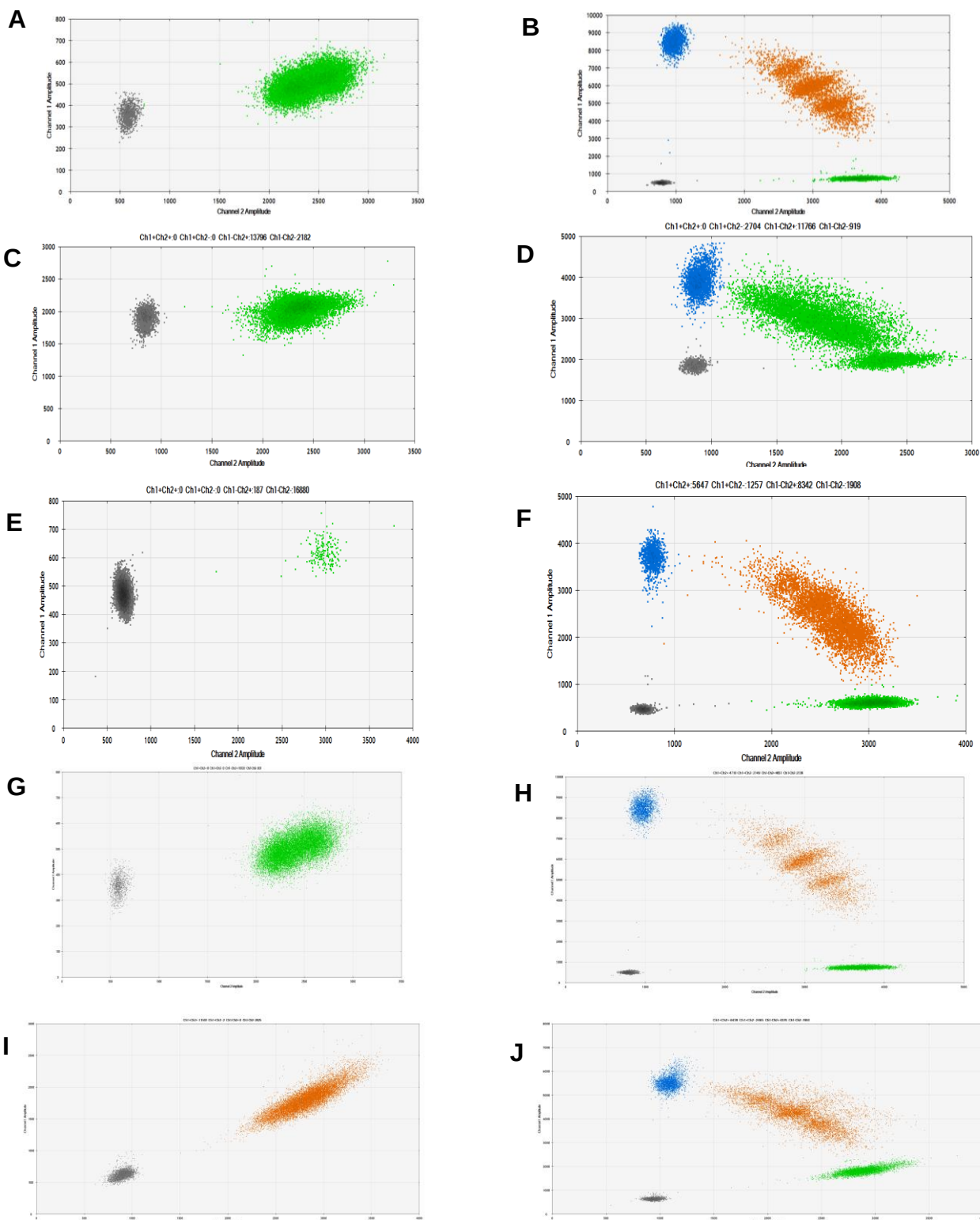


**Metastatic adrenocortical carcinoma displays higher mutation rate and tumor heterogeneity than primary tumors**

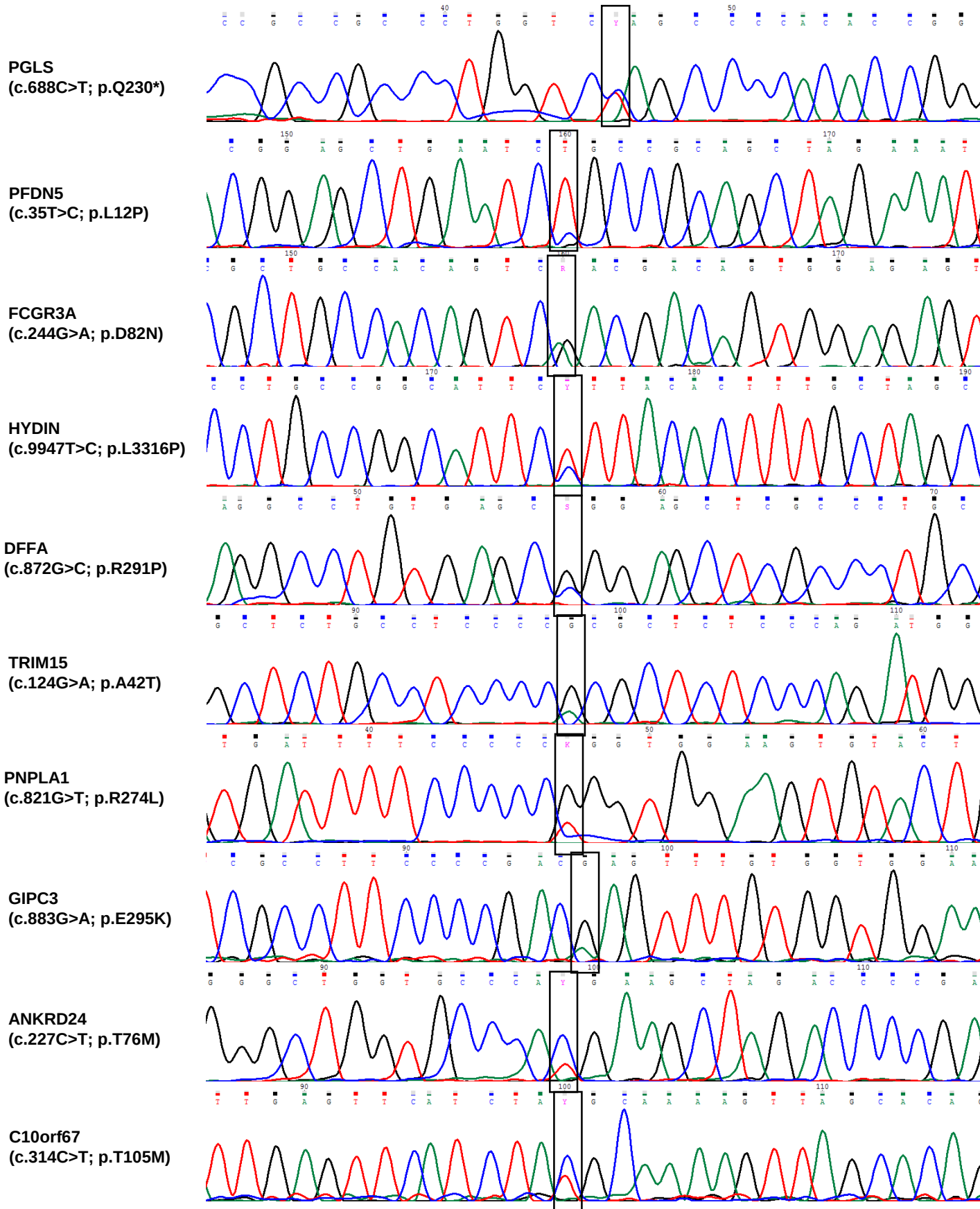
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## **Supplementary Information**

