

Supplementary Tables and Figures

Supplementary Table 2. 151 cancer-associated gene panel

ABCB1	CSF1R	FGFR4	KMT2A	PHF6	SLC22A1	ZMYM3
ABCC2	CTNNB1	FLT1	KRAS	PIK3CA	SLC22A2	
ABL1	CYP19A1	FLT3	LAMA2	PIK3R1	SLC31A1	
ABL2	CYP2A6	FLT4	LCK	PSMB1	SLC34A2	
AKT1	CYP2B6	FSTL5	LTK	PSMB2	SLC45A3	
AKT2	CYP2C19	GNA11	MAP2K1	PSMB5	SLCO1B1	
AKT3	CYP2C9	GNAQ	MAP2K2	PSMD1	SMAD4	
ALK	CYP2D6	GNAS	MAP2K4	PSMD2	SMARCA4	
APC	DDR1	GSTP1	MAP3K1	PTCH1	SMARCB1	
ASXL1	DDR2	H3F3A	MAPK1	PTEN	SMO	
ATM	DDX3X	HNF1A	MED13	PTPN11	SNCAIP	
ATRX	DNMT3A	HRAS	MET	RAF1	SOS1	
BRAF	DPYD	IDH1	MLH1	RARA	SPRED1	
BRCA1	EGFR	IDH2	MPL	RARB	SRC	
BRCA2	ERBB2	IKZF1	MST1R	RARG	STK11	
CBL	ERBB3	IL2RA	MTOR	RB1	SUFU	
CDA	ERBB4	IL2RB	MYC	RET	TAS2R38	
CDH1	ERG	IL2RG	MYD88	ROS1	TET2	
CDKN2A	ESR1	INPP4B	NELL2	RPS6KB1	TP53	
CDKN2B	ESR2	JAK1	NF1	RUNX1	TRRAP	
CEBPA	EZH2	JAK2	NOTCH1	RXRA	TYK2	
CHD7	FBXW7	JAK3	NPM1	RXRB	UGT1A1	
CHIC2	FGFR1	KDM6A	NRAS	RXRG	VHL	
CREBBP	FGFR2	KDR	PDGFRA	SHH	WT1	
CRLF2	FGFR3	KIT	PDGFRB	SHOC2	YES1	

Supplementary Table 3. Supplementary Code

```
R version 4.0.2 (2020-06-22) -- "Taking Off Again"
Copyright (C) 2020 The R Foundation for Statistical Computing
Platform: x86_64-apple-darwin17.0 (64-bit)

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Type 'q()' to quit R.

[R.app GUI 1.72 (7847) x86_64-apple-darwin17.0]

[Workspace restored from /Users/meerapatel/.RData]
[History restored from /Users/meerapatel/.Rapp.history]

> install.packages("maxstat")
--- Please select a CRAN mirror for use in this session ---
trying URL 'https://cran.ma.imperial.ac.uk/bin/macosx/contrib/4.0/maxstat_0.7-25.tgz'
Content type 'application/x-gzip' length 180958 bytes (176 KB)
=====
downloaded 176 KB

The downloaded binary packages are in
  /var/folders/s4/vgt0mphis693dd3ztkl4kcfh80000gn/T//Rtmp7z01jt/downloaded_packages
> install.packages("survival")
trying URL 'https://cran.ma.imperial.ac.uk/bin/macosx/contrib/4.0/survival_3.2-11.tgz'
Content type 'application/x-gzip' length 6803373 bytes (6.5 MB)
=====
downloaded 6.5 MB

The downloaded binary packages are in
  /var/folders/s4/vgt0mphis693dd3ztkl4kcfh80000gn/T//Rtmp7z01jt/downloaded_packages
> install.packages("survminer")
trying URL 'https://cran.ma.imperial.ac.uk/bin/macosx/contrib/4.0/survminer_0.4.9.tgz'
Content type 'application/x-gzip' length 3227677 bytes (3.1 MB)
=====
downloaded 3.1 MB

The downloaded binary packages are in
  /var/folders/s4/vgt0mphis693dd3ztkl4kcfh80000gn/T//Rtmp7z01jt/downloaded_packages
> install.packages("tidyverse")
trying URL 'https://cran.ma.imperial.ac.uk/bin/macosx/contrib/4.0/tidyverse_1.3.1.tgz'
Content type 'application/x-gzip' length 421035 bytes (411 KB)
=====
downloaded 411 KB
```

The downloaded binary packages are in

/var/folders/s4/vgt0mphs693dd3ztkl4kcfh80000gn/T//Rtmp7z01jt/downloaded_packages

```
> library(maxstat)
> library(survival)
> library(survminer)
Loading required package: ggplot2
Loading required package: ggpubr
> library(tidyverse)
— Attaching packages
```

— tidyverse 1.3.1 —

```
✓ tibble 3.1.2 ✓ dplyr 1.0.7
✓ tidyr 1.1.3 ✓ stringr 1.4.0
✓ readr 1.4.0 ✓ forcats 0.5.1
✓ purrr 0.3.4
— Conflicts
```

