61.51868	LTF
positive regulation of osteoblast differentiation (GO:0045669)	Jan-35	0.04956	1	0	0	19.7044	59.20353	LTF
endothelial cell migration (GO:0043542)	Jan-35	0.04956	1	0	0	19.7044	59.20353	S100A2

regulation of cysteine-type endopeptidase activity (GO:2000116)	Jan-36	0.05094	1	0	0	19.1571	57.03264	LTF
epithelial cell migration (GO:0010631)	Jan-36	0.05094	1	0	0	19.1571	57.03264	S100A2
regulation of ATPase activity (GO:0043462)	Jan-40	0.056443	1	0	0	17.2414	49.56075	LTF
lymphocyte chemotaxis (GO:0048247)	Jan-44	0.061915	1	0	0	15.674	43.60488	SAA1
antimicrobial humoral immune response mediated by antimicrobial peptide (GO:0061844)	Jan-49	0.068712	1	0	0	14.0746	37.68938	LTF
negative regulation of viral genome replication (GO:0045071)	Jan-50	0.070066	1	0	0	13.7931	36.6665	LTF

positive regulation of ossification (GO:0045778)	Jan-52	0.072767	1	0	0	13.2626	34.75447	LTF	
neutrophil chemotaxis (GO:0030593)	Jan-53	0.074115	1	0	0	13.0124	33.85988	SAA1	
granulocyte chemotaxis (GO:0071621)	Jan-56	0.078148	1	0	0	12.3153	31.39348	SAA1	
regulation of secretion by cell (GO:1903530)	Jan-56	0.078148	1	0	0	12.3153	31.39348	SAA1	
neutrophil migration (GO:1990266)	Jan-58	0.080827	1	0	0	11.8906	29.91015	SAA1	
cell chemotaxis (GO:0060326)	Jan-60	0.083499	1	0	0	11.4943	28.53939	SAA1	
negative regulation of viral life cycle (GO:1903901)	Jan-61	0.084831	1	0	0	11.3058	27.89247	LTF	
regulation of tumor necrosis factor production (GO:0032680)	Jan-61	0.084831	1	0	0	11.3058	27.89247	LTF	

regulation of viral genome replication (GO:0045069)	Jan-63	0.087492	1	0	0	10.9469	26.66899	LTF
positive regulation of cell adhesion (GO:0045785)	Jan-64	0.088819	1	0	0	10.7759	26.09003	SAA1
regulation of osteoblast differentiation (GO:0045667)	Jan-69	0.095428	1	0	0	9.995	23.48213	LTF
negative regulation of cysteine-type endopeptidase activity (GO:2000117)	Jan-72	0.099371	1	0	0	9.57854	22.11589	LTF
positive regulation of cytokine secretion (GO:0050715)	Jan-73	0.100681	1	0	0	9.44733	21.68914	SAA1
negative regulation of inflammatory response (GO:0050728)	Jan-78	0.107207	1	0	0	8.84173	19.74355	SAA1

regulation of protein serine/threonine kinase activity (GO:0071900)	Jan-80	0.109804	1	0	0	8.62069	19.04359	LTF
negative regulation of defense response (GO:0031348)	Jan-80	0.109804	1	0	0	8.62069	19.04359	SAA1
positive regulation of protein secretion (GO:0050714)	Jan-82	0.112394	1	0	0	8.41043	18.38303	SAA1
negative regulation of endopeptidase activity (GO:0010951)	Jan-83	0.113687	1	0	0	8.3091	18.06655	LTF
cellular response to cytokine stimulus (GO:0071345)	2/456	0.140982	1	0	0	3.0248	5.925972	IGHG4;SAA1
regulation of protein secretion (GO:0050708)	1/107	0.144163	1	0	0	6.44538	12.48347	SAA1

negative regulation of hydrolase activity (GO:0051346)	1/108	0.145411	1	0	0	6.3857	12.31286	LTF
regulation of cytokine production (GO:0001817)	1/108	0.145411	1	0	0	6.3857	12.31286	LTF
negative regulation of cell growth (GO:0030308)	1/115	0.154095	1	0	0	5.997	11.21551	SCGB3A1
cellular protein metabolic process (GO:0044267)	2/484	0.155045	1	0	0	2.84981	5.312168	SAA1;LTF
activation of MAPK activity (GO:0000187)	1/117	0.156561	1	0	0	5.89449	10.93022	SAA1
positive regulation of protein serine/threonine kinase activity (GO:0071902)	1/118	0.157791	1	0	0	5.84454	10.79185	LTF
negative regulation of growth (GO:0045926)	1/120	0.160246	1	0	0	5.74713	10.52325	SCGB3A1