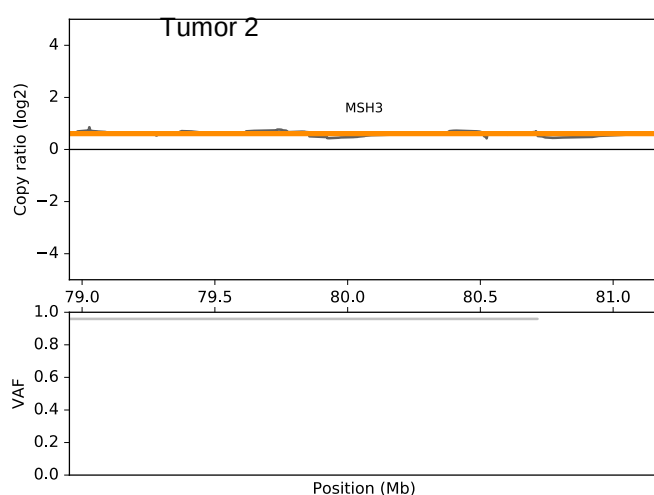
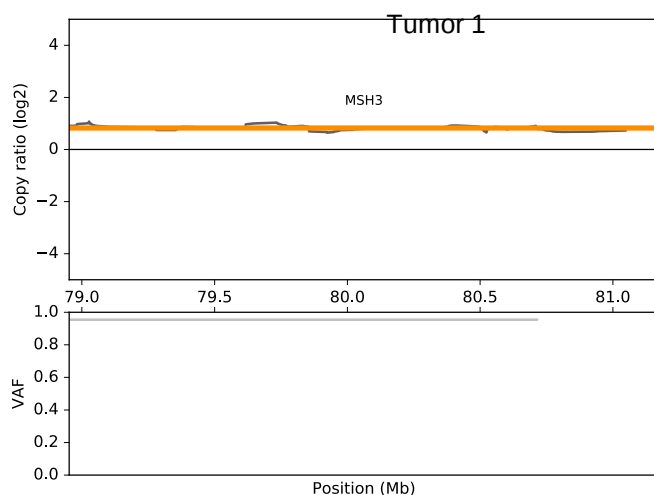
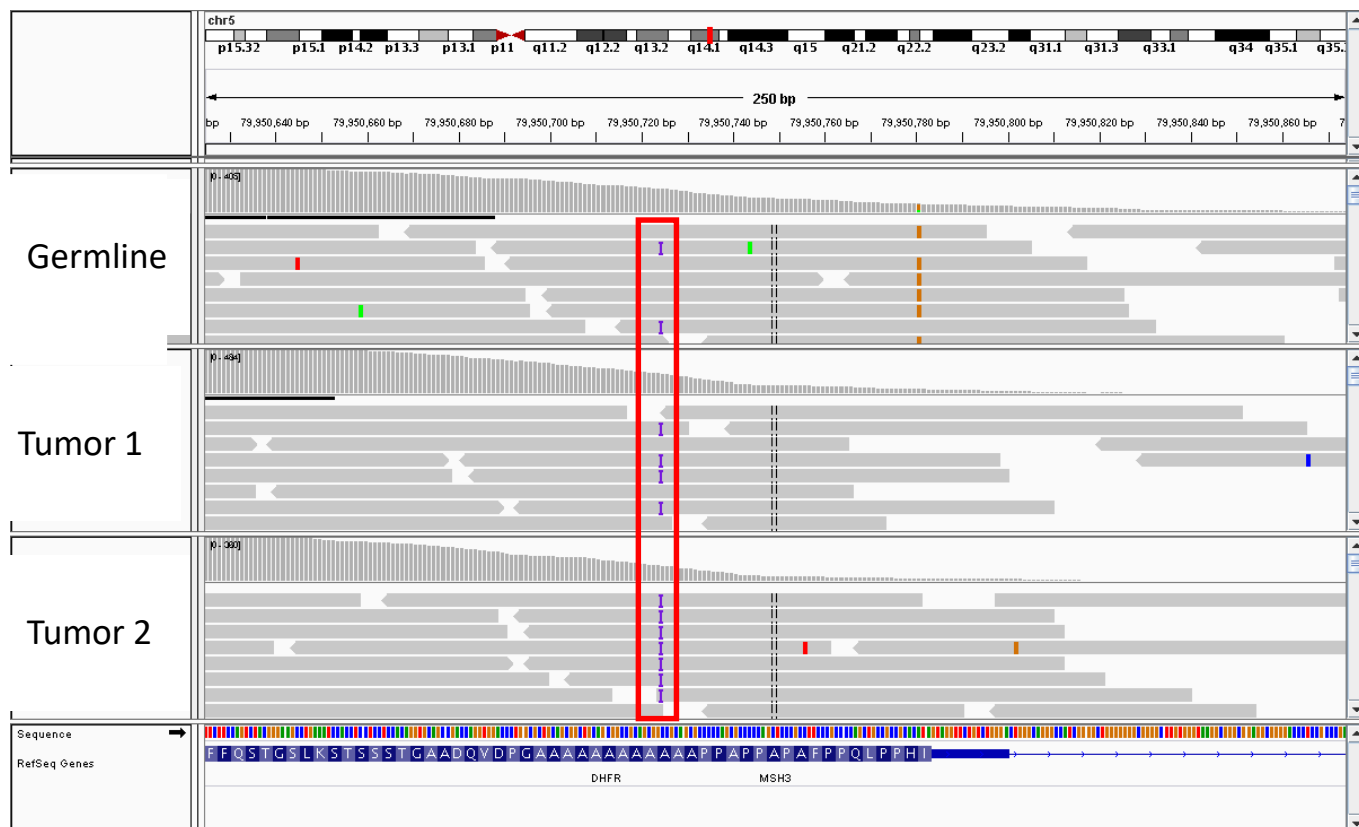


## Supplementary Figure 1

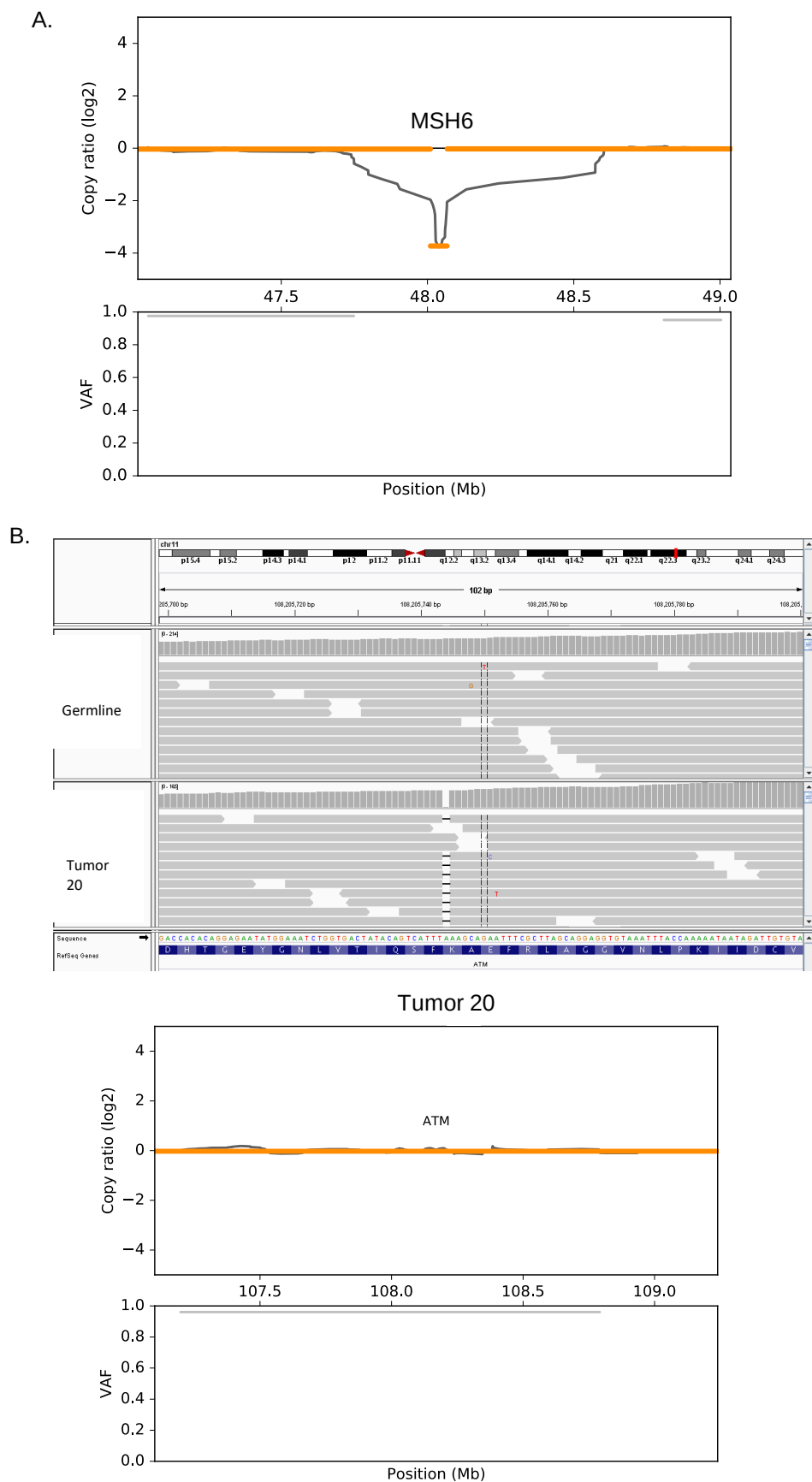
**Validation of genetic variants that was identified in our study through droplet-digital PCR.** The scatter plots represent germline (A,C, E G and I) and tumor samples (B, D, F, H and J) from each case. The selected variants are *CTNNB1*\_pG34R (A&B), *CTNNB1*\_pD32G (C&D), *DNHD1*\_pE2985K (E&F), *WD66*\_pA928S (G&H) and *ENTHD1*\_pN196T (I&J)



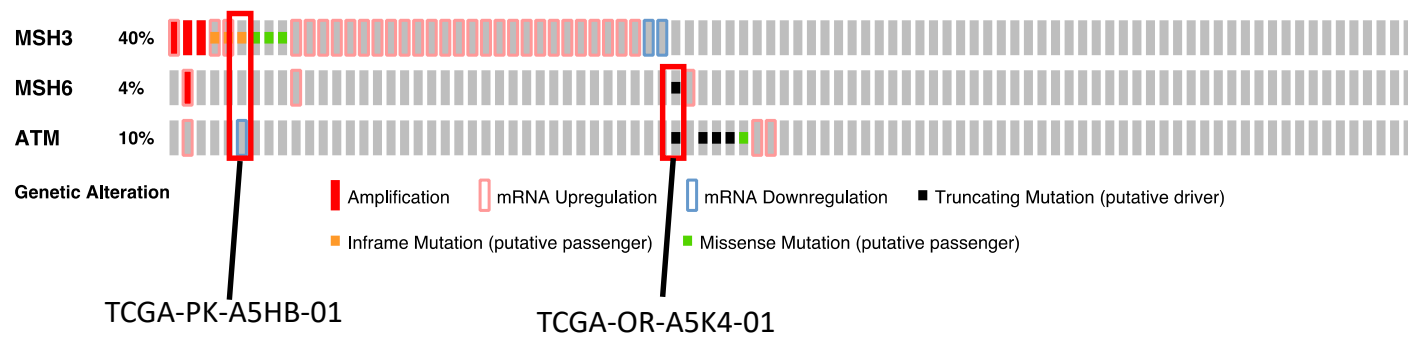
**Supplementary Figure 2: Validation of genetic variants that was identified in our study through Sanger sequencing.** The DNA sequence chromatogram profile of 10 randomly selected genetic variants in different tumors. The cDNA and amino acid change was on the left side of the chromatogram (boxed region in the chromatogram is the location of the mutation)



**Supplementary Figure 3.** *MSH3* loss of function germline mutation in hypervariable ACC metastases tumor 1 and 2. The top panel is an IGV BAM file image illustrating the 9-base INDEL in the germline and two metastases from a single patient. The lower panels show log2 ratios and b-allele frequencies generated with CNVkit. log2 ratios show copy number gain at this locus, and b-allele frequencies show the total loss of heterozygosity, fixing this mutation in both tumor samples.