— tidyverse_conflicts() —

```
✖ dplyr::filter() masks stats::filter()
✖ dplyr::lag() masks stats::lag()
> mydata<-read.csv(file.choose())
> res.cut <- surv_cutpoint(mydata, time="CSS", event="acd", variables = c("cyt"))
> summary(res.cut)
  cutpoint statistic
cyt 111.25 1.350276
>
> plot(res.cut,"cyt")
```

```
> library(maftools)
> IKKlow <- read.maf(file.choose())
-Reading
-Validating
--Removed 115 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
3UTR
inframe_indelstop_gained
inframe_indel
inframe_indelMissense_Mutation
--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 338
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 13.5s elapsed (0.769s cpu)
> IKKhigh <- read.maf(file.choose())
-Reading
-Validating
--Removed 27 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
inframe_indelMissense_Mutation
3UTR
--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 97
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 13.2s elapsed (0.465s cpu)
```

```

> oncoplot(maf=IKKlow,top=10)
> oncoplot(maf=IKKhigh,top=10)
> OncogenicPathways(maf= IKKlow)
  Pathway N n_affected_genes fraction_affected Mutated_samples Fraction_mutated_samples
1: Hippo 38      1  0.02631579      9      0.07086614
2: MYC 13      1  0.07692308      2      0.01574803
3: NRF2 3      1  0.33333333      3      0.02362205
4: TGF-Beta 7      2  0.28571429     33      0.25984252
5: TP53 6      3  0.50000000     95      0.74803150
6: WNT 68      4  0.05882353     110     0.86614173
7: NOTCH 71      7  0.09859155     57      0.44881890
8: Cell_Cycle 15      8  0.53333333     14      0.11023622
9: PI3K 29     11  0.37931034     55      0.43307087
10: RTK-RAS 85     26  0.30588235    111     0.87401575
> OncogenicPathways(maf= IKKhigh)
  Pathway N n_affected_genes fraction_affected Mutated_samples Fraction_mutated_samples
1: MYC 13      1  0.07692308      1      0.03333333
2: NRF2 3      1  0.33333333      1      0.03333333
3: Hippo 38     2  0.05263158      3      0.10000000
4: TGF-Beta 7      2  0.28571429      8      0.26666667
5: WNT 68      4  0.05882353     26      0.86666667
6: TP53 6      4  0.66666667     25      0.83333333
7: Cell_Cycle 15     6  0.40000000      7      0.23333333
8: NOTCH 71      7  0.09859155     17      0.56666667
9: PI3K 29      7  0.24137931     12      0.40000000
10: RTK-RAS 85     22  0.25882353     24      0.80000000
> IKKlow.vs.IKKhigh <- mafCompare(m1 = IKKlow, m2 = IKKhigh, m1Name = 'Low', m2Name = 'High', minMut = 5)
> print(IKKlow.vs.IKKhigh)
$results
  Hugo_Symbol Low High  pval  or  ci.up  ci.low  adjPval
1: ASTE1 8 7 0.01001805 0.2238304 0.8012648 0.06359222 0.4921700
2: SLC23A2 6 6 0.01200415 0.2012461 0.8214793 0.04908922 0.4921700
3: POLE 7 5 0.05385437 0.2947028 1.2768974 0.07343308 0.7519427
4: TTK 12 7 0.05674470 0.3457914 1.1527239 0.11070825 0.7519427
5: BRCA2 13 7 0.06792041 0.3775869 1.2442178 0.12308978 0.7519427
6: B2M 5 4 0.06844821 0.2694396 1.4533705 0.05383565 0.7519427
7: PDGFRA 5 4 0.06844821 0.2694396 1.4533705 0.05383565 0.7519427
8: PTEN 14 0 0.07336026 Inf Inf 0.81936105 0.7519427
9: SMARCA4 6 4 0.09872874 0.3253476 1.6812828 0.07119608 0.8723136
10: AR 30 12 0.10637970 0.4664463 1.1897593 0.18707918 0.8723136
11: EP300 8 5 0.13154671 0.3391165 1.4311206 0.08882791 0.9133470
12: TGFB2 15 7 0.13983790 0.4427883 1.4320047 0.14859127 0.9133470
13: BLM 9 5 0.14570957 0.3842868 1.5876531 0.10455842 0.9133470
14: CREBBP 10 5 0.16625170 0.4301706 1.7467397 0.12067300 0.9133470
15: PBRM1 5 3 0.17910296 0.3718493 2.5384351 0.06752637 0.9133470
16: ARID1A 21 8 0.20046269 0.5471584 1.6169482 0.19929906 0.9133470
17: GATA3 9 0 0.20860635 Inf Inf 0.47031025 0.9133470
18: DICER1 10 0 0.21047644 Inf Inf 0.53763774 0.9133470
19: PTCH1 7 4 0.22327762 0.3821234 1.9125568 0.08914869 0.9133470
20: KRAS 64 11 0.22358246 1.7484577 4.4203978 0.72223406 0.9133470
21: ALK 15 6 0.24106449 0.5381326 1.8704627 0.17395952 0.9133470
22: TM6SF1 8 4 0.24524246 0.4397898 2.1474817 0.10767815 0.9133470
23: RPL22 17 7 0.25618270 0.5103057 1.6264330 0.17504174 0.9133470
24: ERBB3 9 4 0.27465524 0.4983789 2.3859382 0.12660822 0.9384054
25: RET 7 0 0.34778915 Inf Inf 0.33941406 1.0000000
26: ATRX 6 3 0.37458847 0.4490883 2.9473353 0.08898161 1.0000000
27: CIITA 6 3 0.37458847 0.4490883 2.9473353 0.08898161 1.0000000
28: ASXL1 17 6 0.39089864 0.6202814 2.1261121 0.20487592 1.0000000
29: FBXW7 17 6 0.39089864 0.6202814 2.1261121 0.20487592 1.0000000
30: MAP3K1 7 3 0.40433587 0.5275093 3.3623781 0.11122247 1.0000000
31: SETD2 7 3 0.40433587 0.5275093 3.3623781 0.11122247 1.0000000

