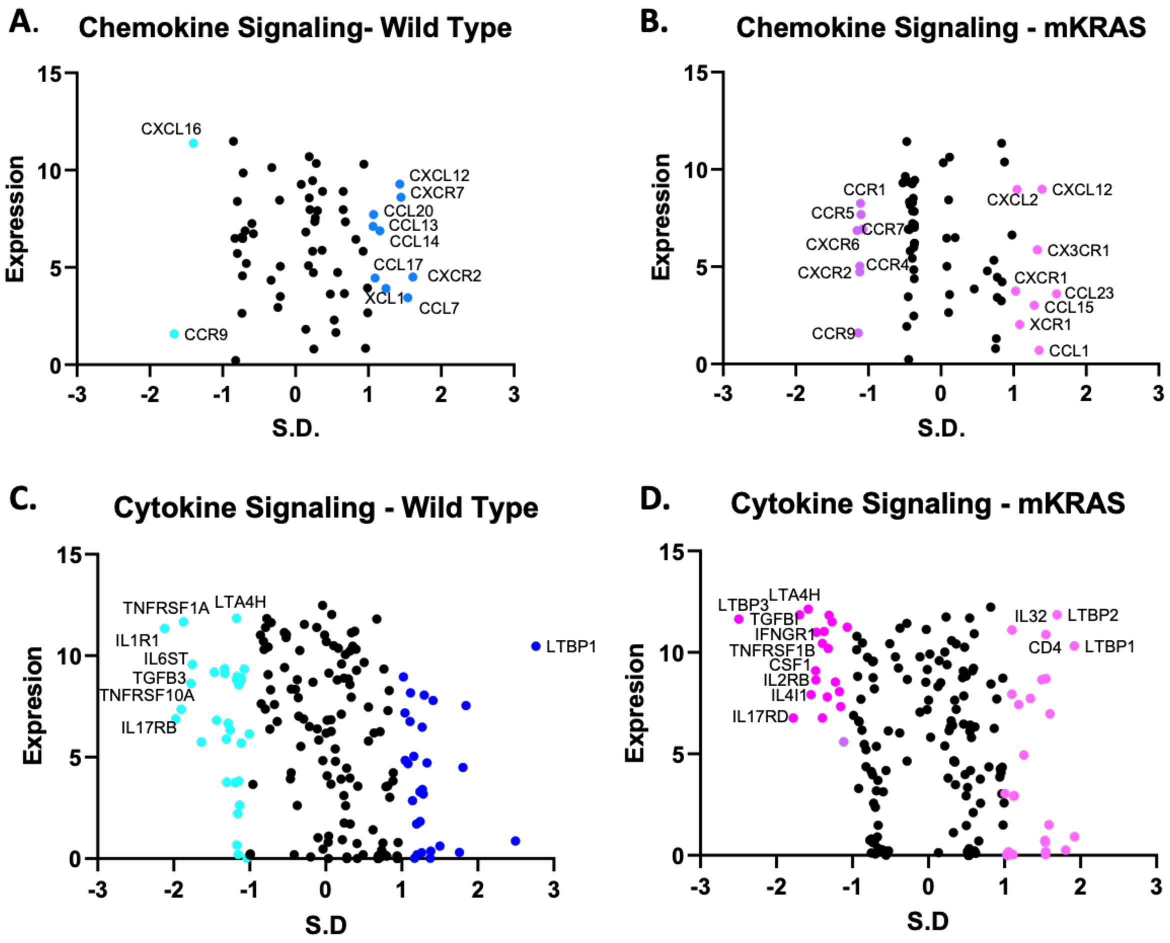
