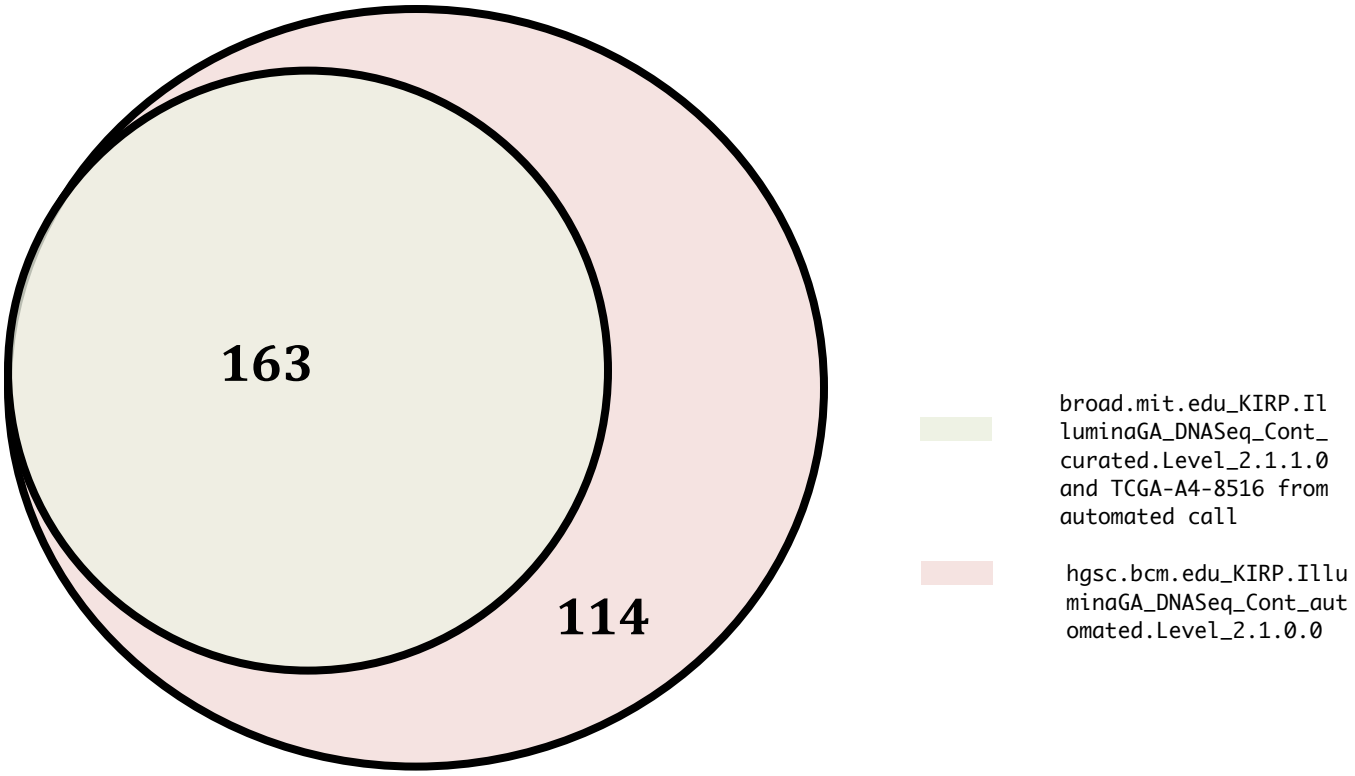

Figure S1. Extended WXS dataset acquisition. An extended WXS dataset of 277 patients were obtained from callsets from two different centers. 100% genotyping concordance was observed for germline rs11762213 in cases of multiple center calling results.