```

```

32: SMO 7 3 0.40433587 0.5275093 3.3623781 0.11122247 1.0000000
33: MTOR 8 3 0.44087494 0.6072447 3.7844407 0.13407620 1.0000000
34: TAF1B 8 3 0.44087494 0.6072447 3.7844407 0.13407620 1.0000000
35: PALB2 11 1 0.46455162 2.7368742 122.3349771 0.36954367 1.0000000
36: ERBB4 12 4 0.51041225 0.6801031 3.1255163 0.18595751 1.0000000
37: NOTCH2 12 4 0.51041225 0.6801031 3.1255163 0.18595751 1.0000000
38: NOTCH4 15 5 0.54214769 0.6715161 2.5836987 0.20622828 1.0000000
39: RAF1 5 0 0.58406150 Inf Inf 0.21393275 1.0000000
40: RNF43 20 6 0.58862733 0.7491340 2.5274659 0.25342227 1.0000000
41: CCDC150 5 2 0.61928362 0.5761261 6.3445321 0.08857889 1.0000000
42: CHEK2 5 2 0.61928362 0.5761261 6.3445321 0.08857889 1.0000000
43: ERBB2 5 2 0.61928362 0.5761261 6.3445321 0.08857889 1.0000000
44: FGFR4 5 2 0.61928362 0.5761261 6.3445321 0.08857889 1.0000000
45: MEN1 5 2 0.61928362 0.5761261 6.3445321 0.08857889 1.0000000
46: RUNX1 6 2 0.64901575 0.6959969 7.4060780 0.11627587 1.0000000
47: TP53 77 20 0.67685460 0.7712589 1.8986671 0.29639510 1.0000000
48: IDH1 7 2 0.68199414 0.8177800 8.4846651 0.14482613 1.0000000
49: CDK12 9 1 0.68844020 2.2028937 100.2063382 0.28480076 1.0000000
50: SF3B1 9 1 0.68844020 2.2028937 100.2063382 0.28480076 1.0000000
51: GNAS 9 3 0.70102725 0.6882524 4.2132295 0.15745888 1.0000000
52: NF1 9 3 0.70102725 0.6882524 4.2132295 0.15745888 1.0000000
53: AIM2 10 3 0.71489808 0.7706056 4.6490741 0.18137706 1.0000000
54: BRCA1 10 3 0.71489808 0.7706056 4.6490741 0.18137706 1.0000000
55: AMER1 11 3 0.73205699 0.8543215 5.0923870 0.20574190 1.0000000
56: RAD50 11 3 0.73205699 0.8543215 5.0923870 0.20574190 1.0000000
57: BRAF 21 4 0.78724197 1.2857464 5.5934097 0.38553581 1.0000000
58: PIK3CA 26 5 0.80052555 1.2851146 4.7152825 0.42508788 1.0000000
59: APC 88 21 1.00000000 0.9672364 2.4501684 0.35636385 1.0000000
60: CTNNB1 10 2 1.00000000 1.1952751 11.8250345 0.23477173 1.0000000
61: NOTCH3 15 3 1.00000000 1.2039815 6.9451405 0.30803454 1.0000000
62: NRAS 10 2 1.00000000 1.1952751 11.8250345 0.23477173 1.0000000
63: ARID1B 8 2 1.00000000 0.9415386 9.5797972 0.17414891 1.0000000
64: ARID2 9 2 1.00000000 1.0673368 10.6929960 0.20416172 1.0000000
65: ATM 21 5 1.00000000 0.9906258 3.6914454 0.32001574 1.0000000
66: ATR 17 4 1.00000000 1.0045168 4.4470226 0.29273495 1.0000000
67: COBLL1 8 1 1.00000000 1.9427024 89.4194012 0.24365629 1.0000000
68: CTCF 7 1 1.00000000 1.6867822 78.8112904 0.20337251 1.0000000
69: GNA11 5 1 1.00000000 1.1872805 58.1277446 0.12575888 1.0000000
70: IDH2 5 1 1.00000000 1.1872805 58.1277446 0.12575888 1.0000000
71: JAK1 5 1 1.00000000 1.1872805 58.1277446 0.12575888 1.0000000
72: KMT2A 12 2 1.00000000 1.4576530 14.1494673 0.29780844 1.0000000
73: MSH2 19 4 1.00000000 1.1425671 5.0096955 0.33828153 1.0000000
74: MSH6 14 3 1.00000000 1.1142903 6.4694426 0.28173609 1.0000000
75: NBN 5 1 1.00000000 1.1872805 58.1277446 0.12575888 1.0000000
76: NOTCH1 18 4 1.00000000 1.0729175 4.7257866 0.31529577 1.0000000
77: PIK3R1 8 1 1.00000000 1.9427024 89.4194012 0.24365629 1.0000000
78: POLQ 11 2 1.00000000 1.3253537 12.9772713 0.26602150 1.0000000
79: ROS1 8 2 1.00000000 0.9415386 9.5797972 0.17414891 1.0000000
80: SMAD4 18 4 1.00000000 1.0729175 4.7257866 0.31529577 1.0000000
81: TEAD2 9 2 1.00000000 1.0673368 10.6929960 0.20416172 1.0000000
82: TSC2 8 2 1.00000000 0.9415386 9.5797972 0.17414891 1.0000000