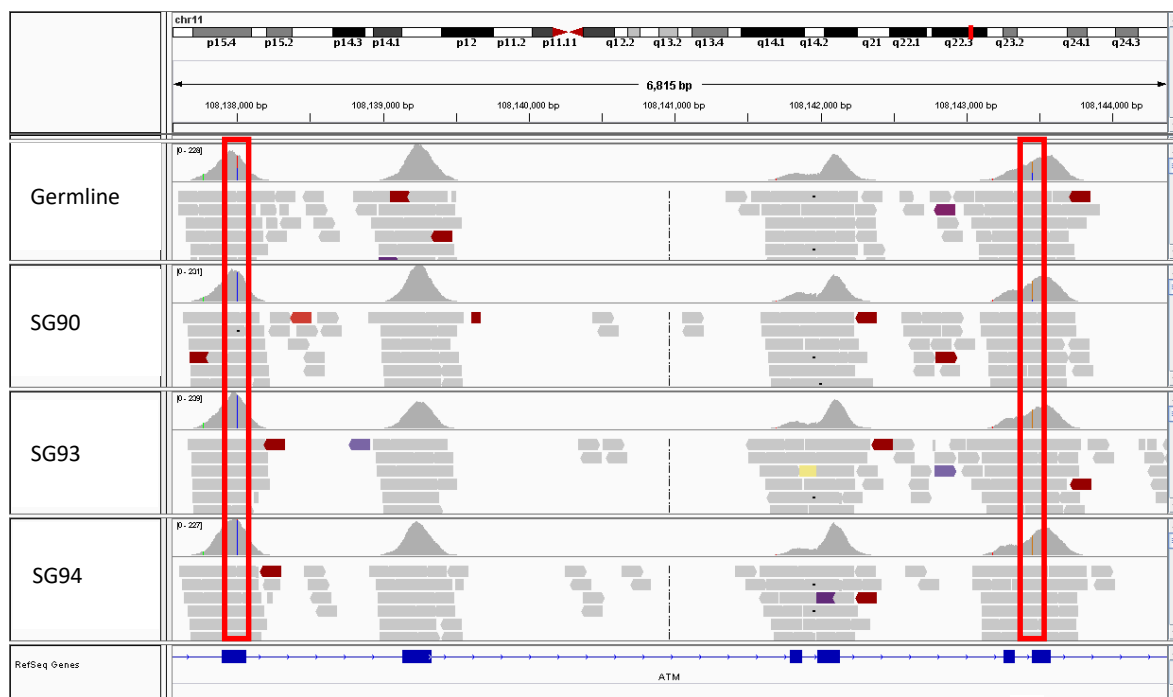


**Supplementary Figure 4.** *MSH6* homozygous deletion (A) and *ATM* frameshift (B) in hypervariable ACC metastasis tumor 20.

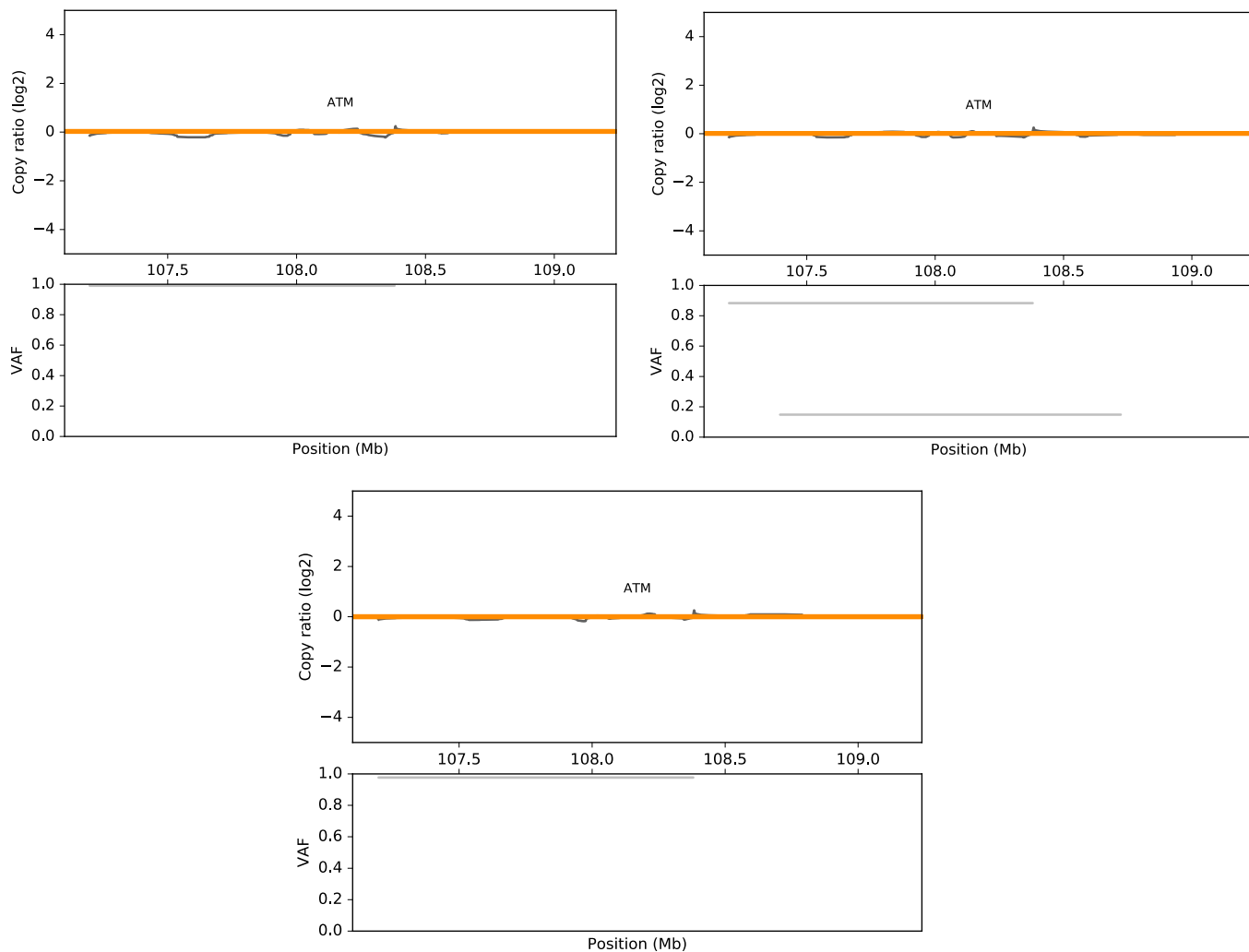


**Supplementary Figure 5.** Frequency of somatic mutations in 92 primary ACCs available in cBioportal for the three genes putatively driving hypermutation in ACC metastases.