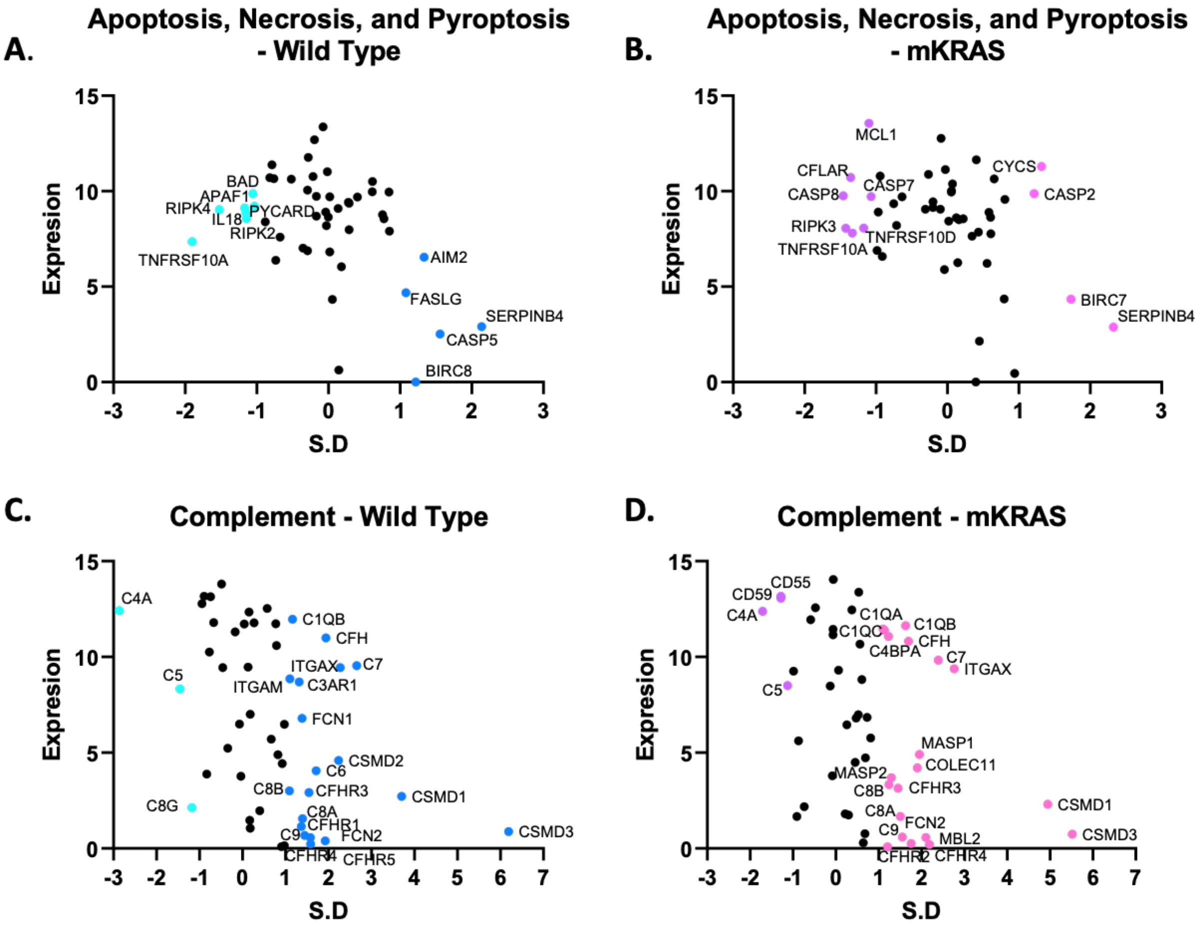
Supplemental Figures