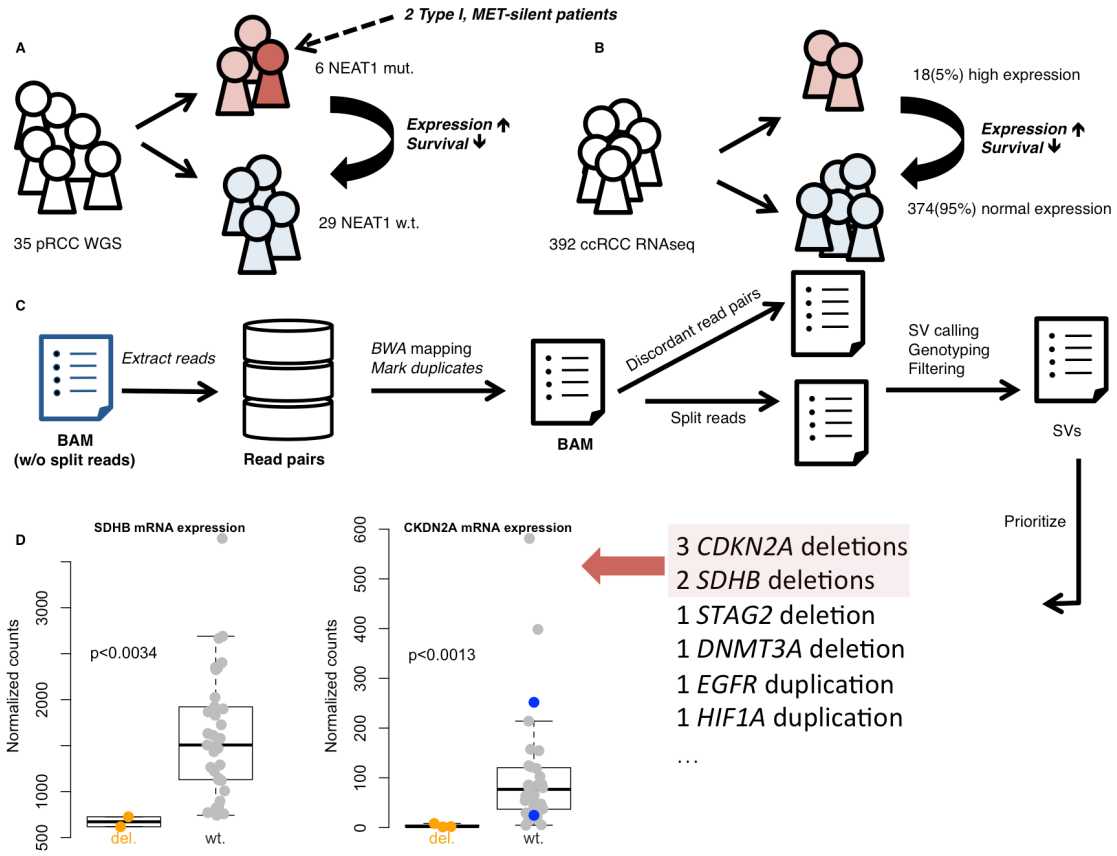

Figure S2. ***NEAT1*** **correlated with survival and SV pipeline and results. A.** Schematics for N*EAT1* survival study. 35 pRCC patients with NEAT1 mutation have significantly higher *NEAT1* expression and worse prognosis (see Fig 2C & 2D). **B.** We then defined expression >2SD as high expression and found 5% of ccRCC patients has high expression level (REF). Those patients have significantly worse survival (p=0.0132, median months of overall survival (OS): 36 versus 77). However, *NEAT1* expression is not statistically significantly associated with survival in an extended TCGA pRCC cohort. **C.** Here we showed how we remapped all the reads, called SVs and prioritized the event by overlapping with known cancer genes. **D.** We showed the expression levels of SDHB and CKDN2A are significantly lower in samples with deletions. One-sided rank sum test. For CKDN2A, TCGA called two other deletions events (blue dots) from array based method that we could not confirm using our SV pipeline.