```

```
Hugo_Symbol Low High pval or ci.up ci.low adjPval
```

```
##SampleSummary
```

```
Cohort SampleSize
```

```
1: Low 127
```

```
2: High 30
```

```
> forestPlot(mafCompareRes = IKKlow.vs.IKKhigh, pVal = 0.05, color = c('royalblue', 'maroon'), geneFontSize = 0.8)
```

```
> genes = c("ASTE1", "SLC23A2", "POLE", "TTK", "BRCA2", "B2M", "PDGFRA", "PTEN", "SMARCA4", "AR")
```

```
> coBarplot(m1 = IKKlow, m2 = IKKhigh, m1Name = 'Low', m2Name = 'High', genes = genes)
```

```

> IKKall <- read.maf(file.choose())
-Reading
-Validating
--Removed 199 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
3UTR
inframe_indellstop_gained
inframe_indel
inframe_indelMissense_Mutation

--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 613
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 3.460s elapsed (0.270s cpu)
> lollipopPlot(maf = IKKall, gene = 'AR', AACol = "VAF")
2 transcripts available. Use arguments refSeqID or proteinID to manually specify tx name.
  HGNC  refseq.ID  protein.ID aa.length
1:  AR  NM_000044  NP_000035   920
2:  AR  NM_001011645  NP_001011645   388
Using longer transcript NM_000044 for now.

> IKKpunctatelow <- read.maf(file.choose())
-Reading
-Validating
Error in validateMaf(maf = maf, isTCGA = isTCGA, rdup = removeDuplicatedVariants, :
  missing required fields from MAF: Hugo_Symbol
> IKKpunctatelow <- read.maf(file.choose())
-Reading
-Validating
--Removed 137 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
3UTR
inframe_indellstop_gained
inframe_indel
inframe_indelMissense_Mutation
--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 425
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 22.0s elapsed (0.854s cpu)
> IKKpunctatehigh <- read.maf(file.choose())
-Reading
-Validating
--Removed 5 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 12
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 6.338s elapsed (0.352s cpu)
> oncoplot(maf=IKKpunctatelow,top=10)

