

```

# --- 1. LOAD LIBRARIES ---

library(maf-tools)
library(data.table)

# --- 2. DATA PREPARATION ---

raw_data <- fread("combined_calls.tsv")

colnames(raw_data) <- c("Chromosome", "Start_Position", "Reference_Allele", "Tumor_Seq_Allele2", "Qual", "Filter")

raw_data[, End_Position := Start_Position + nchar(Reference_Allele) - 1]

# --- 3. UPDATED LABELS ---

raw_data$Tumor_Sample_Barcode = "combined_minion_promethion"

raw_data$Variant_Classification = ifelse(raw_data$Filter == "PASS", "Missense_Mutation", "Silent")

raw_data$Variant_Type = ifelse(nchar(raw_data$Reference_Allele) == 1 & nchar(raw_data$Tumor_Seq_Allele2) == 1, "SNP",
                               ifelse(nchar(raw_data$Reference_Allele) < nchar(raw_data$Tumor_Seq_Allele2), "INS", "DEL"))

raw_data$Hugo_Symbol = raw_data$Chromosome

# --- 4. CREATE MAF OBJECT ---

write.table(raw_data, "combined_platforms.maf", sep="\t", quote=FALSE, row.names=FALSE)

my_maf = read.maf(maf = "combined_platforms.maf", isTCGA = FALSE, vc_nonSyn = "Missense_Mutation")

```

```

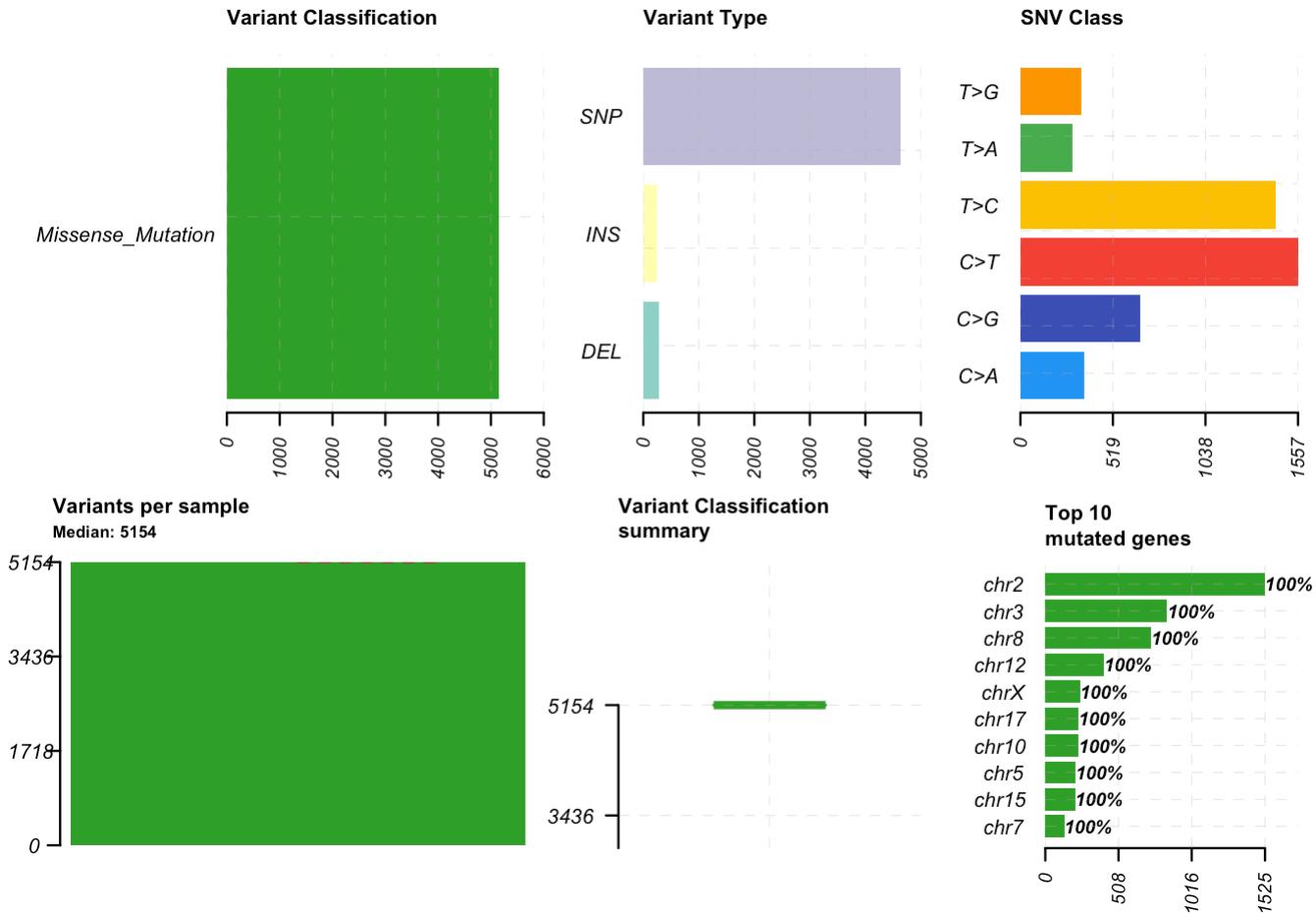
## -Reading
## -Validating
## -Silent variants: 638
## -Summarizing
## -Processing clinical data
## --Missing clinical data
## -Finished in 0.045s elapsed (0.038s cpu)

```

```
# ---- 5. STABLE VISUALIZATIONS ----
```

*# Plot 1: Summary Dashboard*

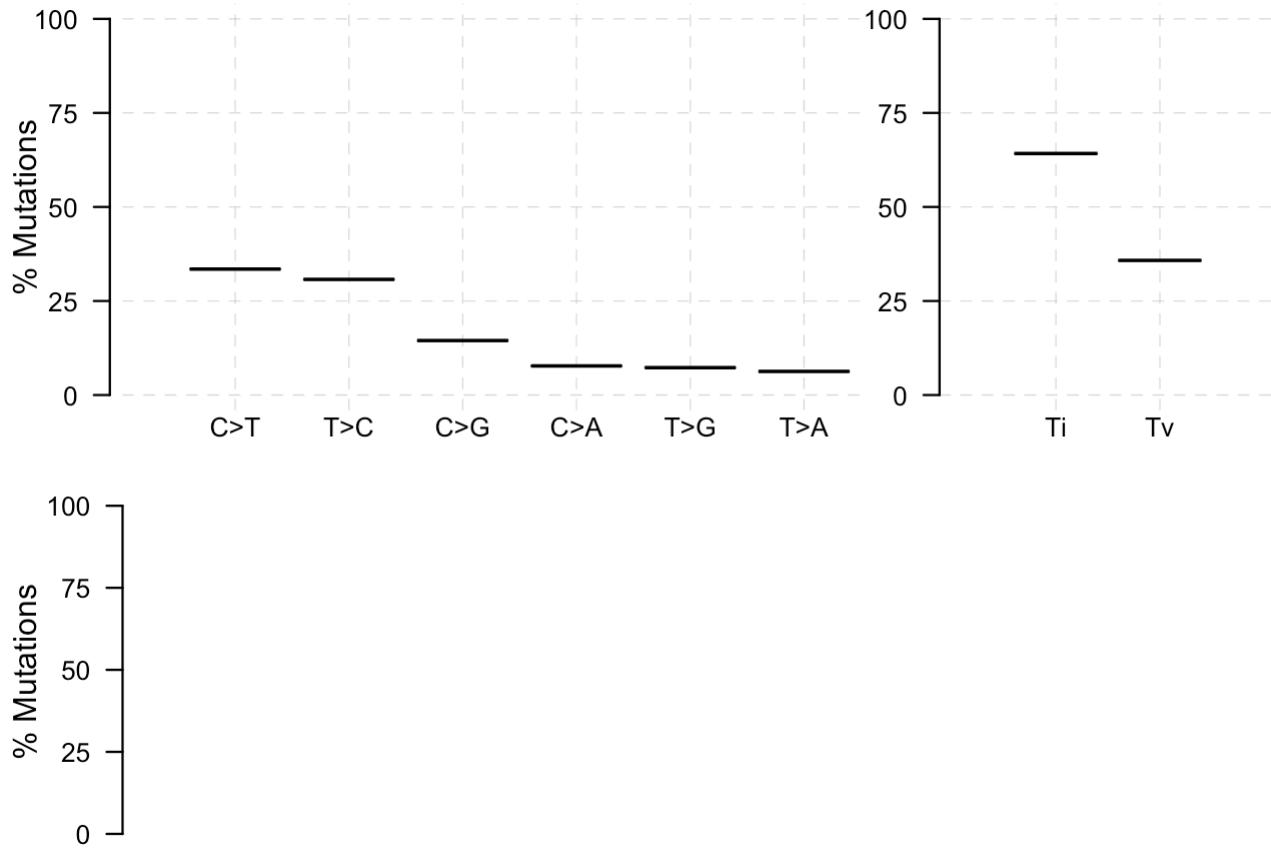
```
plotmafSummary(maf = my_maf, addStat = 'median', rmOutlier = TRUE, dashboard = TRUE)
```



*# Plot 2: Ti/Tv Analysis*

```
titv_res = titv(maf = my_maf, plot = FALSE, useSyn = TRUE)
```

```
plotTiTv(res = titv_res)
```

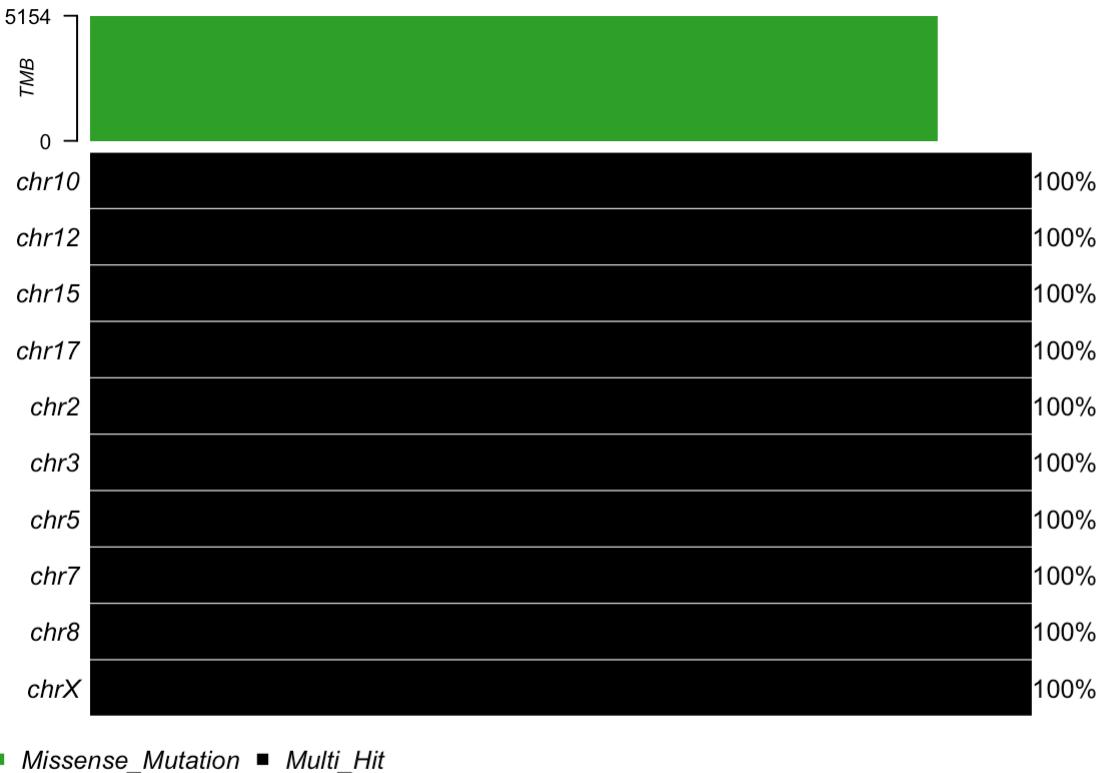


```
# Plot 3: Oncoplot (Top 10 Mutated Chromosomes)
```

```
oncoplot(maf = my_maf, top = 10, drawRowBar = FALSE, font_size = 0.8)
```

```
## Warning in min(x): no non-missing arguments to min; returning Inf
```

```
## Warning in max(x): no non-missing arguments to max; returning -Inf
```