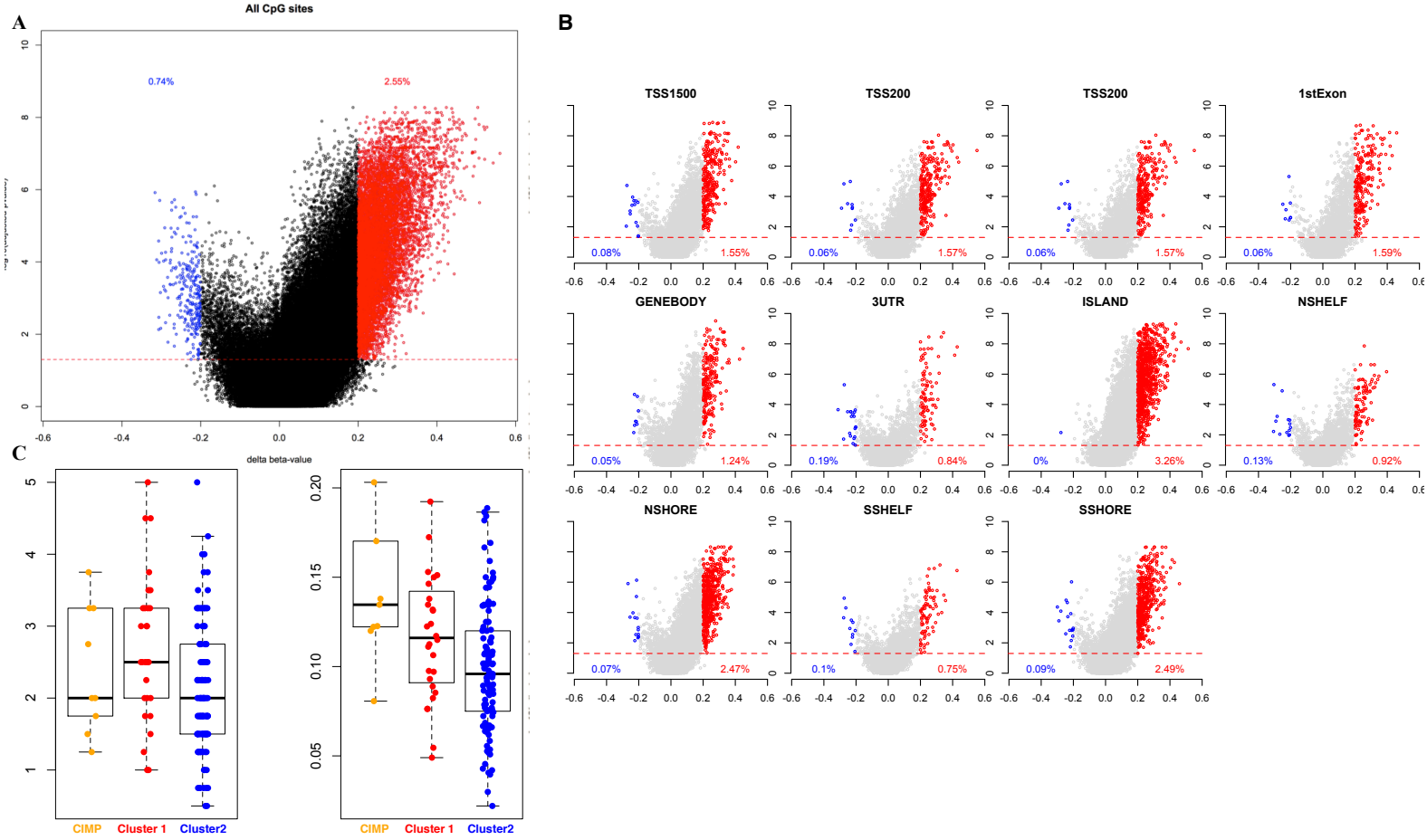

Figure S3. Methylation analyses of pRCC. A. Volcano plot of rank sum test of all CpG probe sites between methylation cluster 1 and 2. Differences in mean beta values are shown on x-axis and log transformed p-value is shown on y-axis. Red dashed line represents 0.05 significance level. **B.** Volcano plot of rank sum test of all CpG probe sites between methylation cluster 1 and 2 after grouped by functional regions. Differences in mean beta values are shown on x-axis and log transformed p-value is shown on y-axis. Red dashed line represents 0.05 significance level. Annotation details please refer to the R "IMA" package. **C.** Comparison of C>T in CpGs mutation counts (per millions) and fractions in pRCC WXS set among three different methylation clusters. CIMP: CpG island methylation phenotype. Cluster 1 versus Cluster 2, $p < 0.013$; CIMP versus Cluster 2: $p < 0.02$ (rank sum test).