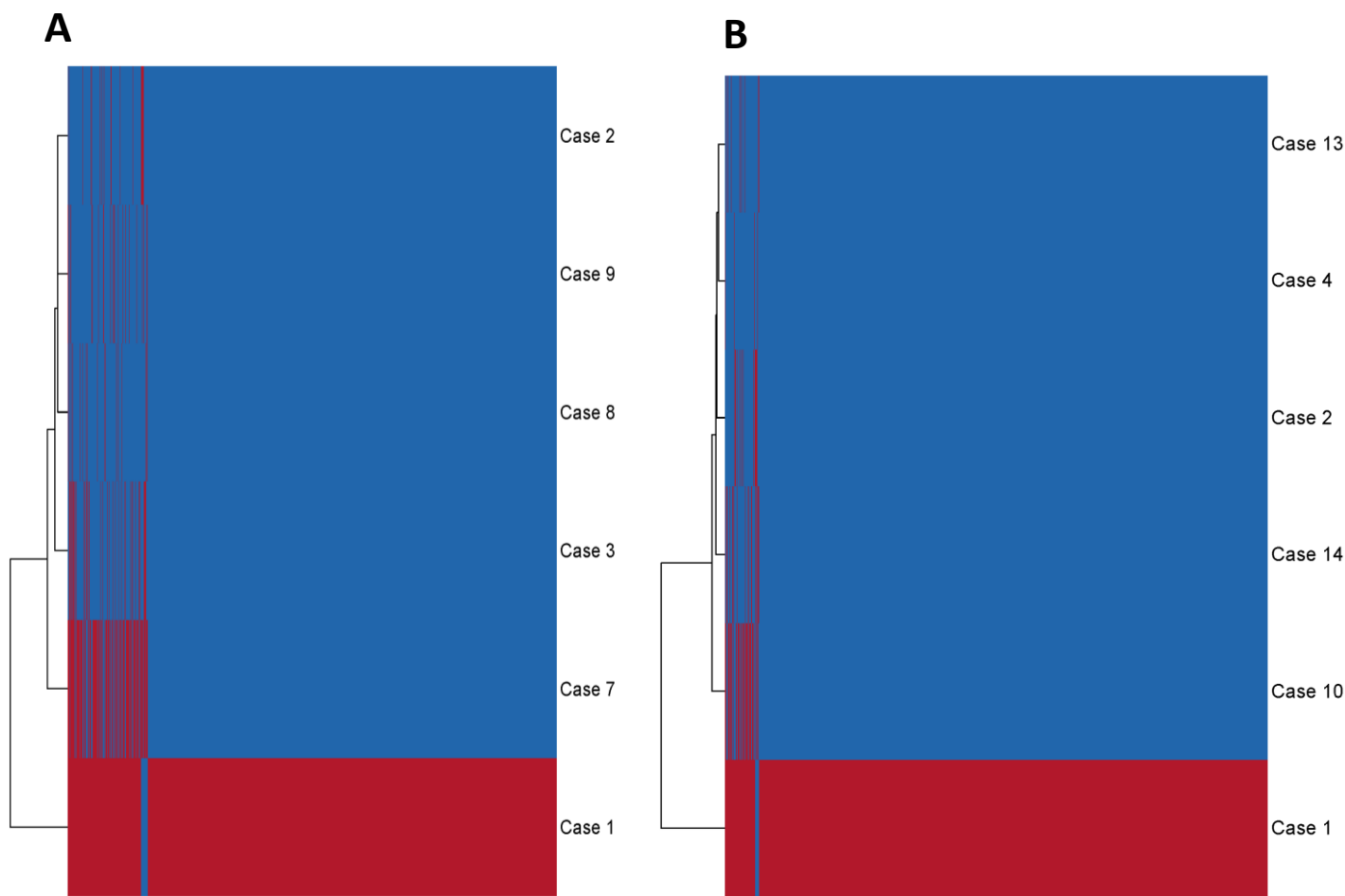
A.



B.

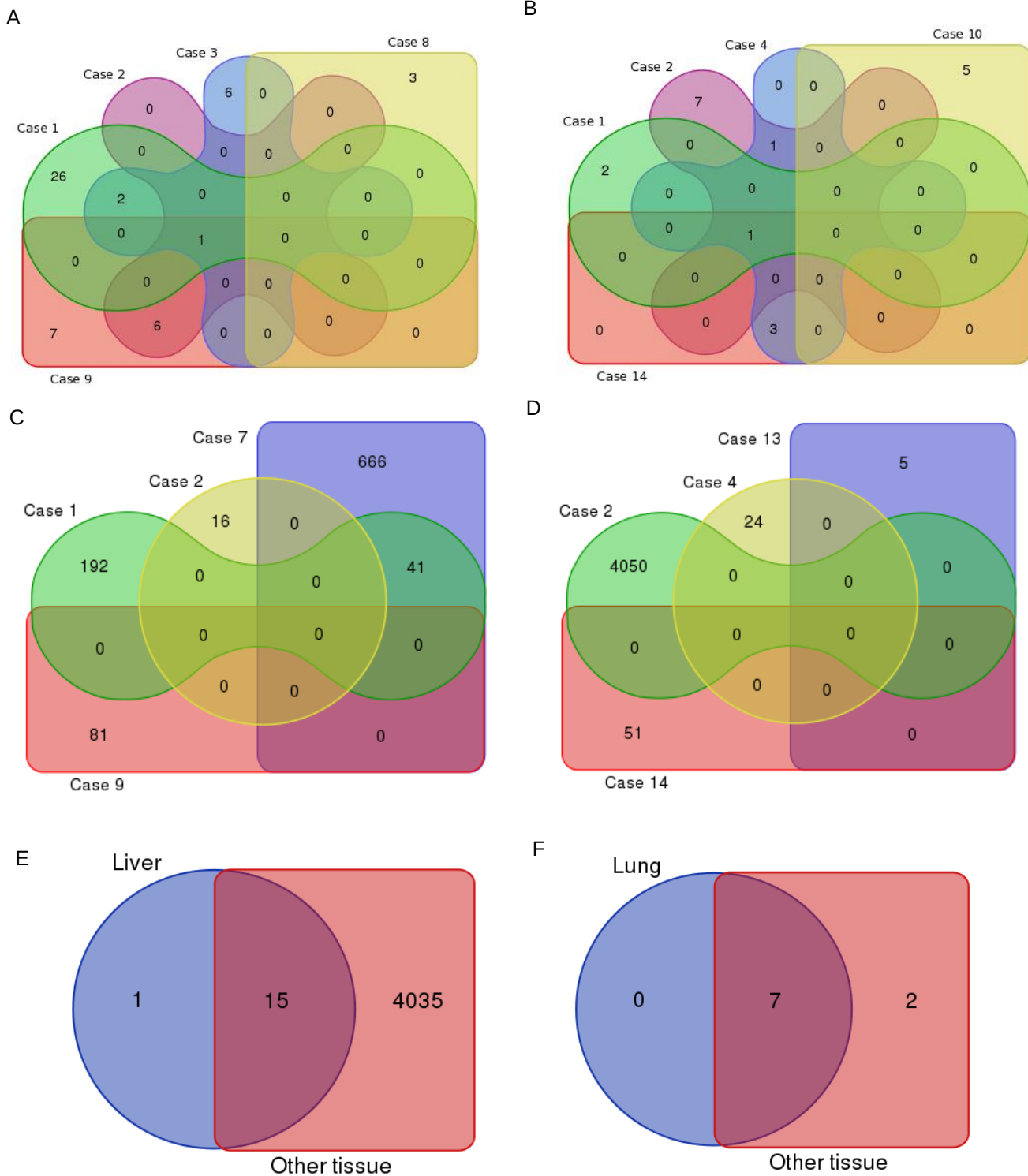


**Supplementary Figure 6.** *ATM* missense mutations in (A) and *ATM* frameshift (B) in hypervariable ACC metastasis tumor 20.



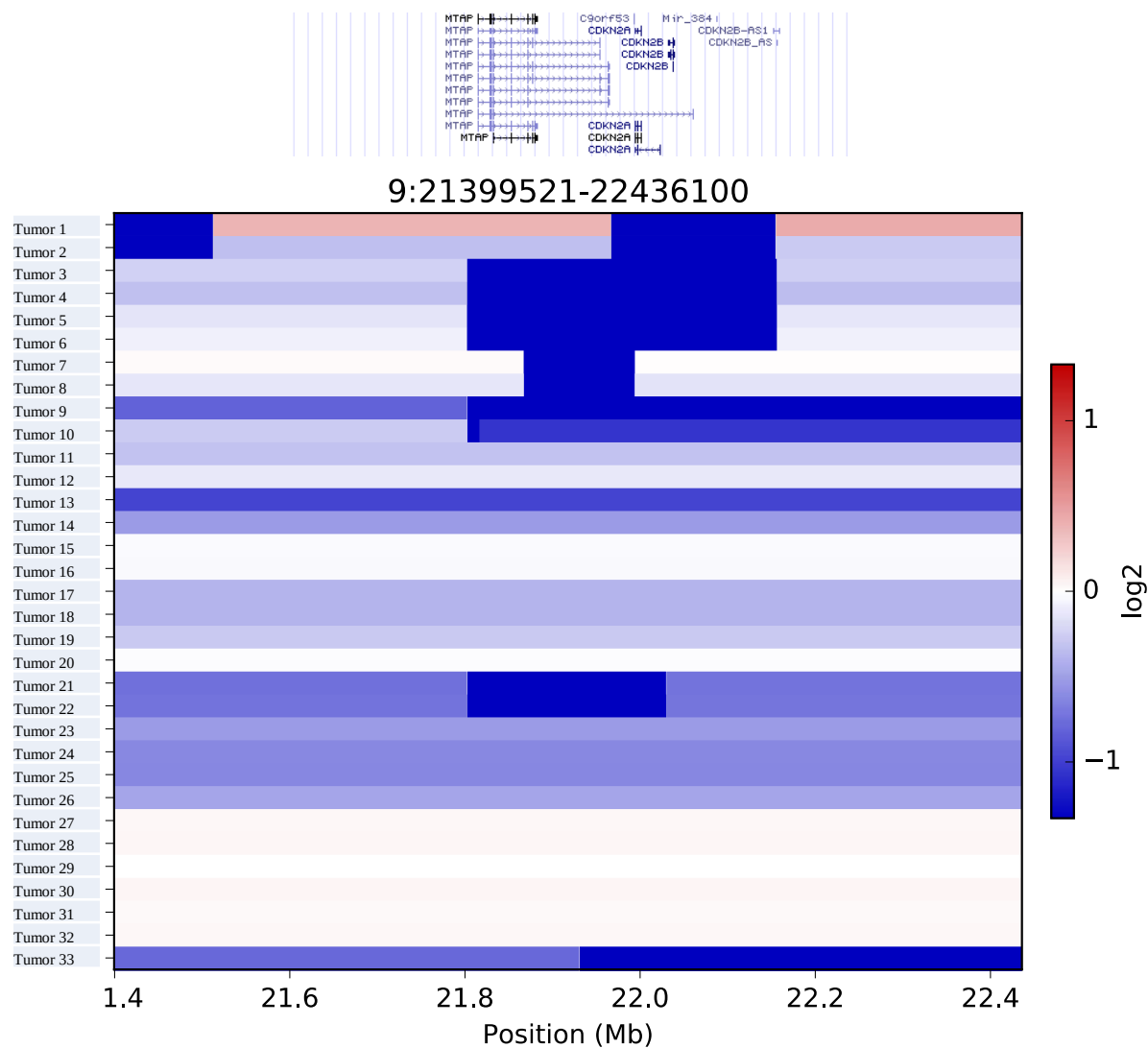
**Supplementary Figure 7.** Heatmaps and clustering of overlapping variants within the genes in metastatic lung (A) and other tumor sites (B) together with the hypermutator case