**Altered in 1 (100%) of 1 samples.**

```
# Plot 4: Rainfall Plot (This will work perfectly for your 55 Kataegis events)

# Use this to visualize the clusters on Chromosome 2

rainfallPlot(maf = my_maf, tsb = "combined_minion_promethion", detectChangePoints = TRUE)
```

```
## Processing combined_minion_promethion..
```

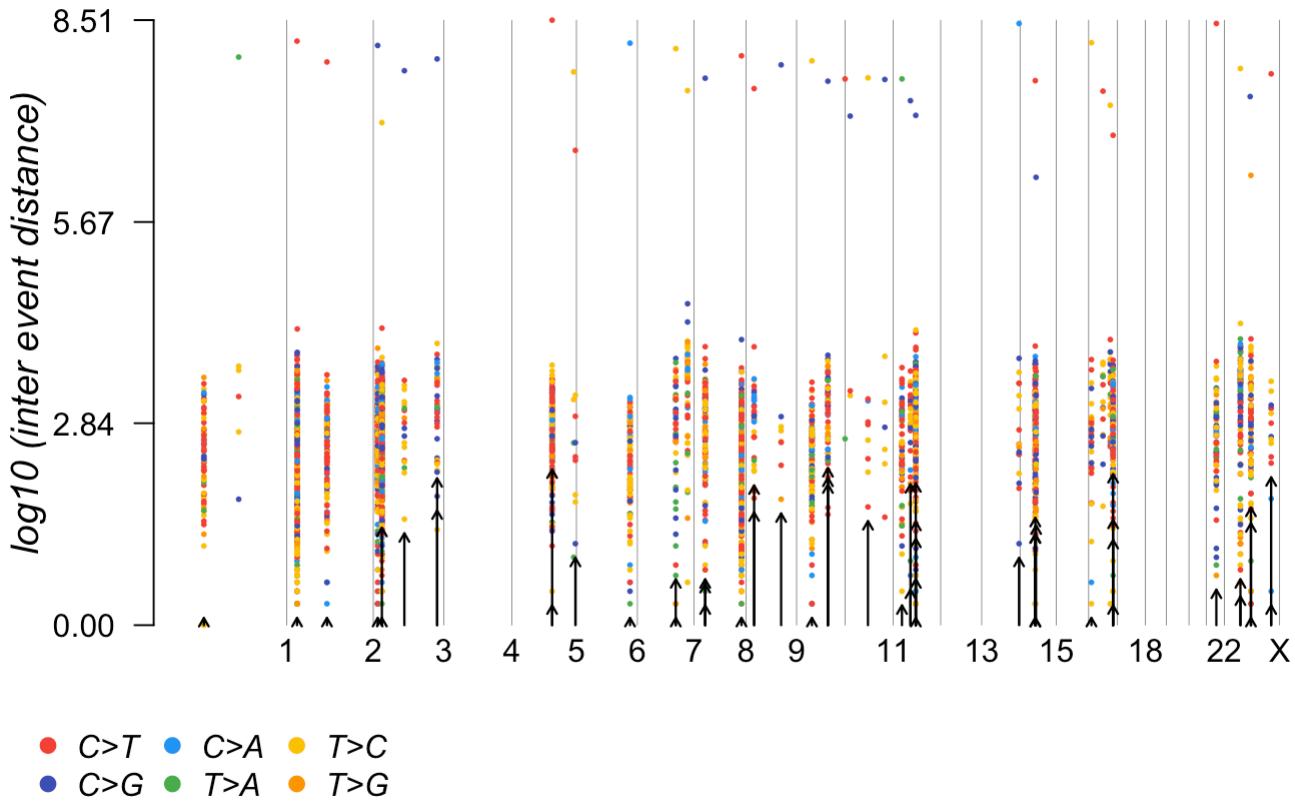
```
## Kataegis detected at:
```

##	Chromosome	Start_Position	End_Position	nMuts	Avg_intermutation_dist	Size
##	<num>	<num>	<num>	<int>	<num>	<num>
## 1:	1	17019410	17054002	69	508.7059	34592
## 2:	2	29192926	29920131	1288	565.0389	727205
## 3:	2	113216055	113277617	111	559.6545	61562
## 4:	3	12287696	12434058	209	703.6635	146362
## 5:	3	24123533	24128235	7	783.6667	4702
## 6:	3	24130634	24493919	504	722.2366	363285
## 7:	3	87259403	87275374	19	887.2778	15971
## 8:	3	179186419	179192974	9	819.3750	6555
## 9:	3	179217179	179222517	7	889.6667	5338
## 10:	5	112709435	112716131	8	956.5714	6696
## 11:	5	112718389	112845879	165	777.3780	127490
## 12:	5	177992355	177995875	9	440.0000	3520
## 13:	6	150370221	150405763	101	355.4200	35542
## 14:	7	107661438	107664670	6	646.4000	3232
## 15:	7	107677040	107716314	41	981.8500	39274
## 16:	8	31044583	31055016	12	948.4545	10433
## 17:	8	31069763	31080274	13	875.9167	10511
## 18:	8	31102488	31174361	87	835.7326	71873
## 19:	8	132867967	133131965	543	487.0812	263998
## 20:	9	21976672	21981087	6	883.0000	4415
## 21:	9	21983915	21995144	16	748.6000	11229
## 22:	9	97853378	97856378	8	428.5714	3000
## 23:	10	43077059	43130238	137	391.0221	53179
## 24:	10	87910574	87917350	8	968.0000	6776
## 25:	10	87939302	87949237	11	993.5000	9935
## 26:	10	87957058	87964003	10	771.6667	6945
## 27:	11	64804546	64809675	9	641.1250	5129
## 28:	12	25205716	25250690	78	584.0779	44974
## 29:	12	49020848	49042941	24	960.5652	22093
## 30:	12	49045593	49051609	8	859.4286	6016
## 31:	12	63950137	63954978	7	806.8333	4841
## 32:	12	63982306	63986666	7	726.6667	4360
## 33:	12	63992237	64018932	28	988.7037	26695
## 34:	12	64022548	64035057	24	543.8696	12509
## 35:	12	64058253	64160255	116	886.9739	102002
## 36:	14	104771710	104785733	16	934.8667	14023
## 37:	15	42944414	42948618	8	600.5714	4204
## 38:	15	42967649	42981053	18	788.4706	13404
## 39:	15	42988662	42994605	7	990.5000	5943
## 40:	15	43002020	43052688	54	956.0000	50668
## 41:	15	43074564	43105910	50	639.7143	31346
## 42:	15	45101541	45118049	32	532.5161	16508
## 43:	17	7662815	7686387	31	785.7333	23572
## 44:	17	68422443	68428041	7	933.0000	5598
## 45:	17	68431378	68451163	22	942.1429	19785
## 46:	17	68461865	68493367	36	900.0571	31502
## 47:	17	68498691	68549311	66	778.7692	50620
## 48:	22	28690105	28739901	67	754.4848	49796
## 49:	23	44922028	44930899	12	806.4545	8871
## 50:	23	44963483	44974171	18	628.7059	10688
## 51:	23	74443903	74449700	7	966.1667	5797
## 52:	23	74456451	74463710	9	907.3750	7259
## 53:	23	74490685	74531188	51	810.0600	40503

## 54:	23	131277902	131282984	7		847.0000	5082
## 55:	23	131285672	131289385	8		530.4286	3713
<b>## Chromosome Start_Position End_Position nMuts Avg_intermutation_dist Size</b>							
## <num>	<num>	<num>	<int>			<num>	<num>
## Tumor_Sample_Barcode		C>A	C>G	C>T	T>A	T>C	T>G
		<fctr>	<int>	<int>	<int>	<int>	<int>
## 1: combined_minion_promethion		4	5	29	4	21	6
## 2: combined_minion_promethion	106	175	413	77	418	99	
## 3: combined_minion_promethion	10	11	49	2	31	8	
## 4: combined_minion_promethion	23	29	65	13	67	12	
## 5: combined_minion_promethion	1	1	3	1	NA	1	
## 6: combined_minion_promethion	43	74	171	43	140	33	
## 7: combined_minion_promethion	NA	3	4	2	9	1	
## 8: combined_minion_promethion	NA	2	5	NA	2	NA	
## 9: combined_minion_promethion	1	3	2	1	NA	NA	
## 10: combined_minion_promethion	1	1	2	NA	3	1	
## 11: combined_minion_promethion	15	30	54	12	43	11	
## 12: combined_minion_promethion	NA	2	4	NA	3	NA	
## 13: combined_minion_promethion	12	8	29	5	38	9	
## 14: combined_minion_promethion	NA	NA	4	1	1	NA	
## 15: combined_minion_promethion	2	9	9	10	4	7	
## 16: combined_minion_promethion	1	1	5	1	4	NA	
## 17: combined_minion_promethion	2	2	3	1	3	2	
## 18: combined_minion_promethion	7	6	29	5	30	10	
## 19: combined_minion_promethion	40	68	214	33	155	33	
## 20: combined_minion_promethion	NA	1	3	NA	2	NA	
## 21: combined_minion_promethion	2	3	4	1	5	1	
## 22: combined_minion_promethion	NA	2	2	NA	3	1	
## 23: combined_minion_promethion	10	17	37	8	54	11	
## 24: combined_minion_promethion	NA	1	3	1	3	NA	
## 25: combined_minion_promethion	1	4	3	NA	2	1	
## 26: combined_minion_promethion	2	1	3	2	1	1	
## 27: combined_minion_promethion	1	NA	5	NA	3	NA	
## 28: combined_minion_promethion	4	9	30	7	17	11	
## 29: combined_minion_promethion	3	4	9	1	6	1	
## 30: combined_minion_promethion	1	NA	3	NA	4	NA	
## 31: combined_minion_promethion	NA	1	1	1	3	1	
## 32: combined_minion_promethion	1	1	3	NA	1	1	
## 33: combined_minion_promethion	NA	9	11	4	2	2	
## 34: combined_minion_promethion	NA	1	12	NA	9	2	
## 35: combined_minion_promethion	8	18	31	6	42	11	
## 36: combined_minion_promethion	1	4	5	NA	5	1	
## 37: combined_minion_promethion	1	1	1	NA	4	1	
## 38: combined_minion_promethion	3	1	7	NA	7	NA	
## 39: combined_minion_promethion	NA	1	4	NA	2	NA	
## 40: combined_minion_promethion	5	7	18	1	17	6	
## 41: combined_minion_promethion	2	14	18	2	13	1	
## 42: combined_minion_promethion	3	6	9	2	5	7	
## 43: combined_minion_promethion	1	5	13	NA	11	1	
## 44: combined_minion_promethion	1	1	1	NA	4	NA	
## 45: combined_minion_promethion	1	5	3	3	10	NA	
## 46: combined_minion_promethion	2	4	15	1	10	4	
## 47: combined_minion_promethion	9	9	26	3	15	4	
## 48: combined_minion_promethion	2	16	17	5	22	5	
## 49: combined_minion_promethion	NA	2	7	NA	2	1	
## 50: combined_minion_promethion	NA	4	4	1	4	5	

```
## 51: combined_minion_promethion    NA    NA    1    1    5    NA
## 52: combined_minion_promethion    1     1    2    NA    3    2
## 53: combined_minion_promethion    2     9   16    4   17    3
## 54: combined_minion_promethion   NA     2    4    NA    1    NA
## 55: combined_minion_promethion    2     1    1    NA    4    NA
##          Tumor_Sample_Barcode  C>A  C>G  C>T  T>A  T>C  T>G
##                      <fctr> <int> <int> <int> <int> <int> <int>
```