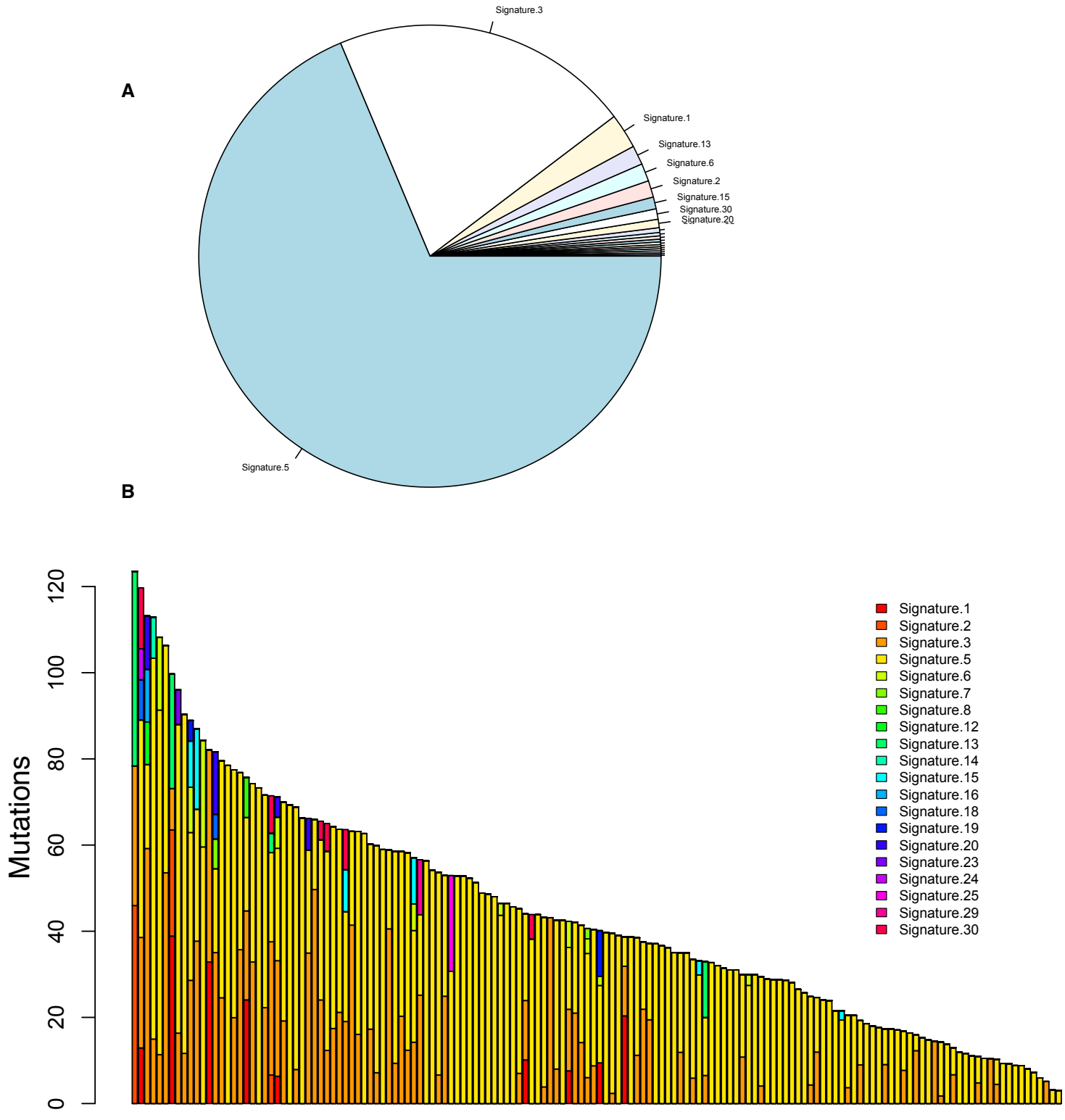

Figure S4. Signatures detected in WXS samples. **A.** Pie chart of signatures contribution percentages by pooling all samples. Signatures contribute less than 5% were not shown. **B**. Bar plot shows signature distribution in each individual samples. The results grossly agreed with previous results (Alexsandrov et al., 2013) with minor disparity in signature 3. A few samples have