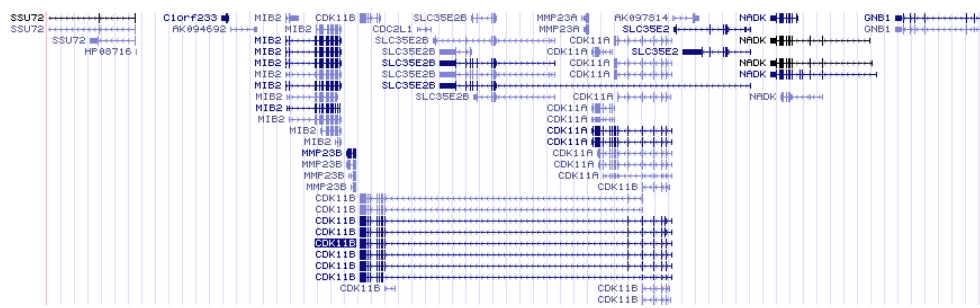


### Supplementary Figure 8

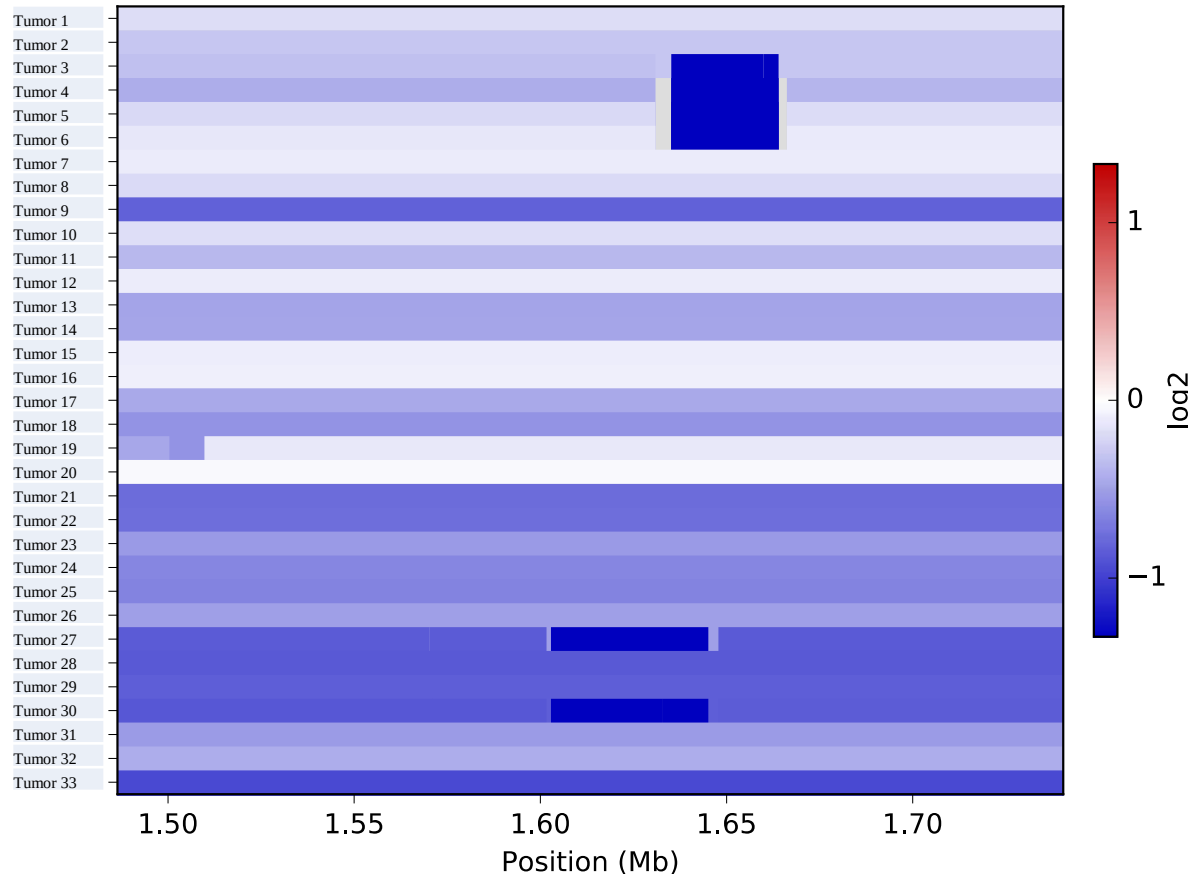
**Copy number variation in metastatic ACC tumors.** Venn diagrams representing the total number of homozygous deletions and high level amplifications in four different metastatic lung (A & C) and other tissue tumors (B & D) respectively. The homozygous deletions (E) and amplifications (F) in a case with two metastatic sites; lung and other tissues.



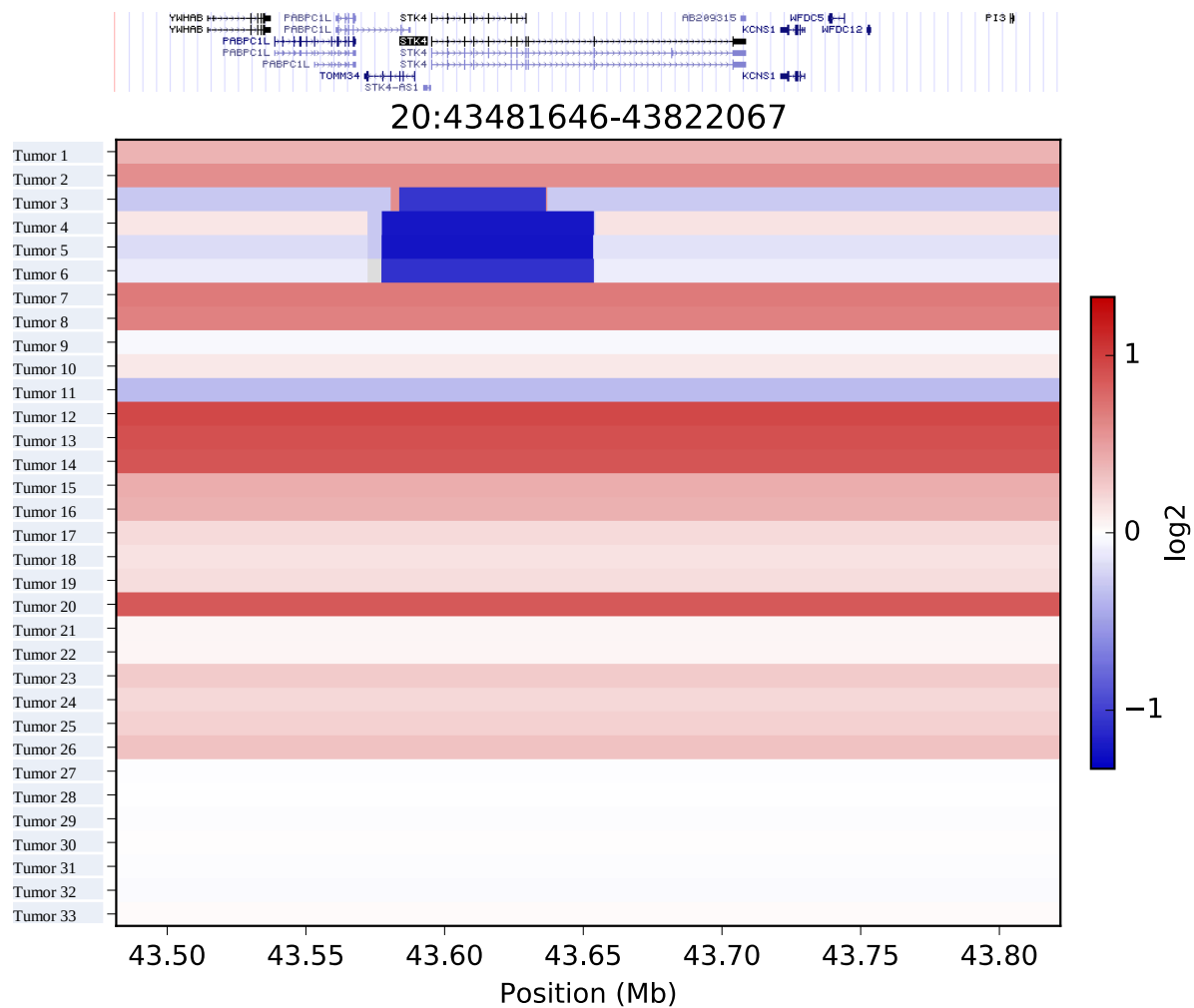
**Supplementary Figure 9.** Heatmap illustration of recurrent *CDKN2A*/*CDKN2B*/*MTAP* deletion