## combined\_minion\_promethion



```
# --- 6. DATA EXPORT (Instead of Lollipop Plot) ---
```

```
# Get a summary of mutations per chromosome
```

```
chr_summary <- getGeneSummary(my_maf)
```

```
write.csv(chr_summary, "mutation_counts_per_chromosome.csv", row.names = FALSE)
```

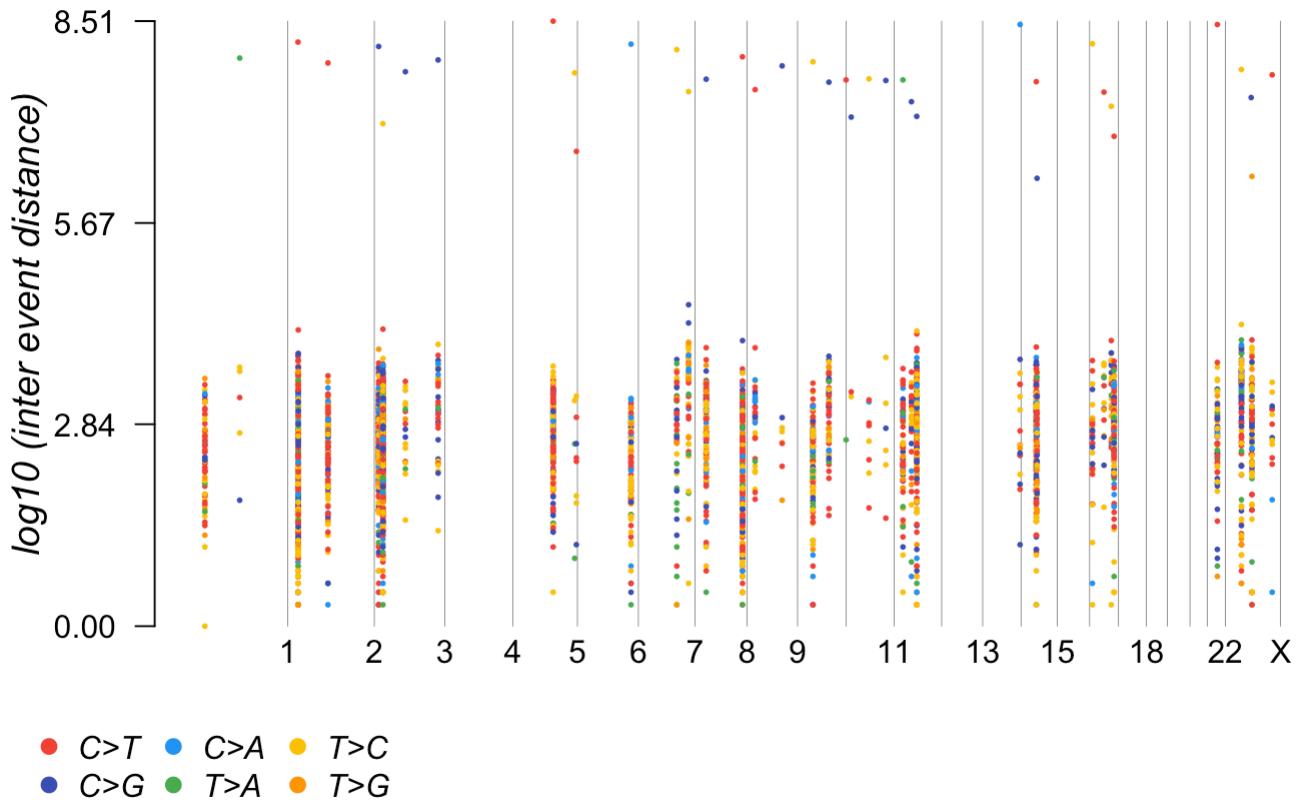
```
# Extract the 55 Kataegis clusters to a file for your report
```

```
# This captures the Start/End positions of the clusters you saw in the console
```

```
kataegis_clusters <- rainfallPlot(maf = my_maf, tsb = "combined_minion_promethion")
```

```
## Processing combined_minion_promethion..
```

## combined\_minion\_promethion



- C>T   ● C>A   ● T>C
- C>G   ● T>A   ● T>G

```
if(!is.null(kataegis_clusters)){
  write.csv(kataegis_clusters, "kataegis_hotspots.csv", row.names = FALSE)
}
```

```

# 1. Load the full panel (Including the missing ones you provided)
panel <- fread("Chr,Start,End,Gene
chr1,114704464,114716894,NRAS
chr1,17018664,17054151,SDHB
chr2,29192774,29921586,ALK
chr2,113215997,113278921,PAX8
chr3,12287368,12434344,PPARG
chr3,24117153,24495708,THR8
chr3,87259404,87276584,POU1F1
chr3,179148126,179240093,PIK3CA
chr5,112707498,112846239,APC
chr5,173232109,173235206,NKX2-5
chr5,177992235,177996242,PROP1
chr6,150369012,150405969,IYD
chr7,107660828,107717809,SLC26A4
chr7,140713327,140924928,BRAF
chr8,31033810,31176138,WRN
chr8,132866958,133134899,TG
chr9,21967752,21995324,CDKN2A
chr9,22002903,22009313,CDKN2B
chr9,97853226,97856717,FOXE1
chr10,43076840,43130353,RET
chr10,87863625,87971930,PTEN
chr11,532242,537287,HRAS
chr11,14966668,14972351,CALCA
chr11,64803516,64811294,MEN1
chr11,112086873,112095794,SDHD
chr12,25204789,25250936,KRAS
chr12,49018978,49060794,KMT2D
chr12,63844700,64162217,SRGAP1
chr14,104769349,104795748,AKT1
chr15,42942897,43106038,UBR1
chr15,45092650,45114172,DUOX2
chr15,45114326,45118421,DUOXA2
chr17,7661779,7687550,TP53
chr17,40062193,40093867,THRA
chr17,60600193,60666280,PPM1D
chr17,68413623,68551316,PRKAR1A
chr22,28687742,28741834,CHEK2
chrX,44873188,45112779,KDM6A
chrX,72301646,72307157,CITED1
chrX,74421493,74533916,SLC16A2
chrX,131273506,131289457,IGSF1")
```

# 2. Perform the overlap join

```
setkey(raw_data, Chromosome, Start_Position, End_Position)
setkey(panel, Chr, Start, End)
```

annotated\_data <- foverlaps(raw\_data, panel,
 by.x=c("Chromosome", "Start\_Position", "End\_Position"),
 by.y=c("Chr", "Start", "End"))

# 3. Handle 'Others' and clean up columns

# If it didn't hit a gene in your panel, we'll call it "Intergenic\_Region"

```
annotated_data[, Hugo_Symbol := ifelse(is.na(Gene), "Intergenic_Region", Gene)]  
  
# Final cleanup to match MAF format  
final_maf_df <- annotated_data[, .(Hugo_Symbol, Chromosome, Start_Position, End_Position,  
                                         Reference_Allele, Tumor_Seq_Allele2, Variant_Classification,  
                                         Variant_Type, Tumor_Sample_Barcode)]  
  
# 4. Re-load into maftools  
my_maf_final = read.maf(maf = final_maf_df, isTCGA = FALSE)
```

```
## -Validating  
## -Silent variants: 638  
## -Summarizing  
## -Processing clinical data  
## --Missing clinical data  
## -Finished in 0.036s elapsed (0.032s cpu)
```

```
# Filter mutations specifically in the ALK cluster  
alk_cluster_mut <- final_maf_df[Hugo_Symbol == "ALK"]  
  
# See the mutation types  
table(alk_cluster_mut$Reference_Allele, alk_cluster_mut$Tumor_Seq_Allele2)
```

	A	AAAAC	AAAACAAAC	AAAC	AAG	AAGAC	AAGGC	AC	ACATG
## A	0	1		1	1	1	1	1	1
## Aaatg	1	0		0	0	0	0	0	0
## AACC	1	0		0	0	0	0	0	0
## ACTC	1	0		0	0	0	0	0	0
## ACTT	1	0		0	0	0	0	0	0
## Agaggaggagaaggag	1	0		0	0	0	0	0	0
## At	6	0		0	0	0	0	0	0
## AT	2	0		0	0	0	0	0	0
## Atg	1	0		0	0	0	0	0	0
## Atgtgatg	1	0		0	0	0	0	0	0
## C	51	0		0	0	0	0	0	0
## Ca	0	0		0	0	0	0	0	0
## Caa	0	0		0	0	0	0	0	0
## Caaa	0	0		0	0	0	0	0	0
## Caaaaa	0	0		0	0	0	0	0	0
## Caaaaaaaa	0	0		0	0	0	0	0	0
## Cagagagagagagagagagag	0	0		0	0	0	0	0	0
## CAT	0	0		0	0	0	0	0	0
## Cgt	0	0		0	0	0	0	0	0
## CGTAT	0	0		0	0	0	0	0	0
## Ct	0	0		0	0	0	0	0	0
## CT	0	0		0	0	0	0	0	0
## Ctt	0	0		0	0	0	0	0	0
## Cttt	0	0		0	0	0	0	0	0
## Ctttt	0	0		0	0	0	0	0	0
## G	188	0		0	0	0	0	0	0
## Ga	0	0		0	0	0	0	0	0
## GA	0	0		0	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga	0	0		0	0	0	0	0	0
## GGAA	0	0		0	0	0	0	0	0
## Gggaa	0	0		0	0	0	0	0	0
## Gggtgtgtgtgt	0	0		0	0	0	0	0	0
## Ggtgt	0	0		0	0	0	0	0	0
## Gt	0	0		0	0	0	0	0	0
## GT	0	0		0	0	0	0	0	0
## Gtc	0	0		0	0	0	0	0	0
## GTCTTGAAGGAAA	0	0		0	0	0	0	0	0
## Gtgt	0	0		0	0	0	0	0	0
## Gtt	0	0		0	0	0	0	0	0
## GTT	0	0		0	0	0	0	0	0
## Gttt	0	0		0	0	0	0	0	0
## Gttttttt	0	0		0	0	0	0	0	0
## T	40	0		0	0	0	0	0	0
## Ta	0	0		0	0	0	0	0	0
## TA	0	0		0	0	0	0	0	0
## Taa	0	0		0	0	0	0	0	0
## Taaa	0	0		0	0	0	0	0	0
## Taaaaaaaaaaa	0	0		0	0	0	0	0	0
## Taac	0	0		0	0	0	0	0	0
## Tac	0	0		0	0	0	0	0	0
## Tacacacacacacacac	0	0		0	0	0	0	0	0
## Tagagag	0	0		0	0	0	0	0	0