positive regulation of NF-kappaB transcription factor activity (GO:0051092)	1/128	0.169998	1	0	0	5.38793	9.547253	LTF
positive regulation of cytosolic calcium ion concentration (GO:0007204)	1/133	0.176037	1	0	0	5.18538	9.007318	SAA1
regulation of cytosolic calcium ion concentration (GO:0051480)	1/137	0.180838	1	0	0	5.03398	8.608884	SAA1
positive regulation of I-kappaB kinase/NF-kappaB signaling (GO:0043123)	1/163	0.211391	1	0	0	4.23101	6.575186	LTF
regulation of inflammatory response (GO:0050727)	1/166	0.214845	1	0	0	4.15455	6.389028	SAA1

positive regulation of protein kinase activity (GO:0045860)	1/172	0.221709	1	0	0	4.00962	6.040061	LTF
positive regulation of MAP kinase activity (GO:0043406)	1/177	0.227384	1	0	0	3.89636	5.770951	SAA1
Fc-epsilon receptor signaling pathway (GO:0038095)	1/182	0.23302	1	0	0	3.78931	5.519638	IGKC
cytokine-mediated signaling pathway (GO:0019221)	2/633	0.233501	1	0	0	2.17901	3.169512	IGHG4;SAA1
Fc receptor signaling pathway (GO:0038093)	1/183	0.234142	1	0	0	3.76861	5.471368	IGKC
positive regulation of cell differentiation (GO:0045597)	1/194	0.246383	1	0	0	3.55492	4.979972	LTF
regulation of cell growth (GO:0001558)	1/201	0.254075	1	0	0	3.43112	4.701068	SCGB3A1

regulation of I-kappaB kinase/NF-kappaB signaling (GO:0043122)	1/204	0.257348	1	0	0	3.38066	4.588662	LTF
positive regulation of sequence-specific DNA binding transcription factor activity (GO:0051091)	1/215	0.269231	1	0	0	3.2077	4.209095	LTF
positive regulation of cytokine production (GO:0001819)	1/220	0.274572	1	0	0	3.1348	4.05186	SAA1
activation of protein kinase activity (GO:0032147)	1/233	0.288281	1	0	0	2.95989	3.681573	SAA1
regulation of immune response (GO:0050776)	1/251	0.306851	1	0	0	2.74763	3.246029	IGKC
negative regulation of signal transduction (GO:0009968)	1/283	0.338716	1	0	0	2.43694	2.63822	LTF

negative regulation of programmed cell death (GO:0043069)	1/408	0.450166	1	0	0	1.69033	1.349117	LTF
positive regulation of cell proliferation (GO:0008284)	1/424	0.46305	1	0	0	1.62655	1.252312	LTF
neutrophil degranulation (GO:0043312)	1/479	0.50515	1	0	0	1.43978	0.983228	LTF
positive regulation of intracellular signal transduction (GO:1902533)	1/479	0.50515	1	0	0	1.43978	0.983228	LTF
neutrophil activation involved in immune response (GO:0002283)	1/483	0.508084	1	0	0	1.42786	0.966815	LTF
negative regulation of apoptotic process (GO:0043066)	1/485	0.509545	1	0	0	1.42197	0.958746	LTF

neutrophil mediated immunity (GO:0002446)	1/487	0.511001	1	0	0	1.41613	0.950766	LTF
negative regulation of cellular process (GO:0048523)	1/534	0.544054	1	0	0	1.29149	0.786139	SCGB3A1
regulation of cell proliferation (GO:0042127)	1/740	0.66517	1	0	0	0.93197	0.379975	SCGB3A1
regulation of apoptotic process (GO:0042981)	1/815	0.701015	1	0	0	0.8462	0.300593	LTF

Data S1: Enrichment analysis for Biological Process using the tool Enrich.