1:1486424-1740451



**Supplementary Figure 10.** Heatmap illustration of recurrent *CDK11A/CDK11B* deletion



**Supplementary Figure 11.** Heatmap illustration of recurrent *STK4/TOMM34* deletion

| Cases   | Sample   | Tumor Purity | Subclonal Genome Fraction | SNP Counts |                  |               | SNPs PerMegabase |                  |               | MuTect Covered Bases | Proportion CNV altered | Proportion LOH |
|---------|----------|--------------|---------------------------|------------|------------------|---------------|------------------|------------------|---------------|----------------------|------------------------|----------------|
|         |          |              |                           | All SNPs   | Coding Nonsilent | Coding Silent | All SNPs         | Coding Nonsilent | Coding Silent |                      |                        |                |
| Case 1  | Tumor 1  | 0.92         | 0.0100                    | 6551       | 2494             | 4057          | 140.8979         | 53.6406          | 87.2573       | 46494669             | 0.4007                 | 0.7930         |
| Case 1  | Tumor 2  | 1.00         | 0.0000                    | 3667       | 1428             | 2239          | 80.6711          | 31.4149          | 49.2562       | 45456191             | 0.9382                 | 0.7243         |
| Case 2  | Tumor 3  | 0.85         | 0.0200                    | 98         | 34               | 64            | 2.2390           | 0.7768           | 1.4622        | 43770135             | 0.7221                 | 0.5048         |
| Case 2  | Tumor 4  | 0.86         | 0.0100                    | 92         | 35               | 57            | 2.1301           | 0.8104           | 1.3197        | 43190006             | 0.6736                 | 0.5447         |
| Case 2  | Tumor 5  | 0.94         | 0.0000                    | 121        | 38               | 83            | 2.7809           | 0.8733           | 1.9076        | 43510708             | 0.5102                 | 0.4739         |
| Case 2  | Tumor 6  | 0.81         | 0.0100                    | 116        | 41               | 75            | 2.6278           | 0.9288           | 1.6990        | 44143875             | 0.4345                 | 0.4110         |
| Case 3  | Tumor 7  | 1.00         | 0.0000                    | 159        | 63               | 96            | 3.5203           | 1.3948           | 2.1255        | 45166882             | 0.3682                 | 0.6762         |
| Case 3  | Tumor 8  | 0.75         | 0.0100                    | 217        | 93               | 124           | 4.7627           | 2.0412           | 2.7215        | 45562460             | 0.3931                 | 0.7054         |
| Case 4  | Tumor 9  | 1.00         | 0.0000                    | 67         | 24               | 43            | 1.5793           | 0.5657           | 1.0136        | 42424559             | 0.2907                 | 0.1974         |
| Case 5  | Tumor 10 | 0.31         | 0.0100                    | 215        | 91               | 124           | 4.9358           | 2.0891           | 2.8467        | 43559540             | 0.3096                 | 0.1629         |
| Case 6  | Tumor 11 | 1.00         | 0.0100                    | 147        | 65               | 82            | 3.2296           | 1.4281           | 1.8016        | 45515892             | 0.4950                 | 0.4108         |
| Case 7  | Tumor 12 | 0.85         | 0.0100                    | 504        | 224              | 280           | 11.2288          | 4.9906           | 6.2382        | 44884404             | 0.4627                 | 0.2320         |
| Case 7  | Tumor 13 | 0.90         | 0.0200                    | 450        | 185              | 265           | 10.1537          | 4.1743           | 5.9794        | 44318620             | 0.6178                 | 0.3827         |
| Case 7  | Tumor 14 | 0.96         | 0.0100                    | 537        | 207              | 330           | 12.1514          | 4.6840           | 7.4673        | 44192542             | 0.5157                 | 0.3144         |
| Case 8  | Tumor 15 | 1.00         | 0.0000                    | 114        | 42               | 72            | 2.5841           | 0.9520           | 1.6320        | 44116768             | 0.2833                 | 0.8075         |
| Case 8  | Tumor 16 | 0.93         | 0.0000                    | 118        | 40               | 78            | 2.6376           | 0.8941           | 1.7435        | 44737744             | 0.2973                 | 0.8082         |
| Case 9  | Tumor 17 | 1.00         | 0.0100                    | 126        | 53               | 73            | 2.7770           | 1.1681           | 1.6089        | 45372897             | 0.4082                 | 0.2999         |
| Case 9  | Tumor 18 | 0.92         | 0.0100                    | 147        | 60               | 87            | 3.2758           | 1.3371           | 1.9388        | 44873924             | 0.3667                 | 0.2583         |
| Case 9  | Tumor 19 | 1.00         | 0.0000                    | 144        | 60               | 84            | 3.1843           | 1.3268           | 1.8575        | 45222271             | 0.4248                 | 0.2650         |
| Case 10 | Tumor 20 | 0.93         | 0.0100                    | 574        | 259              | 315           | 12.3841          | 5.5880           | 6.7962        | 46349581             | 0.1669                 | 0.8387         |
| Case 11 | Tumor 21 | 0.73         | 0.0000                    | 66         | 30               | 36            | 1.5174           | 0.6897           | 0.8277        | 43495518             | 0.5106                 | 0.5091         |
| Case 11 | Tumor 22 | 0.84         | 0.0000                    | 86         | 32               | 54            | 1.9700           | 0.7330           | 1.2370        | 43655497             | 0.5106                 | 0.5163         |
| Case 12 | Tumor 23 | 0.97         | 0.0200                    | 77         | 27               | 50            | 1.7303           | 0.6067           | 1.1236        | 44499729             | 0.9597                 | 0.4837         |
| Case 12 | Tumor 24 | 0.92         | 0.0100                    | 81         | 26               | 55            | 1.8852           | 0.6051           | 1.2801        | 42966871             | 0.9437                 | 0.4996         |
| Case 12 | Tumor 25 | 0.83         | 0.0100                    | 72         | 23               | 49            | 1.7166           | 0.5483           | 1.1682        | 41944315             | 0.9024                 | 0.4981         |
| Case 12 | Tumor 26 | 0.87         | 0.0100                    | 83         | 32               | 51            | 1.8567           | 0.7158           | 1.1408        | 44703883             | 0.9585                 | 0.4884         |
| Case 13 | Tumor 27 | 0.89         | 0.0000                    | 79         | 24               | 55            | 1.7775           | 0.5400           | 1.2375        | 44443520             | 0.5231                 | 0.5472         |
| Case 13 | Tumor 28 | 0.89         | 0.0100                    | 94         | 28               | 66            | 2.1214           | 0.6319           | 1.4895        | 44310782             | 0.5256                 | 0.5356         |
| Case 13 | Tumor 29 | 0.83         | 0.0100                    | 87         | 27               | 60            | 1.9420           | 0.6027           | 1.3393        | 44798925             | 0.5252                 | 0.5473         |
| Case 13 | Tumor 30 | 0.88         | 0.0100                    | 84         | 25               | 59            | 1.8631           | 0.5545           | 1.3086        | 45086784             | 0.5251                 | 0.5456         |
| Case 13 | Tumor 31 | 0.38         | 0.0000                    | 89         | 26               | 63            | 2.0584           | 0.6013           | 1.4571        | 43237553             | 0.5172                 | 0.5461         |
| Case 13 | Tumor 32 | 0.83         | 0.0000                    | 75         | 21               | 54            | 1.6964           | 0.4750           | 1.2214        | 44212491             | 0.5130                 | 0.4979         |
| Case 14 | Tumor 33 | 0.78         | 0.0000                    | 184        | 71               | 113           | 4.0390           | 1.5585           | 2.4805        | 45555279             | 0.4199                 | 0.3524         |
| Mean    |          |              |                           | 464.27     | 179.64           | 284.64        | 10.18            | 3.94             | 6.24          |                      | 0.5277                 | 0.4963         |
| Median  |          |              |                           | 116        | 40               | 73            | 2.63             | 0.89             | 1.63          |                      | 0.5106                 | 0.4996         |

### Supplementary Table 1

Mutational summary of all ACC metastatic tumors. Tumor purity and subclonal genome fraction generated in ABSOLUTE. SNP count and frequency data generated using MuTect. 'All SNPs' refers to exonic (including synonymous), UTR, and splicing mutations; 'Coding Nonsilent' refers to exonic mutations excluding synonymous mutations and splice mutations; 'Coding Silent' refers to synonymous, UTR, and splice mutations. Tumors 1&2 exhibit hyper mutation phenotype belong to the same patient.

| Gene Symbol | Chr | Start Position (hg19) | Stop Position (hg19) | Mutation/Event      | Ref Allele | Tumor Allele | Mutation Location          | Samples Positive  |
|-------------|-----|-----------------------|----------------------|---------------------|------------|--------------|----------------------------|-------------------|
| ATM         | 11  | 108138003             | 108138003            | Missense Mutation   | T          | C            | Germline, with Somatic LoH | Tumors 12, 13 &14 |
| ATM         | 11  | 108143456             | 108143456            | Missense Mutation   | C          | G            | Germline, with Somatic LoH | Tumors 12, 13 &14 |
| ATM         | 11  | 108205744             | 108205744            | FrameShift Deletion | A          | -            | Somatic, with LoH          | Tumor 20          |
| MSH3        | 5   | 79950724              | 79950724             | InFrame Insertion   | G          | GCCGCAGCGC   | Germline, with Somatic LoH | Tumors 1&2        |
| MSH6        | 2   | 48010242              | 48036835             | HomozygousDeletion  | NA         | NA           | Somatic                    | Tumor 20          |