no detectable signature were discharged, mostly because they have too few mutations

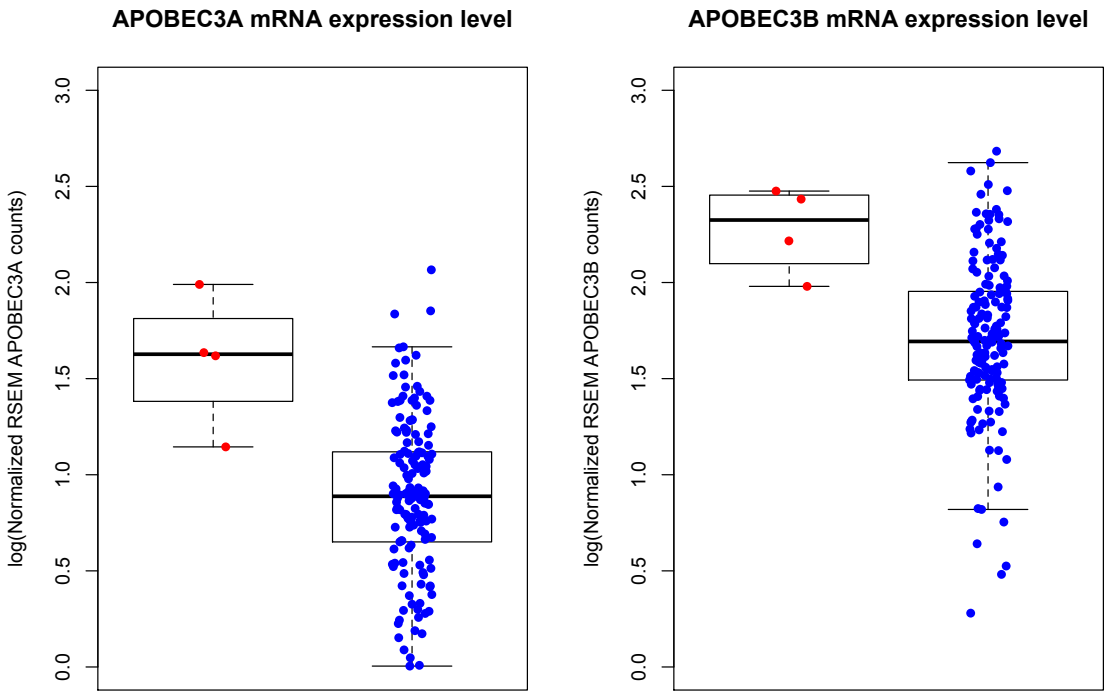

Figure S4. Samples with APOBEC signatures show higher *APOBEC* Expression Level. The expression levels of *APOBEC3A* and *APOBEC3B* are significantly higher in samples carrying APOBEC signatures (red) than the ones do not (blue). $p < 0.0022$ and $p < 0.0039$ respectively, one-sided rank sum test.