Data S2

Data S2	Enrichment analysis for Biological Pathways using the tool Enrich
Reactome_2016	
Tab Content:	
Tab 1	PC1
Tab 2	PC2
Tab 3	PC3

Term	**Overlap**	**P-value**	**Adjusted P-value**	**Old P-value**	**Old Adjusted P-value**	**Odds Ratio**	**Combined Score**	**Genes**
Signaling by MST1 Homo sapiens R-HSA-8852405	05-Jan	0.008224	1	0	0	121.21212	581.9095	HPN

TP53 Regulates Metabolic Genes Homo sapiens R-HSA-5628897	Feb-84	0.008458	1	0	0	14.430014	68.8694	GPX2;TP63
Synthesis of 5-eicosatetraenoic acids Homo sapiens R-HSA-2142688	06-Jan	0.00986	1	0	0	101.0101	466.589	GPX2
Synthesis of 15-eicosatetraenoic acid derivatives Homo sapiens R-HSA-2142770	06-Jan	0.00986	1	0	0	101.0101	466.589	GPX2
Synthesis of 12-eicosatetraenoic acid derivatives Homo sapiens R-HSA-2142712	06-Jan	0.00986	1	0	0	101.0101	466.589	GPX2
Activation of PUMA and translocation to mitochondria Homo sapiens R-HSA-139915	08-Jan	0.013126	1	0	0	75.757576	328.2687	TP63
Zinc influx into cells by the SLC39 gene family Homo sapiens R-HSA-442380	10-Jan	0.016382	1	0	0	60.606061	249.1879	SLC39A2

TP53 Regulates Transcription of Caspase Activators and Caspases Homo sapiens R-HSA-6803207	12-Jan	0.019626	1	0	0	50.505051	198.529	TP63
TP53 Regulates Transcription of Death Receptors and Ligands Homo sapiens R-HSA-6803211	12-Jan	0.019626	1	0	0	50.505051	198.529	TP63
Regulation of TP53 Activity through Association with Co-factors Homo sapiens R-HSA-6804759	14-Jan	0.022861	1	0	0	43.290043	163.5636	TP63
TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain Homo sapiens R-HSA-6803205	14-Jan	0.022861	1	0	0	43.290043	163.5636	TP63
Zinc transporters Homo sapiens R-HSA-435354	17-Jan	0.027694	1	0	0	35.650624	127.863	SLC39A2

TP53 Regulates Transcription of Genes Involved in Cytochrome C Release Homo sapiens R-HSA-6803204	19-Jan	0.030902	1	0	0	31.897927	110.9067	TP63
Common Pathway of Fibrin Clot Formation Homo sapiens R-HSA-140875	22-Jan	0.035696	1	0	0	27.548209	91.81023	SERPINA5
Intrinsic Pathway of Fibrin Clot Formation Homo sapiens R-HSA-140837	22-Jan	0.035696	1	0	0	27.548209	91.81023	SERPINA5
Metal ion SLC transporters Homo sapiens R-HSA-425410	25-Jan	0.040467	1	0	0	24.242424	77.75191	SLC39A2
Activation of BH3-only proteins Homo sapiens R-HSA-114452	29-Jan	0.046793	1	0	0	20.898642	63.99223	TP63
PIWI-interacting RNA (piRNA) biogenesis Homo sapiens R-HSA-5601884	29-Jan	0.046793	1	0	0	20.898642	63.99223	TDRD1

Detoxification of Reactive Oxygen Species Homo sapiens R-HSA-3299685	Jan-33	0.053078	1	0	0	18.365473	53.92095	GPX2
Glutathione conjugation Homo sapiens R-HSA-156590	Jan-38	0.060878	1	0	0	15.948963	44.63934	GSTM1
Formation of Fibrin Clot (Clotting Cascade) Homo sapiens R-HSA-140877	Jan-39	0.06243	1	0	0	15.540016	43.10341	SERPINA5
Intrinsic Pathway for Apoptosis Homo sapiens R-HSA-109606	Jan-42	0.067073	1	0	0	14.430014	38.98955	TP63
TP53 Regulates Transcription of Cell Death Genes Homo sapiens R-HSA-5633008	Jan-43	0.068615	1	0	0	14.094433	37.76233	TP63
Arachidonic acid metabolism Homo sapiens R-HSA-2142753	Jan-53	0.083906	1	0	0	11.435106	28.3369	GPX2
ECM proteoglycans Homo sapiens R-HSA-3000178	Jan-55	0.086934	1	0	0	11.019284	26.91572	COMP