**Supplementary Table 2**  
Putative mutational events underlying hypermutation phenotypes in ACC metastases. LoH = Loss of Heterozygosity

| Cases                | Total genes | Gene name/s                                                                                                                                                                                                                                                     |
|----------------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Case 1 Case 2 Case 7 | 1           | DNAH6                                                                                                                                                                                                                                                           |
| Case 1 Case 3 Case 7 | 2           | MUC5B HELZ2                                                                                                                                                                                                                                                     |
| Case 1 Case 7 Case 8 | 1           | KIAA0100                                                                                                                                                                                                                                                        |
| Case 1 Case 2        | 7           | ZNF646 FHDC1 VSTM2B SNRNP200 TAS2R41 CKAP5 RASGRF2                                                                                                                                                                                                              |
| Case 1 Case 3        | 21          | SALL1 MYO9B ARHGAP21 TENM4 CLEC1B TTLL4 CAMSAP1 LRP1B DCDC1 KCNH3 PFAS ZNF44 CHD7 DMXL2 FSIP2 ITGAX MTFMT SHANK1 CACNA1F MAP2 CFTR                                                                                                                              |
| Case 1 Case 7        | 43          | PLCE1 TET3 SUSD2 AHI1 MEGF10 PIEZO2 COL5A2 FAM120A MKLN1 CD93 KCNN3 CDH11 IKBKAP CCT7 TTC40 TULP1 CNTN1 BRD7 RBP3 MUM1 DRD1 MUC3A PPP6R1 MYH3 ANK2 VWF NEB ZFR2 RNF213 BAG6 TRIM67 PTPRD CACNA1A KCNQ2 TROVE2 IGF1R BCAS1 SALL4 CCDC135 TTN NRCAM COL6A3 FAM65C |
| Case 1 Case 8        | 8           | FN1 CWH43 DNAH7 NAV3 ANKS1B OBSCN RBL2 ADRA2B                                                                                                                                                                                                                   |
| Case 1 Case 9        | 10          | DNAH11 DNHD1 ACTN1 APC TMTC1 KIAA1549L SAMD9L ADAMTS20 SNTB2 MMP9                                                                                                                                                                                               |
| Case 2 Case 7        | 2           | CPNE4 CTNNB1                                                                                                                                                                                                                                                    |
| Case 2 Case 9        | 1           | EME1                                                                                                                                                                                                                                                            |
| Case 3 Case 8        | 1           | MN1                                                                                                                                                                                                                                                             |

### Supplementary Table 3

The list of genes that are frequently mutated in metastatic adrenal tumors from lung.

| Cases                  | Total genes | Gene name                                                                                                                                                                                                                          |
|------------------------|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Case 1 Case 10 Case 4  | 1           | ARHGEF28                                                                                                                                                                                                                           |
| Case 1 Case 10 Case 14 | 1           | PPL                                                                                                                                                                                                                                |
| Case 1 Case 2          | 1           | CACNA2D4                                                                                                                                                                                                                           |
| Case 1 Case 4          | 2           | MUM1L1 ARID1B                                                                                                                                                                                                                      |
| Case 1 Case 10         | 37          | DCHS2 TRIB3 CHD9 FRY DIP2A CCDC141 TMEM63C PLEKHG4 LILRA6 PCLO GRIP1 ANK2 CREBBP HELZ2 SHANK1 TNFRSF1A PIEZO1 NLRX1 SPEG PHRF1 SRCAP KMT2D NCKAP5 MRGPRG DIP2B TTC28 PALM3 FGD1 UNC80 TTC17 HIVEP3 DMWD WDR52 RELN ANO6 COQ2 CDHR2 |
| Case 1 Case 13         | 6           | INF2 VWF KLHL8 ABCA4 TTN SCAF11                                                                                                                                                                                                    |
| Case 1 Case 14         | 13          | MYO9B VANG2 SMCHD1 EOMES DUOX1 PCDH12 ABL1 SYCP2 SHANK2 NHSL1 DDX60L DDR2 PCIF1                                                                                                                                                    |
| Case 10 Case 2         | 2           | CNOT1 DST                                                                                                                                                                                                                          |
| Case 14 Case 2         | 2           | LILRA4 CTNNB1                                                                                                                                                                                                                      |
| Case 10 Case 4         | 1           | PDE4DIP                                                                                                                                                                                                                            |
| Case 10 Case 14        | 1           | GAL3ST3                                                                                                                                                                                                                            |
| Case 13 Case 14        | 2           | PDZRN4 NOVA1                                                                                                                                                                                                                       |

#### Supplementary Table 4

The list of genes that are frequently mutated in metastatic adrenal tumors from other tissue.



| S.No | Primer sequence            | Direction | Gene    |
|------|----------------------------|-----------|---------|
| 1    | CGGATCTGTGCACAGGACTGC      | FP        | TUBA3D  |
| 2    | GAGTTGTAGGGCTCCACCACGG     | RP        |         |
| 3    | CCACTTCTCTGTGTTTAAACAG     | FP        | LTF     |
| 4    | AAGGGGACAGGGTCACTCA        | RP        |         |
| 5    | CACCCAGTGCCCTCATGCAGCATG   | FP        | FAM205A |
| 6    | ATCGCAAGCCCCGTGGCCTCT      | RP        |         |
| 7    | TGCGAGATATCAAGGCCCCG       | FP        | ASXL3   |
| 8    | CAACCGGGTCTCTTTAGAGGTCT    | RP        |         |
| 9    | CATCCGCAATCTGTGCTGCTTG     | FP        | ADAMTS4 |
| 10   | TGCGGTGTGACTGGGGCCT        | RP        |         |
| 11   | GTCACCTTCCCTCTTTGCCCT      | FP        | ITGA9   |
| 12   | CAATCTCTCTGGAACGTGTTTG     | RP        |         |
| 13   | CTGGGCTTGCTCTCCCGTGTG      | FP        | FRS3    |
| 14   | TGCGTGCTCACCTGCTCATCAGGA   | RP        |         |
| 15   | CTTTGTCCCTGCATCCAG         | FP        | DUSP5   |
| 16   | GAAGGGGAATGGCTAAACCTAC     | RP        |         |
| 17   | CGGCACAATAAGGCCACGGAAC     | FP        | GPR65   |
| 18   | CATATCTTCTGTTTCCGTTAC      | RP        |         |
| 19   | CACCAAGCTACCCGAATATG       | FP        | ZFR2    |
| 20   | CATGGCAGGAGGGCGACTGAC      | RP        |         |
| 21   | GCAATGGACAGAATACACTTAG     | FP        | ZNF614  |
| 22   | TGAGTCCTCTGATGCTTGAAGAC    | RP        |         |
| 23   | GAGTATGAAGCCTTGGAGTGGC     | FP        | FAM205A |
| 24   | GATGCTCACGTGGCTAGGGCTGTG   | RP        |         |
| 25   | GGCCCTTTTACTCTTTGATGCC     | FP        | CLIC5   |
| 26   | CCTGTGGGTAGAGCTCTCTTAC     | RP        |         |
| 27   | ATCCATCCCATCCTACTGCCAG     | FP        | PER3    |
| 28   | CTGATGCTGCTGAACCACTTCTGG   | RP        |         |
| 29   | AGTACGGCGGTCACTGGTGT       | FP        | IQSEC3  |
| 30   | TCGGTGAAGGAGTCTCCACG       | RP        |         |
| 31   | ATGGCTCTGGCGGTGGCCC        | FP        | CBLC    |
| 32   | TAGAAAGTCCCCAGAGCCGCCG     | RP        |         |
| 33   | GCTTCGACCACTTCTACGAGGCAGC  | FP        | HOXD11  |
| 34   | CGCTTGCCCACTACCCGGTGCC     | RP        |         |
| 35   | AGTCAATCGTGGGTGCATCATC     | FP        | KCNJ2   |
| 36   | GGGGACACCAAGAAATACGATCG    | RP        |         |
| 37   | TAGGGCTCTGACCTTGTCCAG      | FP        | ZSCAN18 |
| 38   | CTGCTGGATGACGGACTGCCT      | RP        |         |
| 39   | CCATGCTCCGCCCTCTAG         | FP        | KCTD17  |
| 40   | ACAGGCTGAGGCGGGTGGG        | RP        |         |
| 41   | GATGATCAGTACCAAGCTGTAGC    | FP        | ART4    |
| 42   | AGAGGAATTGGCCAATCGAATGG    | RP        |         |
| 43   | GCCCTCTGCTCTGTCTCCAG       | FP        | BP1FB5  |
| 44   | CCAGCCACAGAGCCCTCAC        | RP        |         |
| 45   | GGCTTTACCATCTCTATGCTTTTGGG | FP        | AVPR1B  |
| 46   | TTAGGCTGAGGCTGAGGCTGAG     | RP        |         |
| 47   | CGCCAGTGGGTGCTCTCTG        | FP        | ATAD3A  |
| 48   | CTGGATGGGGTGCCGACGCG       | RP        |         |
| 49   | CCTTGTTCTCTGTGCCACAC       | FP        | ALDH3B2 |
| 50   | TCACAGGAGGGTGACGCTCTG      | RP        |         |
| 51   | GTCAGGTTGCTAAGCAGTGAAAG    | FP        | EME1    |
| 52   | GGGCAGGTAGACAGGTAGGC       | RP        |         |
| 53   | CGGGGGAAGTACAGCGACC        | FP        | CHST11  |
| 54   | GGTGCGCTTCTTCCGCTGGCG      | RP        |         |
| 55   | ACTCCGCTCCGCCCTCTCCT       | FP        | MMP9    |
| 56   | GGCGAGCCCTCACTCAC          | RP        |         |
| 57   | CTGGAACCTCTCTGCCTCC        | FP        | UROC1   |
| 58   | GGTGGAAGGACTGGGTGAC        | RP        |         |
| 59   | CAACCTGACTTTCTTCTTCTCC     | FP        | SFTPD   |
| 60   | GCCCTCTGCTTGGGAATCAGTC     | RP        |         |
| 61   | CTCTCCTTTTGTCTTATCCAC      | FP        | KCNH8   |
| 62   | GTGCTCCGAGTTGTGGACAG       | RP        |         |
| 63   | GCTGAGCGCATGGCCATCCGGCA    | FP        | B3GALT5 |
| 64   | TCATGGTCTCAGGGTCAGATTG     | RP        |         |
| 65   | GTCCCCAGGAGCACCGTGAG       | FP        | TBX5    |
| 66   | GACCAAGGGTGATCACACTCAC     | RP        |         |
| 67   | GCTCACTCATTGAACACGAGAG     | FP        | ZNF419  |
| 68   | GGTCTTTCTCAGAGTGGAATTCTC   | RP        |         |
| 69   | CTCACTCTGTTGCCCTCTACCCC    | FP        | BPI     |
| 70   | CACCCACCCAGAGCCCGGC        | RP        |         |
| 71   | GGAGTGGCTGAATGCTTCTCTC     | FP        | OR10A2  |
| 72   | CACAGACCAAGCTCAGCAGAG      | RP        |         |
| 73   | TGGCTCTATTCTTCCGGCTTC      | FP        | NRP2    |
| 74   | GAAGAGACAGATATTCACATCCC    | RP        |         |
| 75   | TGATCTTTGTCTCCCTCATG       | FP        | ALPPL2  |
| 76   | CTGGCTCACTCAACCGTCACCC     | RP        |         |
| 77   | CAGAGTCCCACCTCCCTCCC       | FP        | CYP4F2  |
| 78   | TCAGCTCAGGGGCTCCACCCG      | RP        |         |