```

```

> oncoplot(maf=IKKpunctatehigh,top=10)
> OncogenicPathways(maf= IKKpunctatelow)
  Pathway N_n_affected_genes fraction_affected Mutated_samples Fraction_mutated_samples
1:  NRF2 3      1  0.33333333      3      0.02040816
2:  Hippo 38     2  0.05263158     12     0.08163265
3:  MYC 13      2  0.15384615      3      0.02040816
4:  TGF-Beta 7     2  0.28571429     38     0.25850340
5:  WNT 68      4  0.05882353     129    0.87755102
6:  TP53 6       4  0.66666667    112    0.76190476
7:  NOTCH 71     7  0.09859155     72     0.48979592
8:  Cell_Cycle 15    8  0.53333333     20     0.13605442
9:  PI3K 29     11  0.37931034     63     0.42857143
10: RTK-RAS 85    28  0.32941176    124    0.84353741
> OncogenicPathways(maf= IKKpunctatehigh)
  Pathway N_n_affected_genes fraction_affected Mutated_samples Fraction_mutated_samples
1: Cell_Cycle 15    1  0.06666667      1      0.09090909
2:  NRF2 3      1  0.33333333      1      0.09090909
3:  WNT 68      2  0.02941176      8      0.72727273
4:  TGF-Beta 7     2  0.28571429      3      0.27272727
5:  NOTCH 71     3  0.04225352      3      0.27272727
6:  TP53 6       3  0.50000000      9      0.81818182
7:  PI3K 29     4  0.13793103      5      0.45454545
8:  RTK-RAS 85    11  0.12941176     11     1.00000000
> IKKpunctatelow.vs.IKKpunctatehigh <- mafCompare(m1 = IKKpunctatelow, m2 = IKKpunctatehigh, m1Name = 'Low', m2Name = 'High', minMut = 5)
> print(IKKpunctatelow.vs.IKKpunctatehigh)
$results
  Hugo_Symbol Low High  pval  or  ci.up  ci.low adjPval
1:  PDGFRA 6 3 0.01693304 0.1168469 0.8512627 0.01983251 1
2:  KRAS 66 9 0.02602932 0.1828151 0.9264554 0.01861796 1
3:  RET 5 2 0.07655128 0.1621296 1.9238916 0.02227786 1
4:  PIK3R1 7 2 0.12135753 0.2286777 2.5660751 0.03550370 1
5:  ROS1 8 2 0.14588678 0.2625954 2.8938770 0.04231794 1
6:  SMAD4 19 3 0.18333364 0.3988933 2.5354896 0.08560004 1
7:  TP53 89 9 0.20833360 0.3429801 1.7419962 0.03485732 1
8:  RNF43 26 0 0.21329377  Inf  Inf 0.50028993 1
9:  BRAF 25 0 0.21481915  Inf  Inf 0.47609327 1
10: AMER1 12 2 0.25246992 0.4031851 4.2530257 0.07060773 1
11: NOTCH3 19 0 0.36280436  Inf  Inf 0.33875949 1
12: CHEK2 6 1 0.40272353 0.4287501 21.5081086 0.04447555 1
13: MEN1 6 1 0.40272353 0.4287501 21.5081086 0.04447555 1
14: CTCF 7 1 0.44623374 0.5028682 24.7613140 0.05468634 1
15: PBRM1 7 1 0.44623374 0.5028682 24.7613140 0.05468634 1
16: PIK3CA 28 3 0.45224205 0.6295333 3.9164291 0.13934373 1
17: GATA3 8 1 0.48684326 0.5780276 28.0613262 0.06507063 1
18: IDH1 8 1 0.48684326 0.5780276 28.0613262 0.06507063 1
19: DICER1 9 1 0.52472732 0.6542535 31.4091629 0.07561369 1
20: ARID2 10 1 0.56005164 0.7315656 34.8058715 0.08632258 1
21: PTCH1 10 1 0.56005164 0.7315656 34.8058715 0.08632258 1
22: TAF1B 10 1 0.56005164 0.7315656 34.8058715 0.08632258 1
23: NF1 11 1 0.59297295 0.8099986 38.2525304 0.09719398 1
24: NRAS 11 1 0.59297295 0.8099986 38.2525304 0.09719398 1
25: POLE 11 1 0.59297295 0.8099986 38.2525304 0.09719398 1
26: SLC23A2 11 1 0.59297295 0.8099986 38.2525304 0.09719398 1
27: TMBIM4 11 1 0.59297295 0.8099986 38.2525304 0.09719398 1
28: BLM 14 0 0.60027905  Inf  Inf 0.23362621 1
29: KMT2A 14 0 0.60027905  Inf  Inf 0.23362621 1
30: AIM2 13 0 0.60133652  Inf  Inf 0.21353998 1
31: EP300 13 0 0.60133652  Inf  Inf 0.21353998 1
32: POLQ 13 0 0.60133652  Inf  Inf 0.21353998 1
33: CREBBP 15 0 0.60146870  Inf  Inf 0.25402248 1
34: ERBB4 16 0 0.60462722  Inf  Inf 0.27472624 1