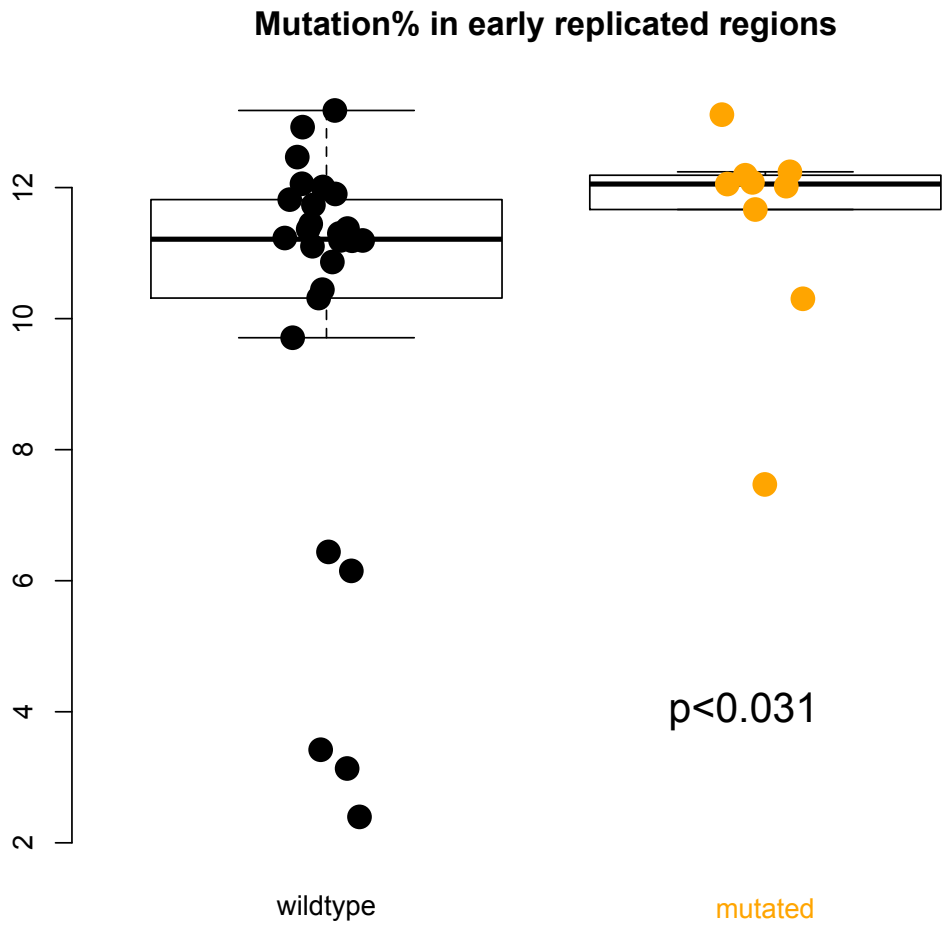

Figure S5. Mutation rate rises in early replicating regions in chromatin remodeling defected samples. Compared to the ones with wild type genes (black), samples with chromatin remodeling genes mutations (orange) have higher percentage of mutations in the early replicating regions. One-sided rank sum test.