| S.No | Primer sequence              | Direction | Gene     |
|------|------------------------------|-----------|----------|
| 79   | CATGATCTCTGGGGTTTGTTC        | FP        | DAPK1    |
| 80   | GGGATCCTGTCTCTGTGCATAC       | RP        |          |
| 81   | GAGAAGGAAAATTATGACGTTTGGGC   | FP        | ARHGAP25 |
| 82   | TTAAGCCTCGGTCTTGGGTTCCTTC    | RP        |          |
| 83   | ACGCCCCAGTCTCCCCCCCC         | FP        | H6PD     |
| 84   | TGCGCAGGGCCACTCACACAC        | RP        |          |
| 85   | TTGCCCCAAATATCACAGTGTGTA     | FP        | TEP1     |
| 86   | CCCGGCTAGAACCCCAACT          | RP        |          |
| 87   | CTCTTCTTCAGTTACAAGTTCCTCC    | FP        | ACSM2B   |
| 88   | CCATGGTTCCTTGGGAACAGG        | RP        |          |
| 89   | GGATCTGTGATGAGAACGGAGCC      | FP        | VWF      |
| 90   | CAGTGGTAAGAGGAGGACCTGGC      | RP        |          |
| 91   | AATCTCGCTCTTCTCTTACCTC       | FP        | ABCA4    |
| 92   | GCATAAGCAGCAGGGGTACCTGG      | RP        |          |
| 93   | GTTTTAGTCCCTGTGCTGTC         | FP        | PCMTD1   |
| 94   | CTGTCTAGAGGCTGAGGAATAAGCTG   | RP        |          |
| 95   | GGCACGGGGGTGTGAACCAAGC       | FP        | PAX2     |
| 96   | CCGGGACAGCTGCGAAGCCCTC       | RP        |          |
| 97   | CTTTCACTCGGGCAAAATATTACTGG   | FP        | TRIM49   |
| 98   | CACAGTCTTAGCTCACATCCAGG      | RP        |          |
| 99   | GAATGTAAGGAATGTGGGAAAACC     | FP        | ZNF717   |
| 100  | CTTCTTGTGGTAGGCCAGGAGG       | RP        |          |
| 101  | GAGGTGGCCAACGGGCTGAGGAAC     | FP        | HHIPL2   |
| 102  | CTTGGCATTGTGGCGAATTTGGG      | RP        |          |
| 103  | CGCTCAACAGAACAGGTTGTC        | FP        | OR13J1   |
| 104  | GACAGGAGGTGGACCACTCAGAG      | RP        |          |
| 105  | GTCCATCTGGGAAGCGGGATTGG      | FP        | BEND5    |
| 106  | GTGACCTACCTCTGACGATGCTTAGTTG | RP        |          |
| 107  | TTCCCCAGCCCTTCGAGATAATCG     | FP        | CADM3    |
| 108  | GACACTGGGTTTGGGAGTCTCAC      | RP        |          |
| 109  | CAGCTGGTCTGTCAATGTCTGTGGG    | FP        | JMJD4    |
| 110  | GGGGGACAGGAGAAGCAGCACATTAC   | RP        |          |
| 111  | TACAGATTCTCAGTGTCTTATATTG    | FP        | CDC27    |
| 112  | GTATCTGTTTGAATCTACCTTGGGG    | RP        |          |
| 113  | CCAGCCCTCCCGCCTCCTGCA        | FP        | CAPN5    |
| 114  | CCTCAAGCCAGCCCCCAAGTAC       | RP        |          |
| 115  | GTCATGTTCTTTTTTCTCTAGAGT     | FP        | SCAF8    |
| 116  | CTGGAGTATTGCTCATAGCAGTGG     | RP        |          |
| 117  | CTTACTCTTCTGCCCTCTCTTCAG     | FP        | PGLS     |
| 118  | GGGCGCGTGCCTGGTCCCG          | RP        |          |
| 119  | GCCAAGCGGGCTGCGGCCGAG        | FP        | C9ORF40  |
| 120  | CGATGCGACCCCCCAGTCTCCCC      | RP        |          |
| 121  | ATGTCGGGACCATAGCCGCTTC       | FP        | KLHL29   |
| 122  | TGGTGACCCGACGACGAGCTGGC      | RP        |          |
| 123  | GCTCAAGCCCTCTTCCCTT          | FP        | PFDN5    |
| 124  | TGGTCCAGCTGGTCTTGAGCATTTC    | RP        |          |
| 125  | AAGATCTCCCAAGGCTGTGGTG       | FP        | FCGR3A   |
| 126  | TTCTCTTCCCTTTCATCAACTC       | RP        |          |
| 127  | TCCCTCCCACCTTGTCTGTCAG       | FP        | HYDIN    |
| 128  | GCTGTCCAATGTGAGTGGTCAGTAC    | RP        |          |
| 129  | GGGCGGTTGGTGGGAGCGGTG        | FP        | GK2      |
| 130  | CTTGTCACGATTACAGTGGTTTCC     | RP        |          |
| 131  | CAAGTGGAGAAGTCTGTCAACGATGC   | FP        | ZNF578   |
| 132  | CTACAATTAAGGCTTCGCCAGTCTC    | RP        |          |
| 133  | CCAAGGAAGACCCCAAGCACTG       | FP        | DFFA     |
| 134  | CTGGCTCGCTTAGGATTCTGCAAGTGC  | RP        |          |
| 135  | TGGCCTCGCTGGGCTCCGA          | FP        | CHRNA1   |
| 136  | GGCCCCAGTGCTCTGTCTCAC        | RP        |          |
| 137  | GCCCGCAACCCGTCCTGAAGGTG      | FP        | TRIM15   |
| 138  | AGTCTCTGCCTGCTCCTCTCTGGC     | RP        |          |
| 139  | CACCCCATGCTATTGTTTATCC       | FP        | PNPLA1   |
| 140  | CCTGCCGTGCTCGAAGGCTTG        | RP        |          |
| 141  | CACCTATTCTTGTGGGG            | FP        | CLTB     |
| 142  | CCTCATGTCCCTACAGCCCTC        | RP        |          |
| 143  | CAGCTTGGTCTCTGGGAACAC        | FP        | GRIN2A   |
| 144  | CCTCTCATCTGCGGTGACGAG        | RP        |          |
| 145  | ATCCCCCTTGGCACGGCCCGCA       | FP        | GIPC3    |
| 146  | CAGGGGGCTGGGCTCCGGGCTG       | RP        |          |
| 147  | AGGAAGCACCAAGTTCAAGATCAAG    | FP        | ZNF8     |
| 148  | GTCAGTGTTCACCGGGCTGTTTCC     | RP        |          |
| 149  | CACCTTCTGGGCGTGCCCTGCAG      | FP        | ANKRD24  |
| 150  | TCACCTCCGGGCTGCGGGCACTC      | RP        |          |
| 151  | CACATTTCAITTCCTTTGTTTTCAGAC  | FP        | C10ORF67 |
| 152  | CAGAACAATTACAGTTTACCTGTGC    | RP        |          |
| 153  | CAGCTACAGATTAGCACCTAAGTATC   | FP        | AADAC    |
| 154  | ATGAACATACCTGTTGAGTCACTGC    | RP        |          |

## Supplementary Table 5

List of genetic variants and primer sequences used for Sanger sequencing