Integrin cell surface interactions Homo sapiens R-HSA-216083	Jan-67	0.104904	1	0	0	9.0456807	20.3954	COMP
Amyloid fiber formation Homo sapiens R-HSA-977225	Jan-68	0.106386	1	0	0	8.912656	19.97045	SEMG1
Transcriptional Regulation by TP53 Homo sapiens R-HSA-3700989	2/348	0.112134	1	0	0	3.4831069	7.62124	GPX2;TP63
Activation of anterior HOX genes in hindbrain development during early embryogenesis Homo sapiens R-HSA-5617472	Jan-89	0.136961	1	0	0	6.8096697	13.53802	HOXC4
Activation of HOX genes during differentiation Homo sapiens R-HSA-5619507	Jan-89	0.136961	1	0	0	6.8096697	13.53802	HOXC4
Phase II conjugation Homo sapiens R-HSA-156580	1/100	0.152569	1	0	0	6.0606061	11.39477	GSTM1

Transport of glucose and other sugars, bile salts and organic acids, metal ions and amine compounds Homo sapiens R-HSA-425366	1/101	0.153975	1	0	0	6.0006001	11.22693	SLC39A2
Gene Silencing by RNA Homo sapiens R-HSA-211000	1/101	0.153975	1	0	0	6.0006001	11.22693	TDRD1
Regulation of TP53 Activity Homo sapiens R-HSA-5633007	1/151	0.22143	1	0	0	4.0136464	6.051177	TP63
Apoptosis Homo sapiens R-HSA-109581	1/163	0.236825	1	0	0	3.7181632	5.355761	TP63
Programmed Cell Death Homo sapiens R-HSA-5357801	1/166	0.240628	1	0	0	3.6509675	5.200813	TP63
Biological oxidations Homo sapiens R-HSA-211859	1/199	0.281263	1	0	0	3.0455307	3.863152	GSTM1
SLC-mediated transmembrane transport Homo sapiens R-HSA-425407	1/268	0.359527	1	0	0	2.2614202	2.313359	SLC39A2

Extracellular matrix organization Homo sapiens R-HSA-1474244	1/283	0.375412	1	0	0	2.1415569	2.098148	COMP
Generic Transcription Pathway Homo sapiens R-HSA-212436	2/812	0.389754	1	0	0	1.4927601	1.406538	GPX2;TP63
Cellular responses to stress Homo sapiens R-HSA-2262752	1/367	0.457555	1	0	0	1.6513913	1.291156	GPX2
Olfactory Signaling Pathway Homo sapiens R-HSA-381753	1/418	0.502208	1	0	0	1.4499058	0.998611	OR51E2
Gene Expression Homo sapiens R-HSA-74160	3/1631	0.511556	1	0	0	1.1147651	0.747225	TDRD1;GPX2;TP63
Hemostasis Homo sapiens R-HSA-109582	1/552	0.603212	1	0	0	1.0979359	0.554992	SERPINA5
Transmembrane transport of small molecules Homo sapiens R-HSA-382551	1/594	0.630556	1	0	0	1.0203041	0.470517	SLC39A2
Metabolism of lipids and lipoproteins Homo sapiens R-HSA-556833	1/659	0.669307	1	0	0	0.9196671	0.369257	GPX2

Developmental Biology Homo sapiens R-HSA-1266738	1/786	0.733971	1	0	0	0.7710695	0.238481	HOXC4
GPCR downstream signaling Homo sapiens R-HSA-388396	1/983	0.81072	1	0	0	0.6165418	0.129371	OR51E2
Metabolism Homo sapiens R-HSA-1430728	Feb-08	0.83641	1	0	0	0.6352837	0.113485	GPX2; GSTM1
Metabolism of proteins Homo sapiens R-HSA-392499	1/1074	0.838451	1	0	0	0.5643022	0.099429	SEMG1
Signaling by GPCR Homo sapiens R-HSA-372790	1/1293	0.890009	1	0	0	0.4687244	0.054618	OR51E2
Signal Transduction Homo sapiens R-HSA-162582	Feb-65	0.926692	1	0	0	0.4917327	0.037438	HPN;OR51E2

Term	**Overlap**	**P-value**	**Adjusted P-value**	**Old P-value**	**Old Adjusted P-value**	**Odds Ratio**	**Combined Score**	**Genes**
Classical antibody-mediated complement activation Homo sapiens R-HSA-173623	Jul-43	3.21E-13	4.92E-10	0	0	105.02626	3021.174	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1