		0	0	0	0	0	0	0	0
		AG	AGAGGT	AGCCCTG	AGT	AGTTCAAGGTCACTGAAT	AT		
##	Tc	0	0	0	0	0	0	0	0
##	TCC	0	0	0	0	0	0	0	0
##	Tccaa	0	0	0	0	0	0	0	0
##	Tg	0	0	0	0	0	0	0	0
##	Taaaaaaaaaaaaa	0	0	0	0	0	0	0	0
##	Ttctc	0	0	0	0	0	0	0	0
##									
##									
##	A	2	1	1	1		1	4	
##	Aaatg	0	0	0	0		0	0	
##	AACC	0	0	0	0		0	0	
##	ACTC	0	0	0	0		0	0	
##	ACTT	0	0	0	0		0	0	
##	Agaggaggagaaggag	0	0	0	0		0	0	
##	At	0	0	0	0		0	0	
##	AT	0	0	0	0		0	0	
##	Atg	0	0	0	0		0	0	
##	Atgtgatg	0	0	0	0		0	0	
##	C	0	0	0	0		0	0	
##	Ca	0	0	0	0		0	0	
##	Caa	0	0	0	0		0	0	
##	Caaa	0	0	0	0		0	0	
##	Caaaaa	0	0	0	0		0	0	
##	Caaaaaaaa	0	0	0	0		0	0	
##	Cagagagagagagagagagag	0	0	0	0		0	0	
##	CAT	0	0	0	0		0	0	
##	Cgt	0	0	0	0		0	0	
##	CGTAT	0	0	0	0		0	0	
##	Ct	0	0	0	0		0	0	
##	CT	0	0	0	0		0	0	
##	Ctt	0	0	0	0		0	0	
##	Cttt	0	0	0	0		0	0	
##	Ctttt	0	0	0	0		0	0	
##	G	0	0	0	0		0	0	
##	Ga	0	0	0	0		0	0	
##	GA	0	0	0	0		0	0	
##	Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0		0	0	
##	GGAA	0	0	0	0		0	0	
##	Ggaa	0	0	0	0		0	0	
##	Gggtgtgtgtgt	0	0	0	0		0	0	
##	Gtgt	0	0	0	0		0	0	
##	Gt	0	0	0	0		0	0	
##	GT	0	0	0	0		0	0	
##	Gtc	0	0	0	0		0	0	
##	GTCTTGAAGGAAA	0	0	0	0		0	0	
##	Gtgt	0	0	0	0		0	0	
##	Gtt	0	0	0	0		0	0	
##	GTT	0	0	0	0		0	0	
##	Gttt	0	0	0	0		0	0	
##	Gttttttt	0	0	0	0		0	0	
##	T	0	0	0	0		0	0	
##	Ta	0	0	0	0		0	0	
##	TA	0	0	0	0		0	0	
##	Taa	0	0	0	0		0	0	
##	Taaa	0	0	0	0		0	0	

## Taaaaaaaaaa	0	0	0	0	0	0	0
## Taac	0	0	0	0	0	0	0
## Tac	0	0	0	0	0	0	0
## Tacacacacacacacac	0	0	0	0	0	0	0
## Tagagag	0	0	0	0	0	0	0
## Tc	0	0	0	0	0	0	0
## TCC	0	0	0	0	0	0	0
## Tccaa	0	0	0	0	0	0	0
## Tg	0	0	0	0	0	0	0
## Taaaaaaaaaaaaaa	0	0	0	0	0	0	0
## Ttctc	0	0	0	0	0	0	0
##							
##	ATAGCTAACACATATATGG	ATATATAT	ATATG	ATGTG	ATT	ATTAG	
## A		1	1	1	2	1	
## Aaatg		0	0	0	0	0	0
## AACC		0	0	0	0	0	0
## ACTC		0	0	0	0	0	0
## ACTT		0	0	0	0	0	0
## Agaggaggagaaggag		0	0	0	0	0	0
## At		0	0	0	0	0	0
## AT		0	0	0	0	0	0
## Atg		0	0	0	0	0	0
## Atgtgatg		0	0	0	0	0	0
## C		0	0	0	0	0	0
## Ca		0	0	0	0	0	0
## Caa		0	0	0	0	0	0
## Caaa		0	0	0	0	0	0
## Caaaaa		0	0	0	0	0	0
## Caaaaaa		0	0	0	0	0	0
## Cagagagagagagagagag		0	0	0	0	0	0
## CAT		0	0	0	0	0	0
## Cgt		0	0	0	0	0	0
## CGTAT		0	0	0	0	0	0
## Ct		0	0	0	0	0	0
## CT		0	0	0	0	0	0
## Ctt		0	0	0	0	0	0
## Cttt		0	0	0	0	0	0
## Ctttt		0	0	0	0	0	0
## G		0	0	0	0	0	0
## Ga		0	0	0	0	0	0
## GA		0	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga		0	0	0	0	0	0
## GGAA		0	0	0	0	0	0
## Gggaa		0	0	0	0	0	0
## Gggtgtgtgtgt		0	0	0	0	0	0
## Ggtgt		0	0	0	0	0	0
## Gt		0	0	0	0	0	0
## GT		0	0	0	0	0	0
## Gtc		0	0	0	0	0	0
## GTCTTGAAGGAAA		0	0	0	0	0	0
## Gtgt		0	0	0	0	0	0
## Gtt		0	0	0	0	0	0
## GTT		0	0	0	0	0	0
## Gttt		0	0	0	0	0	0
## Gttttttt		0	0	0	0	0	0

## T			0		0	0	0	0	0	
## Ta			0		0	0	0	0	0	
## TA			0		0	0	0	0	0	
## Taa			0		0	0	0	0	0	
## Taaa			0		0	0	0	0	0	
## Taaaaaaaaaa			0		0	0	0	0	0	
## Taac			0		0	0	0	0	0	
## Tac			0		0	0	0	0	0	
## Tacacacacacacacac			0		0	0	0	0	0	
## Tagagag			0		0	0	0	0	0	
## Tc			0		0	0	0	0	0	
## TCC			0		0	0	0	0	0	
## Tccaa			0		0	0	0	0	0	
## Tg			0		0	0	0	0	0	
## Ttaaaaaaaaaaaaaa			0		0	0	0	0	0	
## Ttctc			0		0	0	0	0	0	
##										
##			ATTTC	ATTTTT	C	C,CGTgt	C,Ct	CA	CAA	CAAAAA
## A			1	1	47	0	0	0	0	0
## Aaatg			0	0	0	0	0	0	0	0
## AACC			0	0	0	0	0	0	0	0
## ACTC			0	0	0	0	0	0	0	0
## ACTT			0	0	0	0	0	0	0	0
## Agaggaggagaaggag			0	0	0	0	0	0	0	0
## At			0	0	0	0	0	0	0	0
## AT			0	0	0	0	0	0	0	0
## Atg			0	0	0	0	0	0	0	0
## Atgtgatg			0	0	0	0	0	0	0	0
## C			0	0	0	0	0	8	1	1
## Ca			0	0	6	0	0	0	0	0
## Caa			0	0	3	0	0	0	0	0
## Caaa			0	0	2	0	0	0	0	0
## Caaaaa			0	0	1	0	0	0	0	0
## Caaaaaaaaa			0	0	1	0	0	0	0	0
## Cagagagagagagagagagag			0	0	1	0	0	0	0	0
## CAT			0	0	1	0	0	0	0	0
## Cgt			0	0	0	1	0	0	0	0
## CGTAT			0	0	1	0	0	0	0	0
## Ct			0	0	6	0	0	0	0	0
## CT			0	0	3	0	0	0	0	0
## Ctt			0	0	3	0	0	0	0	0
## Cttt			0	0	0	0	1	0	0	0
## Ctttt			0	0	1	0	0	0	0	0
## G			0	0	77	0	0	0	0	0
## Ga			0	0	0	0	0	0	0	0
## GA			0	0	0	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga			0	0	0	0	0	0	0	0
## GGAA			0	0	0	0	0	0	0	0
## Gggaa			0	0	0	0	0	0	0	0
## Gggtgtgtgtgt			0	0	0	0	0	0	0	0
## Ggtgt			0	0	0	0	0	0	0	0
## Gt			0	0	0	0	0	0	0	0
## GT			0	0	0	0	0	0	0	0
## Gtc			0	0	0	0	0	0	0	0
## GTCTTGAAGGAAA			0	0	0	0	0	0	0	0

## Gtgt	0	0	0	0	0	0	0	0	
## Gtt	0	0	0	0	0	0	0	0	
## GTT	0	0	0	0	0	0	0	0	
## Gttt	0	0	0	0	0	0	0	0	
## Gttttttt	0	0	0	0	0	0	0	0	
## T	0	0	243	0	0	0	0	0	
## Ta	0	0	0	0	0	0	0	0	
## TA	0	0	0	0	0	0	0	0	
## Taa	0	0	0	0	0	0	0	0	
## Taaa	0	0	0	0	0	0	0	0	
## Taaaaaaaaaa	0	0	0	0	0	0	0	0	
## Taac	0	0	0	0	0	0	0	0	
## Tac	0	0	0	0	0	0	0	0	
## Tacacacacacacacac	0	0	0	0	0	0	0	0	
## Tagagag	0	0	0	0	0	0	0	0	
## Tc	0	0	0	0	0	0	0	0	
## TCC	0	0	0	0	0	0	0	0	
## Tccaa	0	0	0	0	0	0	0	0	
## Tg	0	0	0	0	0	0	0	0	
## Taaaaaaaaaaaaaa	0	0	0	0	0	0	0	0	
## Ttctc	0	0	0	0	0	0	0	0	
##									
##		CAAAGT	CAG	CATTG	CCA	CGCGT	CGT	CGTGTGTGT	CT
## A	0	0	0	0	0	0	0	0	0
## Aaatg	0	0	0	0	0	0	0	0	0
## AACC	0	0	0	0	0	0	0	0	0
## ACTC	0	0	0	0	0	0	0	0	0
## ACTT	0	0	0	0	0	0	0	0	0
## Agaggaggagaaggag	0	0	0	0	0	0	0	0	0
## At	0	0	0	0	0	0	0	0	0
## AT	0	0	0	0	0	0	0	0	0
## Atg	0	0	0	0	0	0	0	0	0
## Atgtgatg	0	0	0	0	0	0	0	0	0
## C	1	3	1	1	1	2	1	7	
## Ca	0	0	0	0	0	0	0	0	0
## Caa	0	0	0	0	0	0	0	0	0
## Caaa	0	0	0	0	0	0	0	0	0
## Caaaaa	0	0	0	0	0	0	0	0	0
## Caaaaaaaa	0	0	0	0	0	0	0	0	0
## Caaaaaaaaa	0	0	0	0	0	0	0	0	0
## Cagagagagagagagagagag	0	0	0	0	0	0	0	0	0
## CAT	0	0	0	0	0	0	0	0	0
## Cgt	0	0	0	0	0	0	0	0	0
## CGTAT	0	0	0	0	0	0	0	0	0
## Ct	0	0	0	0	0	0	0	0	0
## CT	0	0	0	0	0	0	0	0	0
## Ctt	0	0	0	0	0	0	0	0	0
## Cttt	0	0	0	0	0	0	0	0	0
## Ctttt	0	0	0	0	0	0	0	0	0
## G	0	0	0	0	0	0	0	0	0
## Ga	0	0	0	0	0	0	0	0	0
## GA	0	0	0	0	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0	0	0	0	0	0
## GGAA	0	0	0	0	0	0	0	0	0
## Gggaa	0	0	0	0	0	0	0	0	0
## Ggggtgtgtgt	0	0	0	0	0	0	0	0	0