```


35:	NOTCH2	16	0	0.60462722	Inf	Inf	0.27472624	1
36:	MSH6	17	0	0.60949977	Inf	Inf	0.29574428	1
37:	FBXW7	21	2	0.66303229	0.7514911	7.6238349	0.14073376	1
38:	MSH2	21	2	0.66303229	0.7514911	7.6238349	0.14073376	1
39:	ATM	25	1	0.69324948	2.0416638	92.4064544	0.26796002	1
40:	AR	40	2	0.72867399	1.6773149	16.6166388	0.32669716	1
41:	ALK	20	1	1.00000000	1.5708943	71.6962555	0.20272038	1
42:	ARID1B	10	0	1.00000000	Inf	Inf	0.15502690	1
43:	ATR	20	1	1.00000000	1.5708943	71.6962555	0.20272038	1
44:	CDK12	10	0	1.00000000	Inf	Inf	0.15502690	1
45:	MAP3K1	10	0	1.00000000	Inf	Inf	0.15502690	1
46:	PTEN	13	1	1.00000000	0.9703327	45.3001732	0.11942897	1
47:	RAD50	13	1	1.00000000	0.9703327	45.3001732	0.11942897	1
48:	SETD2	10	0	1.00000000	Inf	Inf	0.15502690	1
49:	SF3B1	10	0	1.00000000	Inf	Inf	0.15502690	1
50:	SMARCA4	10	0	1.00000000	Inf	Inf	0.15502690	1
51:	SMO	10	0	1.00000000	Inf	Inf	0.15502690	1
52:	TSC2	10	0	1.00000000	Inf	Inf	0.15502690	1
53:	TTK	18	1	1.00000000	1.3927159	63.8606786	0.17801415	1
54:	APC	102	8	1.00000000	0.8508612	3.7578728	0.13899153	1
55:	ARID1A	27	2	1.00000000	1.0124222	10.1566173	0.19323340	1
56:	ASTE1	14	1	1.00000000	1.0523028	48.9034785	0.13078601	1
57:	ASXL1	22	1	1.00000000	1.7547234	79.7819907	0.22819906	1
58:	ATRX	9	0	1.00000000	Inf	Inf	0.13609689	1
59:	B2M	9	0	1.00000000	Inf	Inf	0.13609689	1
60:	BRC1A	12	1	1.00000000	0.8896011	41.7502498	0.10822889	1
61:	BRC2A	19	1	1.00000000	1.4811152	67.7479275	0.19027863	1
62:	CASP5	5	0	1.00000000	Inf	Inf	0.06328963	1
63:	CCDC150	7	0	1.00000000	Inf	Inf	0.09909482	1
64:	CIITA	9	0	1.00000000	Inf	Inf	0.13609689	1
65:	COBLL1	9	0	1.00000000	Inf	Inf	0.13609689	1
66:	CTNNA1	12	0	1.00000000	Inf	Inf	0.19374529	1
67:	DNMT3A	6	0	1.00000000	Inf	Inf	0.08103391	1
68:	ERBB2	7	0	1.00000000	Inf	Inf	0.09909482	1
69:	ERBB3	12	1	1.00000000	0.8896011	41.7502498	0.10822889	1
70:	FGFR1	6	0	1.00000000	Inf	Inf	0.08103391	1
71:	FGFR2	7	0	1.00000000	Inf	Inf	0.09909482	1
72:	FGFR3	6	0	1.00000000	Inf	Inf	0.08103391	1
73:	FGFR4	7	0	1.00000000	Inf	Inf	0.09909482	1
74:	GNA11	6	0	1.00000000	Inf	Inf	0.08103391	1
75:	GNAS	12	0	1.00000000	Inf	Inf	0.19374529	1
76:	HGF	5	0	1.00000000	Inf	Inf	0.06328963	1
77:	IDH2	6	0	1.00000000	Inf	Inf	0.08103391	1
78:	JAK1	6	0	1.00000000	Inf	Inf	0.08103391	1
79:	MAP2K4	6	0	1.00000000	Inf	Inf	0.08103391	1
80:	MLH1	5	0	1.00000000	Inf	Inf	0.06328963	1
81:	MTOR	11	0	1.00000000	Inf	Inf	0.17424224	1
82:	NBN	6	0	1.00000000	Inf	Inf	0.08103391	1
83:	NOTCH1	21	1	1.00000000	1.6620859	75.7071114	0.21535957	1
84:	NOTCH4	19	1	1.00000000	1.4811152	67.7479275	0.19027863	1
85:	NTRK1	6	0	1.00000000	Inf	Inf	0.08103391	1
86:	PALB2	12	0	1.00000000	Inf	Inf	0.19374529	1
87:	PIK3CB	5	0	1.00000000	Inf	Inf	0.06328963	1
88:	RB1	5	0	1.00000000	Inf	Inf	0.06328963	1
89:	RPL22	23	1	1.00000000	1.8488417	83.9224367	0.24124265	1
90:	RUNX1	8	0	1.00000000	Inf	Inf	0.11745199	1
91:	TEAD2	11	0	1.00000000	Inf	Inf	0.17424224	1
92:	TGFBR2	21	1	1.00000000	1.6620859	75.7071114	0.21535957	1