Scavenging of heme from plasma Homo sapiens R-HSA-2168880	Jul-46	5.32E-13	4.07E-10	0	0	98.176718	2774.632	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
FCGR activation Homo sapiens R-HSA-2029481	Jul-49	8.52E-13	4.34E-10	0	0	92.165899	2561.447	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
Creation of C4 and C2 activators Homo sapiens R-HSA-166786	Jul-49	8.52E-13	3.26E-10	0	0	92.165899	2561.447	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
Initial triggering of complement Homo sapiens R-HSA-166663	Jul-58	2.95E-12	9.04E-10	0	0	77.864294	2067.165	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1

Role of phospholipids in phagocytosis Homo sapiens R-HSA-2029485	Jul-60	3.78E-12	9.65E-10	0	0	75.268817	1979.574	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
FCERI mediated Ca+2 mobilization Homo sapiens R-HSA-2871809	Jul-62	4.81E-12	1.05E-09	0	0	72.840791	1898.265	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Binding and Uptake of Ligands by Scavenger Receptors Homo sapiens R-HSA-2173782	Jul-74	1.74E-11	3.32E-09	0	0	61.028771	1512.038	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Complement cascade Homo sapiens R-HSA-166658	Jul-80	3.05E-11	5.18E-09	0	0	56.451613	1366.91	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1

Regulation of actin dynamics for phagocytic cup formation Homo sapiens R-HSA-2029482	Jul-97	1.21E-10	1.85E-08	0	0	46.558031	1063.129	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
FCERI mediated NF-kB activation Homo sapiens R-HSA-2871837	7/111	3.15E-10	4.39E-08	0	0	40.685847	890.084	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Fcgamma receptor (FCGR) dependent phagocytosis Homo sapiens R-HSA-2029480	7/120	5.47E-10	6.98E-08	0	0	37.634409	802.5911	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell Homo sapiens R-HSA-198933	7/157	3.60E-09	4.24E-07	0	0	28.765153	559.2261	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1

Role of LAT2/NTAL/LAB on calcium mobilization Homo sapiens R-HSA-2730905	7/162	4.48E-09	4.90E-07	0	0	27.87734	535.877	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
FCERI mediated MAPK activation Homo sapiens R-HSA-2871796	7/289	2.39E-07	2.44E-05	0	0	15.626744	238.259	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
Fc epsilon receptor (FCERI) signaling Homo sapiens R-HSA-2454202	7/395	1.94E-06	1.86E-04	0	0	11.433238	150.3733	IGLV2- 11;IGLV 3- 25;IGLV 1- 40;IGHV 3- 23;IGKV 1- 5;IGLV2- 23;IGKV 4-1
CD22 mediated BCR regulation Homo sapiens R-HSA-5690714	18-Mar	2.71E-06	2.44E-04	0	0	107.52688	1378.414	IGHV3- 23;IGKV 1- 5;IGKV4- 1

Vesicle-mediated transport Homo sapiens R-HSA-5653656	7/492	8.23E-06	7.00E-04	0	0	9.179124	107.4662	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Antigen activates B Cell Receptor (BCR) leading to generation of second messengers Homo sapiens R-HSA-983695	Mar-47	5.22E-05	0.004204	0	0	41.180508	406.0558	IGHV3- 23;IGKV1-5;IGKV4-1
Adaptive Immune System Homo sapiens R-HSA-1280218	7/762	1.34E-04	0.010242	0	0	5.9266785	52.85753	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1
Innate Immune System Homo sapiens R-HSA-168249	7/807	1.91E-04	0.01391	0	0	5.5961946	47.92384	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1

Signaling by the B Cell Receptor (BCR) Homo sapiens R-HSA-983705	3/233	0.005516	0.383581	0	0	8.3067977	43.19689	IGHV3- 23;IGKV1-5;IGKV4-1
Immune System Homo sapiens R-HSA-168256	7/1547	0.008258	0.549342	0	0	2.9192819	14.00252	IGLV2- 11;IGLV3-25;IGLV1-40;IGHV3-23;IGKV1-5;IGLV2-23;IGKV4-1