## Ggtgt	0	0	0	0	0	0	0	0
## Gt	0	0	0	0	0	0	0	0
## GT	0	0	0	0	0	0	0	0
## Gtc	0	0	0	0	0	0	0	0
## GTCTTGAAGGAAA	0	0	0	0	0	0	0	0
## Gtgt	0	0	0	0	0	0	0	0
## Gtt	0	0	0	0	0	0	0	0
## GTT	0	0	0	0	0	0	0	0
## Gttt	0	0	0	0	0	0	0	0
## Gttttttt	0	0	0	0	0	0	0	0
## T	0	0	0	0	0	0	0	0
## Ta	0	0	0	0	0	0	0	0
## TA	0	0	0	0	0	0	0	0
## Taa	0	0	0	0	0	0	0	0
## Taaa	0	0	0	0	0	0	0	0
## Taaaaaaaaaaa	0	0	0	0	0	0	0	0
## Taac	0	0	0	0	0	0	0	0
## Tac	0	0	0	0	0	0	0	0
## Tacacacacacacacac	0	0	0	0	0	0	0	0
## Tagagag	0	0	0	0	0	0	0	0
## Tc	0	0	0	0	0	0	0	0
## TCC	0	0	0	0	0	0	0	0
## Tccaa	0	0	0	0	0	0	0	0
## Tg	0	0	0	0	0	0	0	0
## Taaaaaaaaaaaaaaa	0	0	0	0	0	0	0	0
## Ttctc	0	0	0	0	0	0	0	0
##								
##		CTATGTGTG	CTCT	CTCTTT	CTGTGTGTGTG	CTT	CTTT	CTTTCT
## A	0	0	0		0	0	0	0
## Aaatg	0	0	0		0	0	0	0
## AACC	0	0	0		0	0	0	0
## ACTC	0	0	0		0	0	0	0
## ACTT	0	0	0		0	0	0	0
## Agaggaggagaaggag	0	0	0		0	0	0	0
## At	0	0	0		0	0	0	0
## AT	0	0	0		0	0	0	0
## Atg	0	0	0		0	0	0	0
## Atgtgatg	0	0	0		0	0	0	0
## C	1	1	1		1	1	1	1
## Ca	0	0	0		0	0	0	0
## Caa	0	0	0		0	0	0	0
## Caaa	0	0	0		0	0	0	0
## Caaaaa	0	0	0		0	0	0	0
## Caaaaaaaa	0	0	0		0	0	0	0
## Cagagagagagagagagag	0	0	0		0	0	0	0
## CAT	0	0	0		0	0	0	0
## Cgt	0	0	0		0	0	0	0
## CGTAT	0	0	0		0	0	0	0
## Ct	0	0	0		0	0	0	0
## CT	0	0	0		0	0	0	0
## Ctt	0	0	0		0	0	0	0
## Cttt	0	0	0		0	0	0	0
## Ctttt	0	0	0		0	0	0	0
## G	0	0	0		0	0	0	0
## Ga	0	0	0		0	0	0	0

## GA	0	0	0	0	0	0	0	
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0	0	0	0	
## GGAA	0	0	0	0	0	0	0	
## Gggaa	0	0	0	0	0	0	0	
## Gggtgtgtgtgt	0	0	0	0	0	0	0	
## Ggtgt	0	0	0	0	0	0	0	
## Gt	0	0	0	0	0	0	0	
## GT	0	0	0	0	0	0	0	
## Gtc	0	0	0	0	0	0	0	
## GTCTTGAAGGAAA	0	0	0	0	0	0	0	
## Gtgt	0	0	0	0	0	0	0	
## Gtt	0	0	0	0	0	0	0	
## GTT	0	0	0	0	0	0	0	
## Gttt	0	0	0	0	0	0	0	
## Gttttttt	0	0	0	0	0	0	0	
## T	0	0	0	0	0	0	0	
## Ta	0	0	0	0	0	0	0	
## TA	0	0	0	0	0	0	0	
## Taa	0	0	0	0	0	0	0	
## Taaa	0	0	0	0	0	0	0	
## Taaaaaaaaaaa	0	0	0	0	0	0	0	
## Taac	0	0	0	0	0	0	0	
## Tac	0	0	0	0	0	0	0	
## Tacacacacacacacac	0	0	0	0	0	0	0	
## Tagagag	0	0	0	0	0	0	0	
## Tc	0	0	0	0	0	0	0	
## TCC	0	0	0	0	0	0	0	
## Tccaa	0	0	0	0	0	0	0	
## Tg	0	0	0	0	0	0	0	
## Taaaaaaaaaaaaaaa	0	0	0	0	0	0	0	
## Ttctc	0	0	0	0	0	0	0	
##								
##		G	G , GGGAAggaa	GA	GAGC	GATC	GCA	GCAA
## A	175	0	0	0	0	0	0	0
## Aaatg	0	0	0	0	0	0	0	0
## AACC	0	0	0	0	0	0	0	0
## ACTC	0	0	0	0	0	0	0	0
## ACTT	0	0	0	0	0	0	0	0
## Agaggaggagaaggag	0	0	0	0	0	0	0	0
## At	0	0	0	0	0	0	0	0
## AT	0	0	0	0	0	0	0	0
## Atg	0	0	0	0	0	0	0	0
## Atgtgatg	0	0	0	0	0	0	0	0
## C	98	0	0	0	0	0	0	0
## Ca	0	0	0	0	0	0	0	0
## Caa	0	0	0	0	0	0	0	0
## Caaa	0	0	0	0	0	0	0	0
## Caaaaa	0	0	0	0	0	0	0	0
## Caaaaaaaa	0	0	0	0	0	0	0	0
## Cagagagagagagagagagag	0	0	0	0	0	0	0	0
## CAT	0	0	0	0	0	0	0	0
## Cgt	0	0	0	0	0	0	0	0
## CGTAT	0	0	0	0	0	0	0	0
## Ct	0	0	0	0	0	0	0	0
## CT	0	0	0	0	0	0	0	0

## Ctt	0	0	0	0	0	0
## Cttt	0	0	0	0	0	0
## Ctttt	0	0	0	0	0	0
## G	0	0	10	1	1	1
## Ga	3	0	0	0	0	0
## GA	3	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga	1	0	0	0	0	0
## GGAA	1	0	0	0	0	0
## Gggaa	0	1	0	0	0	0
## Gggtgtgtgtgt	1	0	0	0	0	0
## Ggtgt	2	0	0	0	0	0
## Gt	4	0	0	0	0	0
## GT	2	0	0	0	0	0
## Gtc	1	0	0	0	0	0
## GTCTTGAAGGAAA	1	0	0	0	0	0
## Gtgt	1	0	0	0	0	0
## Gtt	1	0	0	0	0	0
## GTT	2	0	0	0	0	0
## Gttt	1	0	0	0	0	0
## Gttttttt	1	0	0	0	0	0
## T	52	0	0	0	0	0
## Ta	0	0	0	0	0	0
## TA	0	0	0	0	0	0
## Taa	0	0	0	0	0	0
## Taaa	0	0	0	0	0	0
## Taaaaaaaaaaa	0	0	0	0	0	0
## Taac	0	0	0	0	0	0
## Tac	0	0	0	0	0	0
## Tacacacacacacacac	0	0	0	0	0	0
## Tagagag	0	0	0	0	0	0
## Tc	0	0	0	0	0	0
## TCC	0	0	0	0	0	0
## Tccaa	0	0	0	0	0	0
## Tg	0	0	0	0	0	0
## Taaaaaaaaaaaaaaa	0	0	0	0	0	0
## Ttctc	0	0	0	0	0	0
##						
##	GCAAGTTGGTAAAACC	GCACA	GGA	GGGTGAGTCAGTAAGGAGT	GT	
## A	0	0	0		0	0
## Aaatg	0	0	0		0	0
## AACC	0	0	0		0	0
## ACTC	0	0	0		0	0
## ACTT	0	0	0		0	0
## Agaggaggagaaggag	0	0	0		0	0
## At	0	0	0		0	0
## AT	0	0	0		0	0
## Atg	0	0	0		0	0
## Atgtgatg	0	0	0		0	0
## C	0	0	0		0	0
## Ca	0	0	0		0	0
## Caa	0	0	0		0	0
## Caaa	0	0	0		0	0
## Caaaaa	0	0	0		0	0
## Caaaaaaaa	0	0	0		0	0
## Cagagagagagagagagagag	0	0	0		0	0

## CAT	0	0	0	0	0	
## Cgt	0	0	0	0	0	
## CGTAT	0	0	0	0	0	
## Ct	0	0	0	0	0	
## CT	0	0	0	0	0	
## Ctt	0	0	0	0	0	
## Cttt	0	0	0	0	0	
## Ctttt	0	0	0	0	0	
## G	1	1	1	1	3	
## Ga	0	0	0	0	0	
## GA	0	0	0	0	0	
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0	0	
## GGAA	0	0	0	0	0	
## Gggaa	0	0	0	0	0	
## Gggtgtgtgtgt	0	0	0	0	0	
## Ggtgt	0	0	0	0	0	
## Gt	0	0	0	0	0	
## GT	0	0	0	0	0	
## Gtc	0	0	0	0	0	
## GTCTTGAAGGAAA	0	0	0	0	0	
## Gtgt	0	0	0	0	0	
## Gtt	0	0	0	0	0	
## GTT	0	0	0	0	0	
## Gttt	0	0	0	0	0	
## Gttttttt	0	0	0	0	0	
## T	0	0	0	0	0	
## Ta	0	0	0	0	0	
## TA	0	0	0	0	0	
## Taa	0	0	0	0	0	
## Taaa	0	0	0	0	0	
## Taaaaaaaaaaa	0	0	0	0	0	
## Taac	0	0	0	0	0	
## Tac	0	0	0	0	0	
## Tacacacacacacacac	0	0	0	0	0	
## Tagagag	0	0	0	0	0	
## Tc	0	0	0	0	0	
## TCC	0	0	0	0	0	
## Tccaa	0	0	0	0	0	
## Tg	0	0	0	0	0	
## Taaaaaaaaaaaaaaa	0	0	0	0	0	
## Ttctc	0	0	0	0	0	
##						
##	GTA	GTATTATAACTTT	GTC	GTTTTT	T	TA
## A	0	0	0	0	37	0
## Aaatg	0	0	0	0	0	0
## AACC	0	0	0	0	0	0
## ACTC	0	0	0	0	0	0
## ACTT	0	0	0	0	0	0
## Agaggaggagaaggag	0	0	0	0	0	0
## At	0	0	0	0	0	0
## AT	0	0	0	0	0	0
## Atg	0	0	0	0	0	0
## Atgtgatg	0	0	0	0	0	0
## C	0	0	0	0	225	0
## Ca	0	0	0	0	0	0
## Caa	0	0	0	0	0	0