Hugo_Symbol Low High pval or ci.up ci.low adjPval

\$\$SampleSummary

Cohort SampleSize

1: Low 147
2: High 11

```
> forestPlot(mafCompareRes = IKKpunctatelow.vs.IKKpunctatehigh, pVal = 0.05, color = c('royalblue', 'maroon'), geneFontSize = 0.8)
> genes = c("PDGFRA", "KRAS", "RET", "PIK3R1", "ROS1", "SMAD4", "TP53", "RNF43", "BRAF", "AMER1")
> coBarplot(m1 = IKKpunctatelow, m2 = IKKpunctatehigh, m1Name = 'Low', m2Name = 'High', genes = genes)
> IKKall <- read.maf(file.choose())
-Reading
-Validating
--Removed 199 duplicated variants
--Non MAF specific values in Variant_Classification column:
Multi_Hit
3UTR
inframe_indelstop_gained
inframe_indel
inframe_indelMissense_Mutation

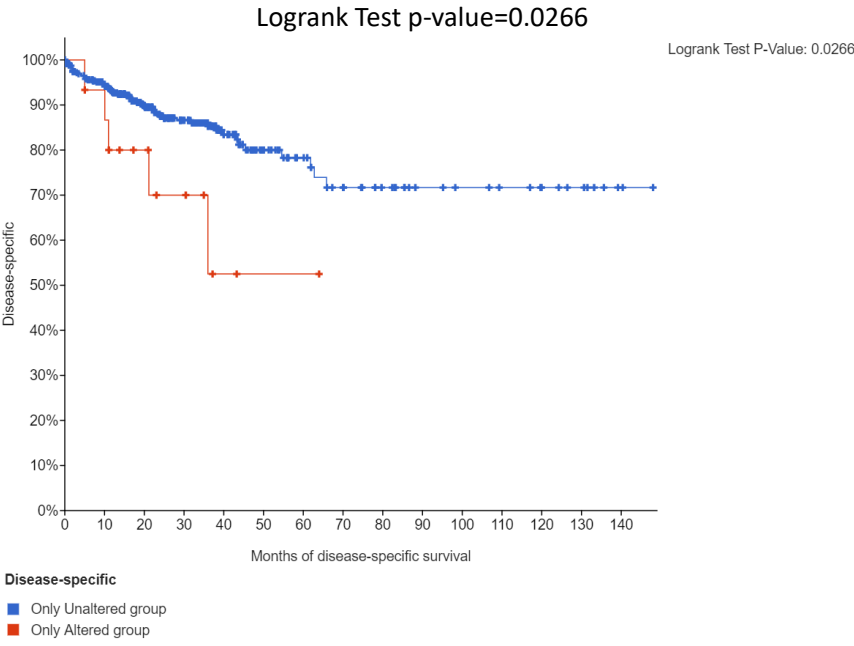
--Non MAF specific values in Variant_Type column:
Complex
-Silent variants: 613
-Summarizing
-Processing clinical data
--Missing clinical data
-Finished in 14.9s elapsed (0.735s cpu)
> plotmafSummary(maf = IKKall, rmOutlier = TRUE, addStat = 'median', dashboard = TRUE, titvRaw = FALSE)
> plotVaf(maf = IKKall, vafCol = 'VAF', top = 10)
```

Supplementary Table 4. Univariate and multivariate analysis in patients undergoing surgery for colorectal cancer

Clinicopathological characteristics	Univariate HR (95% CI)	<i>P</i>	Multivariate analysis	<i>p</i>
Age (<65/>65)	1.25 (0.80 – 1.31)	0.859		
Sex (Female/Male)	1.12 (0.89 – 1.42)	0.348		
Type of surgery (Elective/Emergency)	1.74 (1.33 – 2.28)	<0.001	1.69 (1.23 – 2.33)	0.002
Tumour location (Right/Left/Rectum)	0.74 (0.88 – 1.20)	0.725		
Tumour Characteristics				
TNM stage (I/II/III)	2.63 (2.15 – 3.23)	<0.001	2.42 (1.90 – 3.08)	<0.001
Tumour differentiation (Mod-well/poor)	1.69 (1.22 – 2.35)	<0.001		
Venous invasion (No/Yes)	1.67 (1.31 – 2.13)	<0.001	1.51 (1.12 – 2.02)	0.007
Margin involvement (No/Yes)	3.73 (1.71 – 8.14)	<0.001	2.26 (1.43 – 3.57)	0.001
Necrosis (Absent/Present)	1.13 (0.67 – 1.91)	0.088		
Proliferation (High/Low)	0.79 (0.48 – 1.29)	<0.001		
MMR status (Proficient/Deficient)	1.10 (0.55 – 2.16)	0.176		
Tumour microenvironment				
Klintrup-Mäkinen grade (Weak/Strong)	0.51 (0.28 – 0.93)	<0.001	0.47 (0.32-0.68)	<0.001
Tumour stroma percentage (Low/High)	2.01 (1.22 – 3.54)	<0.001	1.58 (1.16-2.14)	0.005