Term	Overlap	P-value	Adjusted P-value	Old P-value	Old Adjusted P-value	Odds Ratio	Combined Score	Genes
Classical antibody-mediated complement activation Homo sapiens R-HSA-173623	Jun-43	3.14E-11	4.81E-08	0	0	96.23095429	2327.190639	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
FCGR activation Homo sapiens R-HSA-2029481	Jun-49	7.17E-11	5.48E-08	0	0	84.44757213	1972.619435	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
Creation of C4 and C2 activators Homo sapiens R-HSA-166786	Jun-49	7.17E-11	3.65E-08	0	0	84.44757213	1972.619435	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2

Initial triggering of complement Homo sapiens R-HSA-166663	Jun-58	2.06E-10	7.86E-08	0	0	71.34363853	1591.3323	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
Role of phospholipids in phagocytosis Homo sapiens R-HSA-2029485	Jun-60	2.54E-10	7.77E-08	0	0	68.96551724	1523.761332	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
Binding and Uptake of Ligands by Scavenger Receptors Homo sapiens R-HSA-2173782	Jun-74	9.26E-10	2.36E-07	0	0	55.91798695	1163.090332	IGKC;IGLC3;SAA1;IGLC2;IGHA1;IGHA2
Complement cascade Homo sapiens R-HSA-166658	Jun-80	1.49E-09	3.26E-07	0	0	51.72413793	1051.143801	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
Regulation of actin dynamics for phagocytic cup formation Homo sapiens R-HSA-2029482	Jun-97	4.83E-09	9.24E-07	0	0	42.65908283	816.8568044	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2

Scavenging of heme from plasma Homo sapiens R-HSA-2168880	May-46	5.86E-09	9.96E-07	0	0	74.96251874	1420.912392	IGKC;IGLC3;IGLC2;IGHA1;IGHA2
CD22 mediated BCR regulation Homo sapiens R-HSA-5690714	18-Apr	1.08E-08	1.64E-06	0	0	153.256705	2811.987286	IGHM;IGKC;IGLC3;IGLC2
Fcgamma receptor (FCGR) dependent phagocytosis Homo sapiens R-HSA-2029480	6/120	1.75E-08	2.43E-06	0	0	34.48275862	615.9940625	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;IGLC2
Antigen activates B Cell Receptor (BCR) leading to generation of second messengers Homo sapiens R-HSA-983695	Apr-47	6.09E-07	7.76E-05	0	0	58.69405723	840.0151228	IGHM;IGKC;IGLC3;IGLC2
Vesicle-mediated transport Homo sapiens R-HSA-5653656	6/492	6.31E-05	0.00743	0	0	8.410428932	81.33626304	IGKC;IGLC3;SAA1;IGLC2;IGHA1;IGHA2

FCERI mediated Ca+2 mobilization Homo sapiens R-HSA-2871809	Mar-62	9.79E-05	0.0107	0	0	33.37041157	308.0737308	IGKC;IGLC3;IGLC2
Innate Immune System Homo sapiens R-HSA-168249	7/807	1.22E-04	0.0124	0	0	5.982139042	53.92865104	IGHG3;IGHG4;IGHG2;IGKC;IGLC3;SAA1;IGLC2
Immune System Homo sapiens R-HSA-168256	9/1547	2.34E-04	0.02236	0	0	4.012214966	33.54636585	IGHG3;IGHM;IGHG4;IGHG2;IGKC;IGLC3;SAA1;IGLC2;LTF
Signaling by the B Cell Receptor (BCR) Homo sapiens R-HSA-983705	4/233	3.39E-04	0.03052	0	0	11.83957378	94.58824954	IGHM;IGKC;IGLC3;IGLC2
FCERI mediated NF-kB activation Homo sapiens R-HSA-2871837	3/111	5.47E-04	0.04652	0	0	18.63932898	139.9930224	IGKC;IGLC3;IGLC2

Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell Homo sapiens R-HSA-198933	3/157	0.001493	0.1202	0	0	13.17812431	85.752336	IGKC;IGLC3;IGLC2
Role of LAT2/NTAL/LAB on calcium mobilization Homo sapiens R-HSA-2730905	3/162	0.001633	0.12492	0	0	12.77139208	81.9589089	IGKC;IGLC3;IGLC2
Amyloid fiber formation Homo sapiens R-HSA-977225	Feb-68	0.004358	0.31753	0	0	20.28397566	110.2570502	SAA1;LTF
Scavenging by Class B Receptors Homo sapiens R-HSA-3000471	05-Jan	0.00723	0.50279	0	0	137.9310345	679.9401122	SAA1
FCERI mediated MAPK activation Homo sapiens R-HSA-2871796	3/289	0.008264	0.54975	0	0	7.159050233	34.33349591	IGKC;IGLC3;IGLC2