Supplemental Figure 1. Conservation profiles in chemokine genes (A-B) and cytokine genes (C-D). Gene conservation score, measure as the standard residual from the regression line (SR) graphed against genes expression levels (Log2) for WT (A and C) and mKRAS (B and D). Conserved genes (SR ≤ -1.0) and over-mutated genes (SR ≥ 1.0) are colored and labelled with text. (Standard residual (SR)



Supplemental Figure 2. Conservation profiles in cell death pathways (A-B) and complement system (C-D) genes. Gene conservation score, measure as the standard residual from the regression line (SR) graphed against genes expression levels (Log2) for WT (A) and mKRAS (B). Conserved genes (SR ≤ -1.0) and over-mutated genes (SR ≥ 1.0) are colored and labelled with text. Standard residual (SR).

Supplementary Tables

Process	Gene Symbols (Reference)
Antigen processing and presentation	B2M (1-5), CD1A (6-8), CD1B (6, 7), CD1C (6, 7), CD1D (6, 7), CD1E (6, 7) (9), CIITA (10, 11), ERAP1 (12-14), ERAP2 (12-14), HLA-A (1, 4)HLA-B (1, 4), HLA-C (1, 4), HLA-DMA (11), HLA-DMB (11), HLA-DOA (11), HLA-DOB (11), HLA-DPA1 (11), HLA-DPB1 (11), HLA-DQA1 (11), HLA-DQA2 (11), HLA-DQB1 (11), HLA-DQB2 (11), HLA-DRA (11), HLA-DRB1 (11), HLA-DRB5 (11), HLA-E (2), HLA-F (15), MEX3C (16), MTTP (6, 9), NLRC5 (4, 16), NPC1 (9, 17), NPC2 (9, 17), PSAP (9), PSMB8 (1) (18) (2, 16), PSMB9 (1, 18) (2, 16), RFX1 (19), RFX2 (19), RFX5 (10, 16), RFXANK (10, 16), TAP1 (1, 5, 18), TAPBP (1, 18)
Immune Modulating Proteins	ADAM17 (20), C10orf54, CCL2 (1), CD274 (1, 2) (5, 21), CD276 (1, 2) (5, 21), CD40 (21), CD47 (22), CD48 (23), CD80 (21), CD86 (21), CTLA4,ENTPD1 (24), FASLG (1), HCST, HLA-A (25), HLA-B (25), HLA-C (25), HLA-G (2), IDO1 (1, 20) (18), IDO2, LGALS1 (1), LGALS2 (1), LGALS3 (1), LGALS9 (1), MICA (2) (25), MICB (2, 26), NT5E (18, 20, 27), PDCD1LG2, PTGS1, PTGS2 (1), PVR (21, 26, 27), PVRIG (27), PVRL1 (26), PVRL2 (27, 28), PVRL3 (27, 28), PVRL4, RAET1E (2, 29), TGFB1 (1, 20, 30) (18), TNFRSF14 (27), TNFRSF6B, TNFSF4 (18, 21), TNFSF9 (21), ULBP1 (2, 29), ULBP2 (2, 29), ULBP3 (2, 29)
Innate immune receptor signaling	AGER (31), AIM2 (31), BTK (32), CASP1 (11, 33), CASP8 (31), CD14 (32), CIITA (11, 33), CTNNB1 (34), DDX3X, DDX41, DDX58 (11, 35), DHX58 (11, 35), DOK3, DOK4, DTX4, FADD (31),HMGB1 (31), IFI16 (31, 36), IFIH1 (11, 31), IL18 (33),