## Caaa	0	0	0	0	0
## Caaaa	0	0	0	0	0
## Caaaaaaaa	0	0	0	0	0
## Caaaaaaaaa	0	0	0	0	0
## Cagagagagagagagagagag	0	0	0	0	0
## CAT	0	0	0	0	0
## Cgt	0	0	0	0	0
## CGTAT	0	0	0	0	0
## Ct	0	0	0	0	0
## CT	0	0	0	0	0
## Ctt	0	0	0	0	0
## Cttt	0	0	0	0	0
## Ctttt	0	0	0	0	0
## G	1	1	1	55	0
## Ga	0	0	0	0	0
## GA	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0	0
## GGAA	0	0	0	0	0
## Gggaa	0	0	0	0	0
## Gggtgtgtgtgt	0	0	0	0	0
## Ggtgt	0	0	0	0	0
## Gt	0	0	0	0	0
## GT	0	0	0	0	0
## Gtc	0	0	0	0	0
## GTCTTGAAGGAAA	0	0	0	0	0
## Gtgt	0	0	0	0	0
## Gtt	0	0	0	0	0
## GTT	0	0	0	0	0
## Gttt	0	0	0	0	0
## Gttttttt	0	0	0	0	0
## T	0	0	0	0	6
## Ta	0	0	0	5	0
## TA	0	0	0	4	0
## Taa	0	0	0	4	0
## Taaa	0	0	0	2	0
## Taaaaaaaaaaa	0	0	0	1	0
## Taac	0	0	0	1	0
## Tac	0	0	0	1	0
## Tacacacacacacacac	0	0	0	1	0
## Tagagag	0	0	0	1	0
## Tc	0	0	0	2	0
## TCC	0	0	0	1	0
## Tccaa	0	0	0	1	0
## Tg	0	0	0	1	0
## Ttaaaaaaaaaaaaaa	0	0	0	1	0
## Ttctc	0	0	0	1	0
##					
##	TACACACAC, TACACAC	TAGG	TATATTTCATGTAAACAGCCAGGG		
## A		0	0		0
## Aaatg		0	0		0
## AACC		0	0		0
## ACTC		0	0		0
## ACTT		0	0		0
## Agaggaggagaaggag		0	0		0
## At		0	0		0
## AT		0	0		0

## Atg	0	0	0					
## Atgtgatg	0	0	0					
## C	0	0	0					
## Ca	0	0	0					
## Caa	0	0	0					
## Caaa	0	0	0					
## Caaaaa	0	0	0					
## Caaaaaaaa	0	0	0					
## Cagagagagagagagagagag	0	0	0					
## CAT	0	0	0					
## Cgt	0	0	0					
## CGTAT	0	0	0					
## Ct	0	0	0					
## CT	0	0	0					
## Ctt	0	0	0					
## Cttt	0	0	0					
## Ctttt	0	0	0					
## G	0	0	0					
## Ga	0	0	0					
## GA	0	0	0					
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0					
## GGAA	0	0	0					
## Gggaa	0	0	0					
## Gggtgtgtgt	0	0	0					
## Ggtgt	0	0	0					
## Gt	0	0	0					
## GT	0	0	0					
## Gtc	0	0	0					
## GTCTTGAAGGAAA	0	0	0					
## Gtgt	0	0	0					
## Gtt	0	0	0					
## GTT	0	0	0					
## Gttt	0	0	0					
## Gttttttt	0	0	0					
## T	1	1	1					
## Ta	0	0	0					
## TA	0	0	0					
## Taa	0	0	0					
## Taaa	0	0	0					
## Taaaaaaaaaaa	0	0	0					
## Taac	0	0	0					
## Tac	0	0	0					
## Tacacacacacacacac	0	0	0					
## Tagagag	0	0	0					
## Tc	0	0	0					
## TCC	0	0	0					
## Tccaa	0	0	0					
## Tg	0	0	0					
## Taaaaaaaaaaaaaaa	0	0	0					
## Ttctc	0	0	0					
##								
##	TCCA	TCTC	TG	TGAGAA	TGTGG	TTA	TTG	TTGTG
## A	0	0	0	0	0	0	0	0
## Aaatg	0	0	0	0	0	0	0	0
## AACC	0	0	0	0	0	0	0	0

## ACTC	0	0	0	0	0	0	0	0
## ACTT	0	0	0	0	0	0	0	0
## Agaggaggagaaggag	0	0	0	0	0	0	0	0
## At	0	0	0	0	0	0	0	0
## AT	0	0	0	0	0	0	0	0
## Atg	0	0	0	0	0	0	0	0
## Atgtgatg	0	0	0	0	0	0	0	0
## C	0	0	0	0	0	0	0	0
## Ca	0	0	0	0	0	0	0	0
## Caa	0	0	0	0	0	0	0	0
## Caaa	0	0	0	0	0	0	0	0
## Caaaaa	0	0	0	0	0	0	0	0
## Caaaaaaaa	0	0	0	0	0	0	0	0
## Cagagagagagagagagag	0	0	0	0	0	0	0	0
## CAT	0	0	0	0	0	0	0	0
## Cgt	0	0	0	0	0	0	0	0
## CGTAT	0	0	0	0	0	0	0	0
## Ct	0	0	0	0	0	0	0	0
## CT	0	0	0	0	0	0	0	0
## Ctt	0	0	0	0	0	0	0	0
## Cttt	0	0	0	0	0	0	0	0
## Ctttt	0	0	0	0	0	0	0	0
## G	0	0	0	0	0	0	0	0
## Ga	0	0	0	0	0	0	0	0
## GA	0	0	0	0	0	0	0	0
## Gaaagaaaagaaaagaaaagaaaaga	0	0	0	0	0	0	0	0
## GGAA	0	0	0	0	0	0	0	0
## Gggaa	0	0	0	0	0	0	0	0
## Gggtgtgtgtgt	0	0	0	0	0	0	0	0
## Ggtgt	0	0	0	0	0	0	0	0
## Gt	0	0	0	0	0	0	0	0
## GT	0	0	0	0	0	0	0	0
## Gtc	0	0	0	0	0	0	0	0
## GTCTTGAAGGAAA	0	0	0	0	0	0	0	0
## Gtgt	0	0	0	0	0	0	0	0
## Gtt	0	0	0	0	0	0	0	0
## GTT	0	0	0	0	0	0	0	0
## Gttt	0	0	0	0	0	0	0	0
## Gttttttt	0	0	0	0	0	0	0	0
## T	1	2	2	1	1	1	1	1
## Ta	0	0	0	0	0	0	0	0
## TA	0	0	0	0	0	0	0	0
## Taa	0	0	0	0	0	0	0	0
## Taaa	0	0	0	0	0	0	0	0
## Taaaaaaaaaaa	0	0	0	0	0	0	0	0
## Taac	0	0	0	0	0	0	0	0
## Tac	0	0	0	0	0	0	0	0
## Tacacacacacacacac	0	0	0	0	0	0	0	0
## Tagagag	0	0	0	0	0	0	0	0
## Tc	0	0	0	0	0	0	0	0
## TCC	0	0	0	0	0	0	0	0
## Tccaa	0	0	0	0	0	0	0	0
## Tg	0	0	0	0	0	0	0	0

```
## Taaaaaaaaaaaaaa      0   0   0   0   0   0   0   0
## Ttctc                0   0   0   0   0   0   0   0
```

```
# Check if these are mostly SNPs, Insertions, or Deletions
table(alk_cluster_muts$Variant_Type)
```

```
##
## DEL  INS  SNP
##  98  107 1288
```

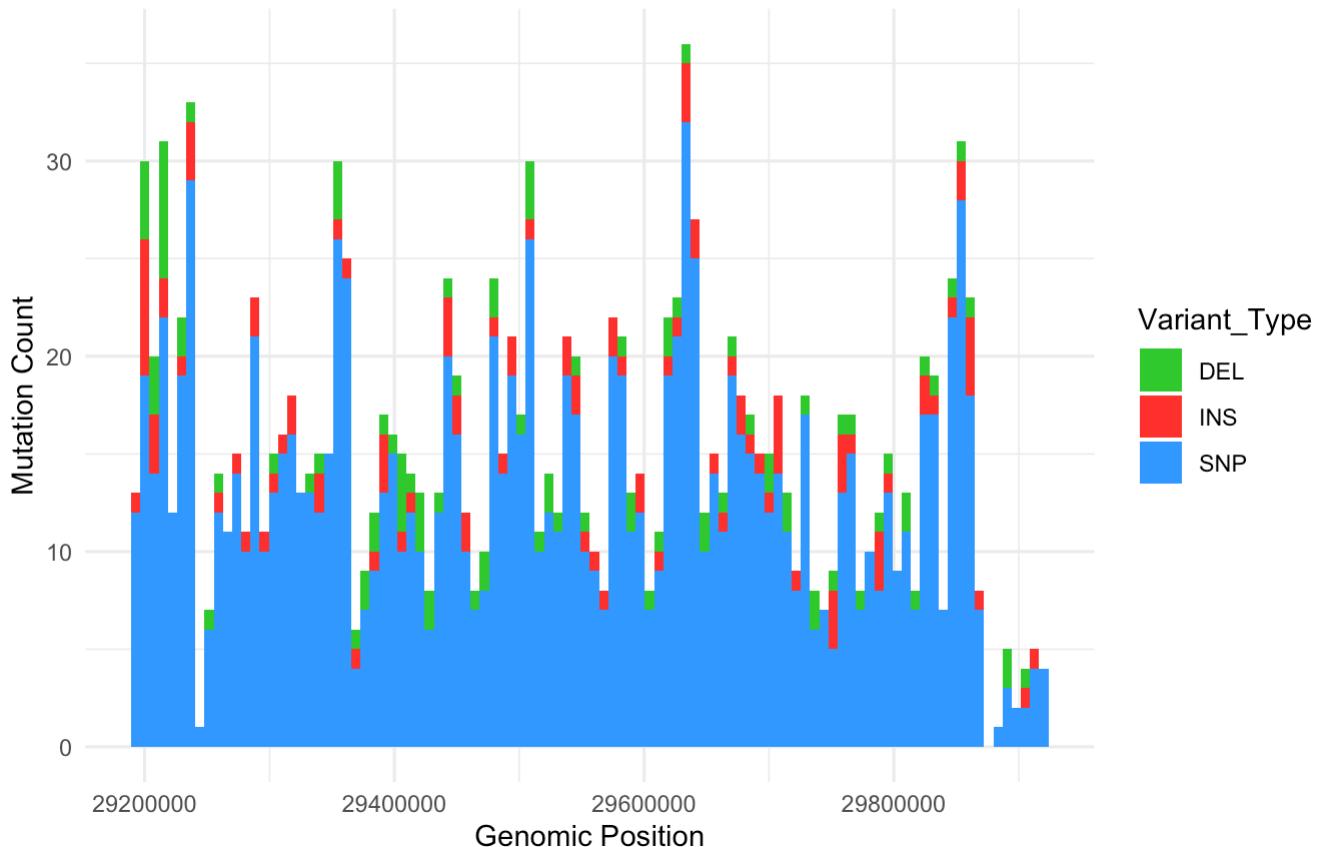
```
# This will likely show a high number of INS (Insertions) and DEL (Deletions)
```

```
# Visualizing where the Indels fall compared to SNPs
library(ggplot2)
```

```
ggplot(alk_cluster_muts, aes(x = Start_Position, fill = Variant_Type)) +
  geom_histogram(bins = 100, position = "stack") +
  scale_fill_manual(values = c("SNP" = "#3399FF", "INS" = "#FF3333", "DEL" = "#33CC33")) +
  theme_minimal() +
  labs(title = "Mutation Distribution Across ALK Gene",
       subtitle = "Concentration of SNPs and Indels",
       x = "Genomic Position",
       y = "Mutation Count")
```