Formyl peptide receptors bind formyl peptides and many other ligands Homo sapiens R-HSA-	08-Jan	0.011543	0.73588	0	0	86.20689655	384.6257661	SAA1
DEx/H-box helicases activate type I IFN and inflammatory cytokines production Homo sapiens R-HSA-3134963	13-Jan	0.018692	1	0	0	53.05039788	211.1217133	SAA1
Advanced glycosylation endproduct receptor signaling Homo sapiens R-HSA-879415	13-Jan	0.018692	1	0	0	53.05039788	211.1217133	SAA1
Fc epsilon receptor (FCERI) signaling Homo sapiens R-HSA-2454202	3/395	0.019101	1	0	0	5.237887385	20.73170498	IGKC;IGLC3;IGLC2

Adaptive Immune System Homo sapiens R-HSA-1280218	4/762	0.023289	1	0	0	3.620237126	13.61128337	IGHM;IGKC;IGLC3;IGLC2
RIP-mediated NFkB activation via ZBP1 Homo sapiens R-HSA-1810476	21-Jan	0.030027	1	0	0	32.8407225	115.128225	SAA1
TRAF6 mediated NF-kB activation Homo sapiens R-HSA-933542	24-Jan	0.034245	1	0	0	28.73563218	96.96019099	SAA1
ZBP1(DAI) mediated induction of type I IFNs Homo sapiens R-HSA-1606322	26-Jan	0.037047	1	0	0	26.52519894	87.41553486	SAA1
TAK1 activates NFkB by phosphorylation and activation of IKKs complex Homo sapiens R-HSA-445989	26-Jan	0.037047	1	0	0	26.52519894	87.41553486	SAA1

ROS, RNS production in response to bacteria Homo sapiens R-HSA-1222556	Jan-34	0.048177	1	0	0	20.28397566	61.51868449	LTF
Cytosolic sensors of pathogen-associated DNA Homo sapiens R-HSA-1834949	Jan-66	0.091468	1	0	0	10.44932079	24.99232926	SAA1
TRAF6 Mediated Induction of proinflammatory cytokines Homo sapiens R-HSA-168180	Jan-72	0.099371	1	0	0	9.578544061	22.1158904	SAA1
RIG-I/MDA5 mediated induction of IFN-alpha/beta pathways Homo sapiens R-HSA-168928	Jan-79	0.108506	1	0	0	8.729812309	19.3884414	SAA1

Toll Like Receptor 10 (TLR10) Cascade Homo sapiens R-HSA-168142	Jan-82	0.112394	1	0	0	8.410428932	18.38302695	SAA1
Toll Like Receptor 5 (TLR5) Cascade Homo sapiens R-HSA-168176	Jan-82	0.112394	1	0	0	8.410428932	18.38302695	SAA1
MyD88 cascade initiated on plasma membrane Homo sapiens R-HSA-975871	Jan-82	0.112394	1	0	0	8.410428932	18.38302695	SAA1
TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation Homo sapiens R-HSA-975138	Jan-83	0.113687	1	0	0	8.309098463	18.06655067	SAA1
MyD88 dependent cascade initiated on endosome Homo sapiens R-HSA-975155	Jan-85	0.116266	1	0	0	8.113590264	17.45943983	SAA1

Toll Like Receptor 7/8 (TLR7/8) Cascade Homo sapiens R-HSA-168181	Jan-85	0.116266	1	0	0	8.113590264	17.45943983	SAA1
Toll Like Receptor 9 (TLR9) Cascade Homo sapiens R-HSA-168138	Jan-88	0.120121	1	0	0	7.836990596	16.60858299	SAA1
MyD88:Mal cascade initiated on plasma membrane Homo sapiens R-HSA-166058	Jan-92	0.125236	1	0	0	7.496251874	15.57387177	SAA1
Toll Like Receptor TLR1:TLR2 Cascade Homo sapiens R-HSA-168179	Jan-92	0.125236	1	0	0	7.496251874	15.57387177	SAA1
Toll Like Receptor TLR6:TLR2 Cascade Homo sapiens R-HSA-168188	Jan-92	0.125236	1	0	0	7.496251874	15.57387177	SAA1