	IL1B (33), IRF3 (31, 32), IRF7 (31, 32), LRRFIP1, MAL (32), MAVS (11, 35), MB21D1 (35, 37), MyD88 (31), NLRC3 (11, 33), NLRC4 (11, 33), NLRC5 (11, 33), NLRP1 (11, 33), NLRP10 (11, 33), NLRP11 (11, 33), NLRP12 (11, 33), NLRP13 (11, 33), NLRP14 (11, 33), NLRP2 (11, 33), NLRP3 (11, 33), NLRP4 (11, 33), NLRP5 (11, 33), NLRP6 (11, 33), NLRP7 (11, 33), NLRP8 (11, 33), NLRP9 (11, 33), NLRX1 (11, 33, 38), NOD1 (11, 33), NOD2 (11, 33), OAS1 (11, 33), PYCARD (31), RIPK1 (31), TANK (32), TBK1 (35), TICAM1 (32), TLR1 (11, 32), TLR10 (11, 32), TLR2 (11, 32), TLR3 (11, 32), TLR4 (11, 32), TLR5 (11, 32), TLR6 (11, 32), TLR7 (11, 32), TLR8 (11, 32), TLR9 (11, 32), TMEM173 (37), TNIP1 (39), TRAF3 (32), TRAF6 (32), TRAM1 (32), TRIM56 (40), TUFM (38), ZBP1 (36)
Interferon Signaling	CREBBP, DOCK2, IFNA1, IFNA10, IFNA13, IFNA14, IFNA16, IFNA17, IFNA2, IFNA21, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNAR1, IFNAR2, IFNB1, IFNE, IFNG, IFNGR1, IFNGR2, IL10RB, IL28A, IL28B, IL28RA, IL29, IRF1, IRF2, IRF2BP1, IRF2BP2, IRF2BPL, IRF3, IRF4, IRF5, IRF6, IRF7, IRF8, IRF9, JAK1, JAK2, JAK3, MAVS, PIAS1, PIAS2, PIAS3, PIAS4, PIK3CA, PTPN11, RAC1, RAC2, RAC3, SIRT1, SIRT2, SIRT3, SIRT4, SIRT5, SIRT7, SMARCA4, SOCS2, SOCS3, SOCS4, SOCS5, SOCS6, SOCS7, STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, STAT6, TYK2, ULK1, USP18
chemokine signaling	CCL1, CCL11, CCL13 ,CCL14, CCL15, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23, CCL24, CCL25, CCL26, CCL2, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL4L2, CCL5, CCL7, CCL8, CCR1, CCR10, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCRL1, CX3CL1, CX3CR1, CXCL1, CXCL10, CXCL11,

	CXCL12, CXCL13, CXCL14, CXCL16, CXCL17, CXCL2, CXCL3, CXCL5,CXCL6, CXCL9, CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, CXCR6, CXCR7, XCL1, XCL2, XCR1
cytokine signaling	CD27, CD4, CD40, CD40LG, CD70, CNTF, CSF1, CSF1R, CSF2, CSF2RA, CSF2RB, CSF3, CSF3R, Epo, EpoR, FAS, FASLG, FLT3, FLT3LG, IFNA1, IFNA10, IFNA13, IFNA14, IFNA16, IFNA17, IFNA2, IFNA21, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNB1, IFNE, IFNG, IFNGR1, IFNGR2, IFNK, IFNW1, IL10, IL10RA, IL10RB, IL11RA, IL12A, IL12B, IL12RB1, IL12RB2, IL13, IL13RA1, IL13RA2, IL15, IL16, IL17A, IL17B, IL17C, IL17D, IL17F, IL17RA, IL17RB, IL17RC, IL17RD, IL17RE, IL17REL, IL18, IL18BP, IL18R1, IL18RAP, IL19, IL1A, IL1F10, IL1R1, IL1R2, IL1RAP, IL1RAPL1, IL1RAPL2, IL2, IL20, IL20RA, IL20RB, IL21, IL21R, IL22, IL23, IL23R, IL24, IL25, IL26, IL27, IL27RA, IL28A, IL28B, IL28RA, IL29, IL2RA, IL2RB, IL2RG, IL3, IL31, IL31RA, IL32, IL33, IL34, IL36A, IL36B, IL36G, IL36RN, IL37, IL3RA, IL4, IL4I1, IL4R, IL5, IL5RA, IL6, IL6R, IL6ST, IL7, IL7R, IL8, IL9, KIT, KITLG, LIF, LIFR, LTA, LTA4H, LTB, LTB4R, LTB4R2, LTBP1, LTBP2, LTBP3, LTBR, MPL, MST1, MST1R, NFKB1, OSM, OSMR, SPP1, TGFB1, TGFB1I1, TGFB2, TGFB3, TGFBI, TGFBR1, TGFBR2, TGFBR3, TNF, TNFRSF10A, TNFRSF10B, TNFRSF10C, TNFRSF10D, TNFRSF11A, TNFRSF11B,TNFRSF12A, TNFRSF13B, TNFRSF13C, TNFRSF14, TNFRSF17, TNFRSF19, TNFRSF1A, TNFRSF1B, TNFRSF4, TNFRSF6B, TNFRSF8, TNFRSF9, TNFSF10, TNFSF11, TNFSF12, TNFSF13B, TNFSF14, TNFSF18, TNFSF4, TNFSF8, TNFSF9, Tpo, TRAF3IP2, TSLP, TXLNA
apoptosis, necrosis, and pyroptosis	Aim2 (41), APAF1, BAD (42), Bcl-2 (2) (43) (44), BCL2L1 (2), BIRC5 (45) (46),