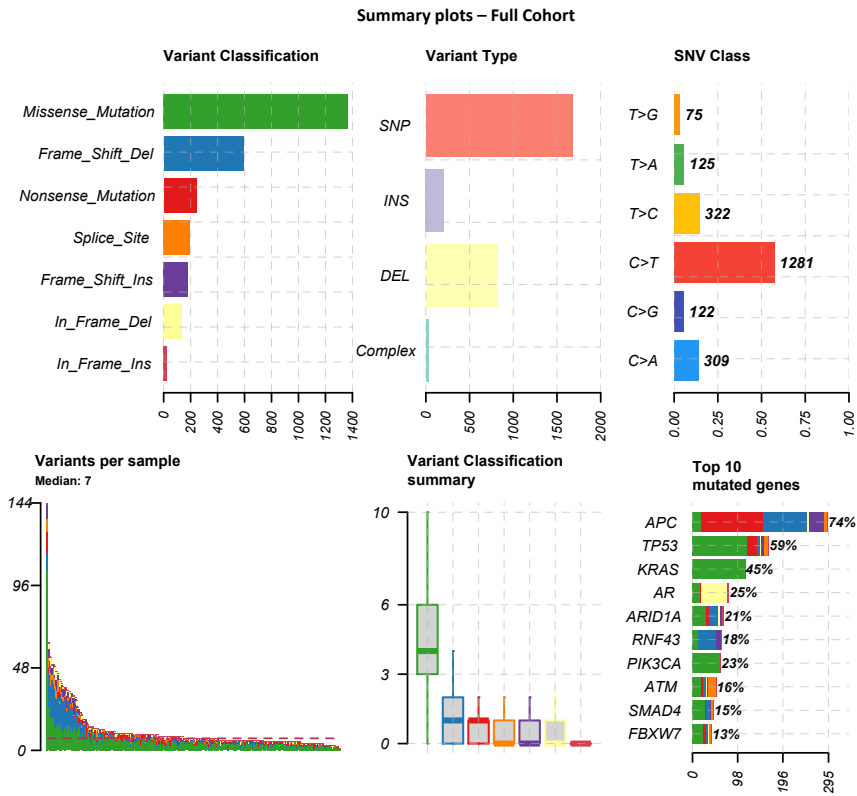
Adjuvant therapy (No/Yes)	1.05 (0.63 – 1.74)	0.994		
Cytoplasmic IKK-α (Low/High)	1.56 (0.87 – 2.78)	0.240		
Punctate IKK-α (Low/High)	2.22 (1.14 – 4.30)	<0.001	1.97 (1.26 –3.08)	0.006

Supplementary Figure 1. Altered CHUK gene signature and survival in patients from the TCGA panCancer atlas colorectal cohort

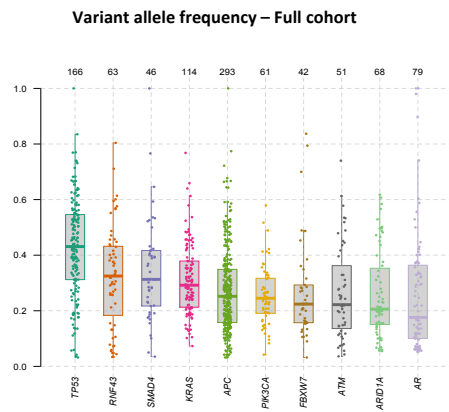


Supplementary Figure 2. Mutational cohort characteristics

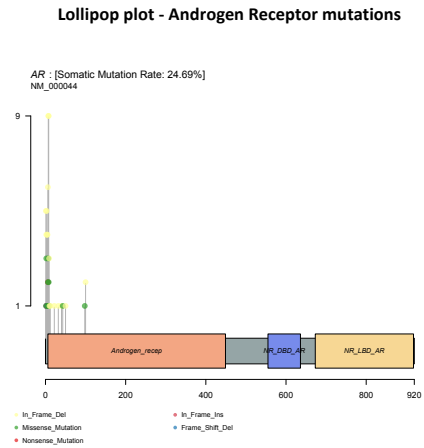
A



B



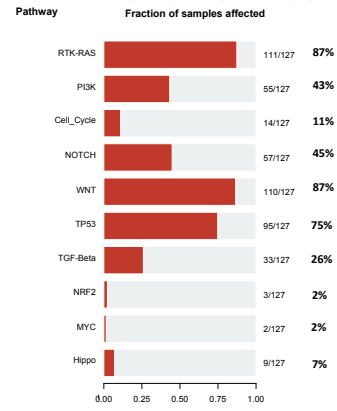
C



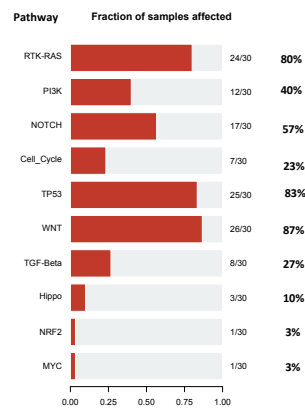
Supplementary Figure 3. Mutations in oncogenic pathways in low vs high cytoplasmic and low vs. high punctate IKK α

A

Mutations in oncogenic pathways -Low Cytoplasmic IKK α

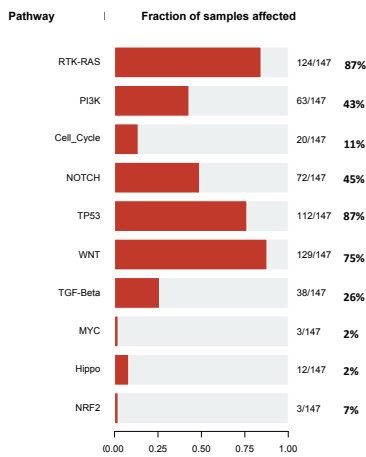


Mutations in oncogenic pathways -High Cytoplasmic IKK α



B

Mutations in oncogenic pathways -Low punctate IKK α



Mutations in oncogenic pathways -High punctate IKK α