Toll Like Receptor 2 (TLR2) Cascade Homo sapiens R-HSA-181438	Jan-92	0.125236	1	0	0	7.496251874	15.57387177	SAA1

MyD88-independent TLR3/TLR4 cascade Homo sapiens R-HSA-166166	Jan-97	0.13159	1	0	0	7.109847138	14.41925158	SAA1
Toll Like Receptor 3 (TLR3) Cascade Homo sapiens R-HSA-168164	Jan-97	0.13159	1	0	0	7.109847138	14.41925158	SAA1
TRIF-mediated TLR3/TLR4 signaling Homo sapiens R-HSA-937061	Jan-97	0.13159	1	0	0	7.109847138	14.41925158	SAA1
Activated TLR4 signalling Homo sapiens R-HSA-166054	1/112	0.150384	1	0	0	6.157635468	11.66604345	SAA1
Toll Like Receptor 4 (TLR4) Cascade Homo sapiens R-HSA-166016	1/122	0.162694	1	0	0	5.652911249	10.265023	SAA1

Toll-Like Receptors Cascades Homo sapiens R-HSA- 168898	1/140	0.184421	1	0	0	4.926108374	8.327763361	SAA1
G alpha (q) signalling events Homo sapiens R-HSA- 416476	1/191	0.243064	1	0	0	3.610760065	5.107173062	SAA1
Peptide ligand-binding receptors Homo sapiens R-HSA- 375276	1/193	0.245278	1	0	0	3.573342862	5.021837388	SAA1
G alpha (i) signalling events Homo sapiens R-HSA- 418594	1/240	0.295559	1	0	0	2.873563218	3.502546682	SAA1
Class A/1 (Rhodopsin-like receptors) Homo sapiens R-HSA- 373076	1/323	0.376562	1	0	0	2.135155333	2.085348299	SAA1
Infectious disease Homo sapiens R-HSA-5663205	1/348	0.399144	1	0	0	1.981767737	1.820119503	LTF
Metabolism of proteins Homo sapiens R-HSA- 392499	2/1074	0.46633	1	0	0	1.284274064	0.979722471	SAA1;LTF

Gastrin-CREB signalling pathway via PKC and MAPK Homo sapiens R-HSA- 881907	1/432	0.469381	1	0	0	1.59642401	1.207439229	SAA1
GPCR ligand binding Homo sapiens R-HSA- 500792	1/447	0.48106	1	0	0	1.542852735	1.129004505	SAA1
Disease Homo sapiens R-HSA-1643685	1/725	0.657519	1	0	0	0.951248514	0.398841023	LTF
GPCR downstream signaling Homo sapiens R-HSA- 388396	1/983	0.76837	1	0	0	0.701582068	0.184855213	SAA1
Signaling by GPCR Homo sapiens R-HSA- 372790	1/1293	0.856238	1	0	0	0.533376003	0.082783637	SAA1
Signal Transduction Homo sapiens R-HSA- 162582	Jan-65	0.978012	1	0	0	0.279778975	0.006220549	SAA1

Data S2: Enrichment analysis for Biological Pathways using the tool Enrich.

Data S3

Data S3	Correlations among PCs and selected clinical features of PRAD (TCGA, Cell 2015)
Tab Content:	
Tab 1	Correlation between major clinical features of PRAD
Tab 2	Correlation between major clinical features and PCs

Correlations			
	erg	**ar**	**cel**
gleason	0.02	-0.09	0.26
erg		-0.24	-0.06
ar			0.18
P-values			
	erg	**ar**	**cel**
gleason	0.73	0.11	0.00
erg		0.00	0.31
ar			0.00

Correlations			
	PC1	**PC2**	**PC3**
gleason	0.26	-0.16	0.04
erg	0.02	-0.18	0.24
ar	0.23	0.32	0.45
cel	0.37	0.14	0.19
P-values			
	PC1	**PC2**	**PC3**
gleason	0.00	0.01	0.52
erg	0.66	0.00	0.00
ar	0.00	0.00	0.00
cel	0.00	0.02	0.00

Data S3: Correlations among PCs and selected clinical features of PRAD (TCGA, Cell 2015).