	BIRC6, BIRC7, BIRC8, CASP1 (41), CASP10, CASP14, CASP2 (42), CASP3, CASP4 (41), CASP5 (41), CASP6 (42), CASP7, CASP8 (42), CASP8AP2, CASP9, CFLAR (47) (48) CYCS, CYLD, FADD (1), FAS (1) (49), FASLG, GSDMD (41), IL18 (41), IL1B (41), MCL1 (42), Nlrc4 (41), NLRP1 (41), PYCARD (31), RIPK1 (41), RIPK2, RIPK3 (41), RIPK4, SERPINB4 (50), SERPINB9 (51) (52) (53) {topfer2011}, STAT3 (2), TNFRSF10A (1), TNFRSF10B (1), TNFRSF10C (1), TNFRSF10D (1), TNFRSF11B (1), TNFRSF6B (1) (2), TNFSF10 (1)
Complement	C1QA, C1QB, C1QC, C1S, C2, C3, C3AR1, C4A, C4B, C4BPA, C4BPB, C5, C6, C7, C8A, C8B, C8G, C9, CD46, CD55, CD59, CD93, CFB, CFDP1, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5, CFP, COLEC10, COLEC11, CR1, CR2, CSMD1, CSMD2, CSMD3, ELANE, F2, FCN1, FCN2, FCN3, ITGAM, ITGAX, ITGB2, MASP1, MASP2, MBL2, SERPING1, VSIG4, VTN

Supplemental Table 1. Gene lists for broad categories of tumor-immune interactions.

	Mutant KRAS	Wild Type
Average # of gene mutations/tumor	300	348
# of conserved genes (SR ≤ -1.0)	3,011	2,587
# of highly conserved genes (SR ≤ -2.0)	160	248
# of hypermutated genes (SR ≥ 1.0)	2,581	2,398
# of highly hypermutated genes (SR ≥ 2.0)	518	593
# of frequently mutated genes (≥10% of patients)	157	208
# of genes mutated in 0 patients	5,621	2,323

Supplemental Table 2. The number of total genes conserved or hypermutated varied between mutant KRAS and wild-type lung tumours. Mutation rates of 17,615 genes were calculated in mutant KRAS (n= 163 patients) and wild-type (n=313 patients) lung tumours. Numbers of conserved or hypermutated genes out of 17,615 genes examined. Genes with an SR ≥ 1.0 are hypermutated and genes with an SR ≤ -1.0 are conserved genes (under mutated). Others have an expected number of mutations (Background mutations). Standard residual (SR).

	Gene	mutated samples	total samples	SR score
Wild-type	TP53	177	313	11.94
	CSMD3	135	313	6.19
	KEAP1	59	313	6.07
	RYR2	125	313	5.58
	STK11	27	313	5.52
	ZFHX4	104	313	5.49
	COL11A1	82	313	5.44
	ZNF536	69	313	5.42
	CDH10	59	313	5.35
	NRXN1	65	313	5.07
mKRAS	KRAS	163	163	15.14
	TP53	57	163	8.18

STK11	32	163	7.72
ZFHX4	60	163	5.83
KEAP1	31	163	5.64
CSMD3	65	163	5.52
RYR2	66	163	5.44
ZNF536	37	163	5.22
LRP1B	66	163	5.04
CSMD1	46	163	4.95

Supplemental Table 3. Genes with the highest mutation score for mutant KRAS and wild-type cohorts. Non-synonymous mutation rates of 17,615 genes were calculated in mutant KRAS (n= 163 patients) and wild-type (n=313 patients) lung tumours. Standard residual (SR).

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