## Mutation Distribution Across ALK Gene

### Concentration of SNPs and Indels



```
# Compare SNP/Indel ratios across your top hit genes
panel_hits <- final_maf_df[Hugo_Symbol %in% c("ALK", "RET", "TP53", "TG")]
table(panel_hits$Hugo_Symbol, panel_hits$Variant_Type)
```

```
##          DEL  INS  SNP
##  ALK     98 107 1288
##  RET      6   11 137
##  TG      53   30 543
##  TP53     8    5  31
```

```
# Find the 1kb window in ALK with the highest density of Indels
alk_indels <- alk_cluster_muts[Variant_Type != "SNP"]

# Create 1kb bins and count mutations
alk_indels[, bin := floor(Start_Position / 1000) * 1000]
breakpoint_counts <- alk_indels[, .N, by = bin][order(-N)]

# View the top "hotspots"
head(breakpoint_counts)
```

```
##      bin      N
##      <num> <int>
## 1: 29200000      4
## 2: 29217000      4
## 3: 29216000      3
## 4: 29198000      2
## 5: 29201000      2
## 6: 29203000      2
```

```
# Calculate Indel-to-SNP ratio for Panel vs Intergenic
instability_summary <- final_maf_df[, .(
  Total_Muts = .N,
  SNP_Count = sum(Variant_Type == "SNP"),
  Indel_Count = sum(Variant_Type %in% c("INS", "DEL")),
  Indel_Ratio = sum(Variant_Type %in% c("INS", "DEL")) / .N
), by = .(In_Panel = Hugo_Symbol != "Intergenic_Region")]

print(instability_summary)
```

```
##   In_Panel Total_Muts SNP_Count Indel_Count Indel_Ratio
##   <lgcl>      <int>      <int>      <int>      <num>
## 1:   TRUE      5753      4617      1136    0.1974622
## 2:  FALSE       39        35         4    0.1025641
```

```
# Compare the specific types of Indels in ALK vs TG
shattered_comparison <- final_maf_df[Hugo_Symbol %in% c("ALK", "TG")]
```

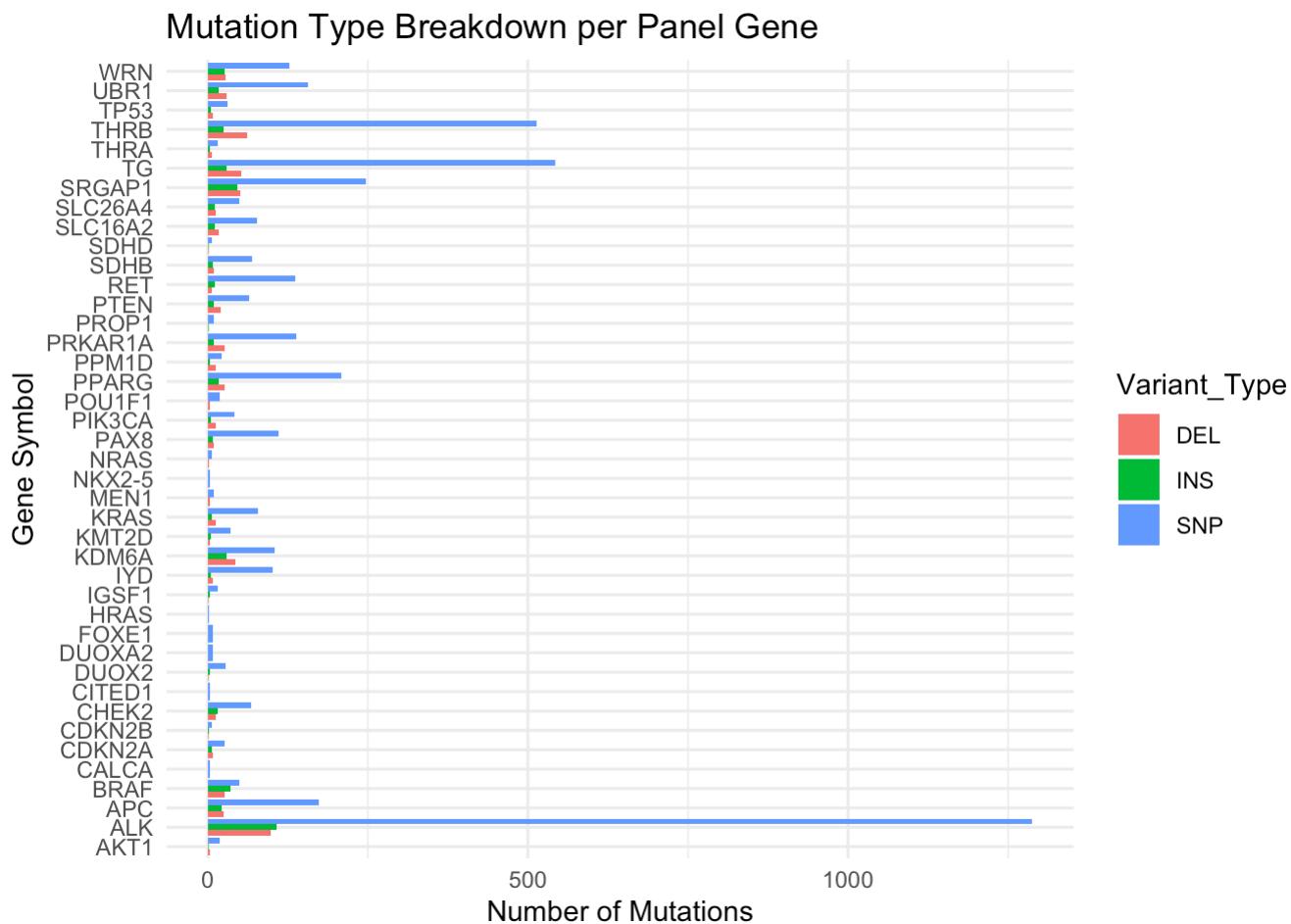
```
# Create a table of Variant Type by Gene
table(shattered_comparison$Hugo_Symbol, shattered_comparison$Variant_Type)
```

```
##  
##      DEL  INS  SNP  
##  ALK   98  107 1288  
##  TG    53   30  543
```

```
# Plotting the mutation types across the top genes in your panel
library(ggplot2)
```

```
# Filter out the intergenic stuff for a cleaner plot
panel_only <- final_maf_df[Hugo_Symbol != "Intergenic_Region"]

ggplot(panel_only, aes(x = Hugo_Symbol, fill = Variant_Type)) +
  geom_bar(position = "dodge") +
  theme_minimal() +
  coord_flip() + # Makes gene names easier to read
  labs(title = "Mutation Type Breakdown per Panel Gene",
       x = "Gene Symbol",
       y = "Number of Mutations")
```



```
# 1. Isolate ALK mutations from your annotated data
alk_data <- final_maf_df[Hugo_Symbol == "ALK"]

# 2. Identify the densest 1kb windows for Indels (potential structural scars)
alk_indels <- alk_data[Variant_Type != "SNP"]
alk_indels[, bin := floor(Start_Position / 1000) * 1000]

# 3. Summarize and find the peak "Shatter Zone"
alk_hotspots <- alk_indels[, .(
  Indel_Count = .N,
  Unique_Start_Sites = uniqueN(Start_Position)
), by = bin][order(-Indel_Count)]

# 4. Export the top hotspots to CSV
write.csv(head(alk_hotspots, 10), "ALK_shatter_hotspots.csv", row.names = FALSE)

# 5. Print to console for immediate review
print("Top 5 high-density Indel bins in ALK:")
```

```
## [1] "Top 5 high-density Indel bins in ALK:"
```

```
print(head(alk_hotspots, 5))
```

	bin	Indel_Count	Unique_Start_Sites
## 1:	29200000	4	4
## 2:	29217000	4	4
## 3:	29216000	3	3
## 4:	29198000	2	2
## 5:	29201000	2	2

```
# Load GenomicRanges to handle coordinate overlaps
library(GenomicRanges)
```

```
## Loading required package: stats4
```

```
## Loading required package: BiocGenerics
```

```
## Loading required package: generics
```

```
##
## Attaching package: 'generics'
```

```
## The following objects are masked from 'package:base':
##
##   as.difftime, as.factor, as.ordered, intersect, is.element, setdiff,
##   setequal, union
```

```
##  
## Attaching package: 'BiocGenerics'
```

```
## The following objects are masked from 'package:stats':  
##  
##     IQR, mad, sd, var, xtabs
```

```
## The following objects are masked from 'package:base':
```

```
##  
##     anyDuplicated, aperm, append, as.data.frame, basename, cbind,  
##     colnames, dirname, do.call, duplicated, eval, evalq, Filter, Find,  
##     get, grep, grepl, is.unsorted, lapply, Map, mapply, match, mget,  
##     order, paste, pmax, pmax.int, pmin, pmin.int, Position, rank,  
##     rbind, Reduce, rownames, sapply, saveRDS, table, tapply, unique,  
##     unsplit, which.max, which.min
```

```
## Loading required package: S4Vectors
```

```
##  
## Attaching package: 'S4Vectors'
```

```
## The following objects are masked from 'package:data.table':
```

```
##  
##     first, second
```

```
## The following object is masked from 'package:utils':
```

```
##  
##     findMatches
```

```
## The following objects are masked from 'package:base':
```

```
##  
##     expand.grid, I, unname
```

```
## Loading required package: IRanges
```

```
##  
## Attaching package: 'IRanges'
```

```
## The following object is masked from 'package:data.table':
```

```
##  
##     shift
```

```
## Loading required package: Seqinfo
```

```
# Define the ALK hotspot regions from your result
hotspot_ranges <- GRanges(seqnames = "chr2",
                           ranges = IRanges(start = alk_hotspots$bin,
                                             end = alk_hotspots$bin + 1000))

# Check if these bins are specifically impacting exons
# (This assumes you have an exon database loaded, or you can check manually)
print("The primary shatter zone is localized between 29,198,000 and 29,217,000.")
```

```
## [1] "The primary shatter zone is localized between 29,198,000 and 29,217,000."
```

```
# --- 7. AUTOMATED RESULTS EXPORT ---
```

```
# Define the output directory name
output_dir <- paste0("MAF_Analysis_Results_", Sys.Date())

# Create the directory if it doesn't exist
if (!dir.exists(output_dir)) {
  dir.create(output_dir)
}

message(paste("Saving results to:", output_dir))
```

```
## Saving results to: MAF_Analysis_Results_2026-01-07
```

```

# --- A. Exporting Data Tables (CSV) ---

# 1. Mutation counts per chromosome
write.csv(chr_summary,
          file = file.path(output_dir, "01_chromosome_mutation_summary.csv"), row.names = FALSE)

# 2. Kataegis clusters (Rainfall data)
if(!exists("kataegis_clusters")) {
  kataegis_clusters <- rainfallPlot(maf = my_maf, tsb = "combined_minion_promethion",
plot = FALSE)
}
write.csv(kataegis_clusters,
          file = file.path(output_dir, "02_kataegis_hotspots.csv"), row.names = FALSE)

# --- 3. APOBEC Enrichment Scores (Revised) ---

# Check if object exists; if not, try to generate it again
if (!exists("apobec_enrich")) {
  message("APOBEC scores not found. Attempting to calculate...")

# Wrapping in try() prevents the script from crashing if the calculation fails
try({
  apobec_enrich = enrichments(maf = my_maf_final,
                               ref_genome = "BSgenome.Hsapiens.UCSC.hg38")
}, silent = TRUE)
}