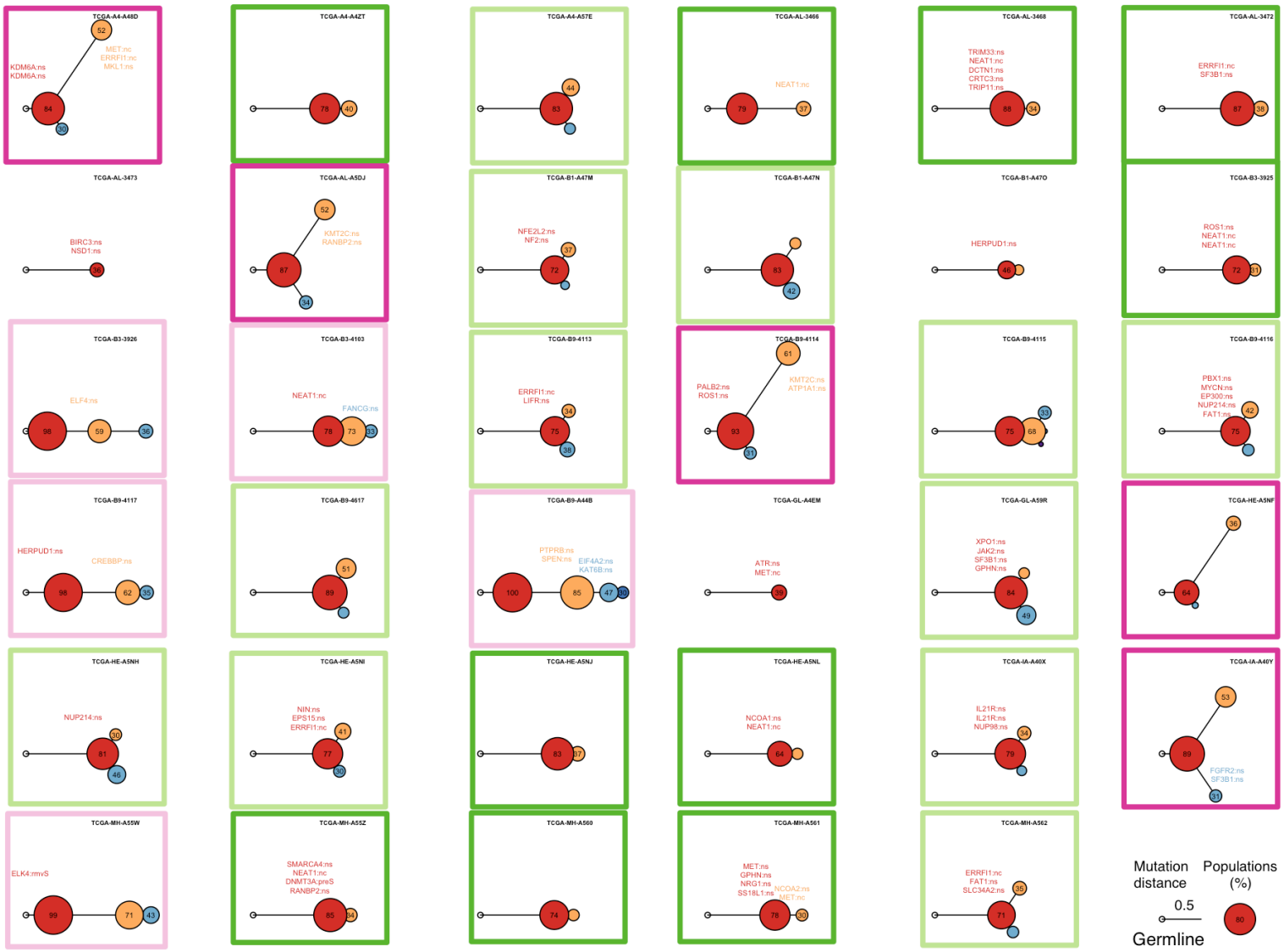

Figure S6. Individual evolutionary trees. Frame colors indicates four different topology types (See Figure 4). Mutations in cancer related gene are shown in colors corresponding to where it first appear. Three trees without frame are the ones with largest population fraction <0.5, indicating unreliable inference of tree structures (due to low mutation counts, sequence error or very high heterogeneity etc.). They are excluded from downstream analysis.

Table S1. Extra somatic mutations in *MET* found among 111 additional pRCC cases and rs11672213 genotype and cancer-specific survival (CSS) of all 277 patients and 96 type 2 patients.

Table S2. Molecular summary (non-coding region mutations, mutation fraction in DHS regions etc.) of 32 WGS patients

Table S3. Structural variants found by DELLY using WGS data

Table S4. APOBEC mutation signatures and pattern enrichment analysis using WXS data