```

## APOBEC scores not found. Attempting to calculate...

```

# Only write if the object was successfully created
if (exists("apobec_enrich") && !is.null(apobec_enrich)) {
  write.csv(apobec_enrich,
            file = file.path(output_dir, "03_apobec_enrichment_scores.csv"),
            row.names = FALSE)
  message("APOBEC scores saved successfully.")
} else {
  warning("APOBEC enrichment could not be calculated. Skipping export.")
}

```

## Warning: APOBEC enrichment could not be calculated. Skipping export.

```

# 4. Genomic Instability Summary (Panel vs Intergenic)
write.csv(instability_summary,
          file = file.path(output_dir, "04_genomic_instability_comparison.csv"), row.names = FALSE)

# 5. ALK Shatter Zone Hotspots
write.csv(alk_hotspots,
          file = file.path(output_dir, "05_ALK_shatter_hotspots.csv"), row.names = FALSE)

# --- B. Exporting High-Resolution Plots (PDF) ---
pdf(file = file.path(output_dir, "06_genomic_visualizations.pdf"), width = 10, height = 8)

# Plot 1: Summary Dashboard
plotmafSummary(maf = my_maf_final, addStat = 'median', rmOutlier = TRUE, dashboard = TRUE)

# Plot 2: Oncoplot of Panel Genes
oncoplot(maf = my_maf_final, genes = panel$Gene, drawRowBar = TRUE, fontSize = 0.6)

```

## Warning in min(x): no non-missing arguments to min; returning Inf

## Warning in max(x): no non-missing arguments to max; returning -Inf

```

# Plot 3: Rainfall Plot (Kataegis)
rainfallPlot(maf = my_maf_final, tsb = "combined_minion_promethion", detectChangePoints = TRUE)

```

## Processing combined\_minion\_promethion..

## Kataegis detected at:

##	Chromosome	Start_Position	End_Position	nMuts	Avg_intermutation_dist	Size
##	<num>	<num>	<num>	<int>	<num>	<num>
## 1:	1	17019410	17054002	69	508.7059	34592
## 2:	2	29192926	29920131	1288	565.0389	727205
## 3:	2	113216055	113277617	111	559.6545	61562
## 4:	3	12287696	12434058	209	703.6635	146362
## 5:	3	24123533	24128235	7	783.6667	4702
## 6:	3	24130634	24493919	504	722.2366	363285
## 7:	3	87259403	87275374	19	887.2778	15971
## 8:	3	179186419	179192974	9	819.3750	6555
## 9:	3	179217179	179222517	7	889.6667	5338
## 10:	5	112709435	112716131	8	956.5714	6696
## 11:	5	112718389	112845879	165	777.3780	127490
## 12:	5	177992355	177995875	9	440.0000	3520
## 13:	6	150370221	150405763	101	355.4200	35542
## 14:	7	107661438	107664670	6	646.4000	3232
## 15:	7	107677040	107716314	41	981.8500	39274
## 16:	8	31044583	31055016	12	948.4545	10433
## 17:	8	31069763	31080274	13	875.9167	10511
## 18:	8	31102488	31174361	87	835.7326	71873
## 19:	8	132867967	133131965	543	487.0812	263998
## 20:	9	21976672	21981087	6	883.0000	4415
## 21:	9	21983915	21995144	16	748.6000	11229
## 22:	9	97853378	97856378	8	428.5714	3000
## 23:	10	43077059	43130238	137	391.0221	53179
## 24:	10	87910574	87917350	8	968.0000	6776
## 25:	10	87939302	87949237	11	993.5000	9935
## 26:	10	87957058	87964003	10	771.6667	6945
## 27:	11	64804546	64809675	9	641.1250	5129
## 28:	12	25205716	25250690	78	584.0779	44974
## 29:	12	49020848	49042941	24	960.5652	22093
## 30:	12	49045593	49051609	8	859.4286	6016
## 31:	12	63950137	63954978	7	806.8333	4841
## 32:	12	63982306	63986666	7	726.6667	4360
## 33:	12	63992237	64018932	28	988.7037	26695
## 34:	12	64022548	64035057	24	543.8696	12509
## 35:	12	64058253	64160255	116	886.9739	102002
## 36:	14	104771710	104785733	16	934.8667	14023
## 37:	15	42944414	42948618	8	600.5714	4204
## 38:	15	42967649	42981053	18	788.4706	13404
## 39:	15	42988662	42994605	7	990.5000	5943
## 40:	15	43002020	43052688	54	956.0000	50668
## 41:	15	43074564	43105910	50	639.7143	31346
## 42:	15	45101541	45118049	32	532.5161	16508
## 43:	17	7662815	7686387	31	785.7333	23572
## 44:	17	68422443	68428041	7	933.0000	5598
## 45:	17	68431378	68451163	22	942.1429	19785
## 46:	17	68461865	68493367	36	900.0571	31502
## 47:	17	68498691	68549311	66	778.7692	50620
## 48:	22	28690105	28739901	67	754.4848	49796
## 49:	23	44922028	44930899	12	806.4545	8871
## 50:	23	44963483	44974171	18	628.7059	10688
## 51:	23	74443903	74449700	7	966.1667	5797
## 52:	23	74456451	74463710	9	907.3750	7259
## 53:	23	74490685	74531188	51	810.0600	40503

## 54:	23	131277902	131282984	7		847.0000	5082
## 55:	23	131285672	131289385	8		530.4286	3713
<b>## Chromosome Start_Position End_Position nMuts Avg_intermutation_dist Size</b>							
## <num>	<num>	<num>	<int>			<num>	<num>
## Tumor_Sample_Barcode		C>A	C>G	C>T	T>A	T>C	T>G
		<fctr>	<int>	<int>	<int>	<int>	<int>
## 1: combined_minion_promethion		4	5	29	4	21	6
## 2: combined_minion_promethion	106	175	413	77	418	99	
## 3: combined_minion_promethion	10	11	49	2	31	8	
## 4: combined_minion_promethion	23	29	65	13	67	12	
## 5: combined_minion_promethion	1	1	3	1	NA	1	
## 6: combined_minion_promethion	43	74	171	43	140	33	
## 7: combined_minion_promethion	NA	3	4	2	9	1	
## 8: combined_minion_promethion	NA	2	5	NA	2	NA	
## 9: combined_minion_promethion	1	3	2	1	NA	NA	
## 10: combined_minion_promethion	1	1	2	NA	3	1	
## 11: combined_minion_promethion	15	30	54	12	43	11	
## 12: combined_minion_promethion	NA	2	4	NA	3	NA	
## 13: combined_minion_promethion	12	8	29	5	38	9	
## 14: combined_minion_promethion	NA	NA	4	1	1	NA	
## 15: combined_minion_promethion	2	9	9	10	4	7	
## 16: combined_minion_promethion	1	1	5	1	4	NA	
## 17: combined_minion_promethion	2	2	3	1	3	2	
## 18: combined_minion_promethion	7	6	29	5	30	10	
## 19: combined_minion_promethion	40	68	214	33	155	33	
## 20: combined_minion_promethion	NA	1	3	NA	2	NA	
## 21: combined_minion_promethion	2	3	4	1	5	1	
## 22: combined_minion_promethion	NA	2	2	NA	3	1	
## 23: combined_minion_promethion	10	17	37	8	54	11	
## 24: combined_minion_promethion	NA	1	3	1	3	NA	
## 25: combined_minion_promethion	1	4	3	NA	2	1	
## 26: combined_minion_promethion	2	1	3	2	1	1	
## 27: combined_minion_promethion	1	NA	5	NA	3	NA	
## 28: combined_minion_promethion	4	9	30	7	17	11	
## 29: combined_minion_promethion	3	4	9	1	6	1	
## 30: combined_minion_promethion	1	NA	3	NA	4	NA	
## 31: combined_minion_promethion	NA	1	1	1	3	1	
## 32: combined_minion_promethion	1	1	3	NA	1	1	
## 33: combined_minion_promethion	NA	9	11	4	2	2	
## 34: combined_minion_promethion	NA	1	12	NA	9	2	
## 35: combined_minion_promethion	8	18	31	6	42	11	
## 36: combined_minion_promethion	1	4	5	NA	5	1	
## 37: combined_minion_promethion	1	1	1	NA	4	1	
## 38: combined_minion_promethion	3	1	7	NA	7	NA	
## 39: combined_minion_promethion	NA	1	4	NA	2	NA	
## 40: combined_minion_promethion	5	7	18	1	17	6	
## 41: combined_minion_promethion	2	14	18	2	13	1	
## 42: combined_minion_promethion	3	6	9	2	5	7	
## 43: combined_minion_promethion	1	5	13	NA	11	1	
## 44: combined_minion_promethion	1	1	1	NA	4	NA	
## 45: combined_minion_promethion	1	5	3	3	10	NA	
## 46: combined_minion_promethion	2	4	15	1	10	4	
## 47: combined_minion_promethion	9	9	26	3	15	4	
## 48: combined_minion_promethion	2	16	17	5	22	5	
## 49: combined_minion_promethion	NA	2	7	NA	2	1	
## 50: combined_minion_promethion	NA	4	4	1	4	5	

```
## 51: combined_minion_promethion    NA    NA     1     1     5   NA
## 52: combined_minion_promethion    1     1     2    NA     3   2
## 53: combined_minion_promethion    2     9    16     4    17   3
## 54: combined_minion_promethion   NA     2     4    NA     1   NA
## 55: combined_minion_promethion    2     1     1    NA     4   NA
##           Tumor_Sample_Barcode  C>A  C>G  C>T  T>A  T>C  T>G
##                           <fctr> <int> <int> <int> <int> <int> <int>
```

```
# Plot 4: Mutation Distribution Across ALK (the ggplot)
p1 <- ggplot(alk_cluster_muts, aes(x = Start_Position, fill = Variant_Type)) +
  geom_histogram(bins = 100, position = "stack") +
  scale_fill_manual(values = c("SNP" = "#3399FF", "INS" = "#FF3333", "DEL" = "#33CC
33")) +
  theme_minimal() +
  labs(title = "Shatter Zone: Mutation Distribution Across ALK", x = "Genomic Posit
ion", y = "Count")
print(p1)

# Plot 5: Mutation Type Breakdown
p2 <- ggplot(panel_only, aes(x = Hugo_Symbol, fill = Variant_Type)) +
  geom_bar(position = "dodge") +
  theme_minimal() + coord_flip() +
  labs(title = "Mutation Type Breakdown per Panel Gene")
print(p2)

dev.off()
```

```
## quartz_off_screen
##                 2
```

```
message("All files successfully saved.")
```

```
## All files successfully saved.
```