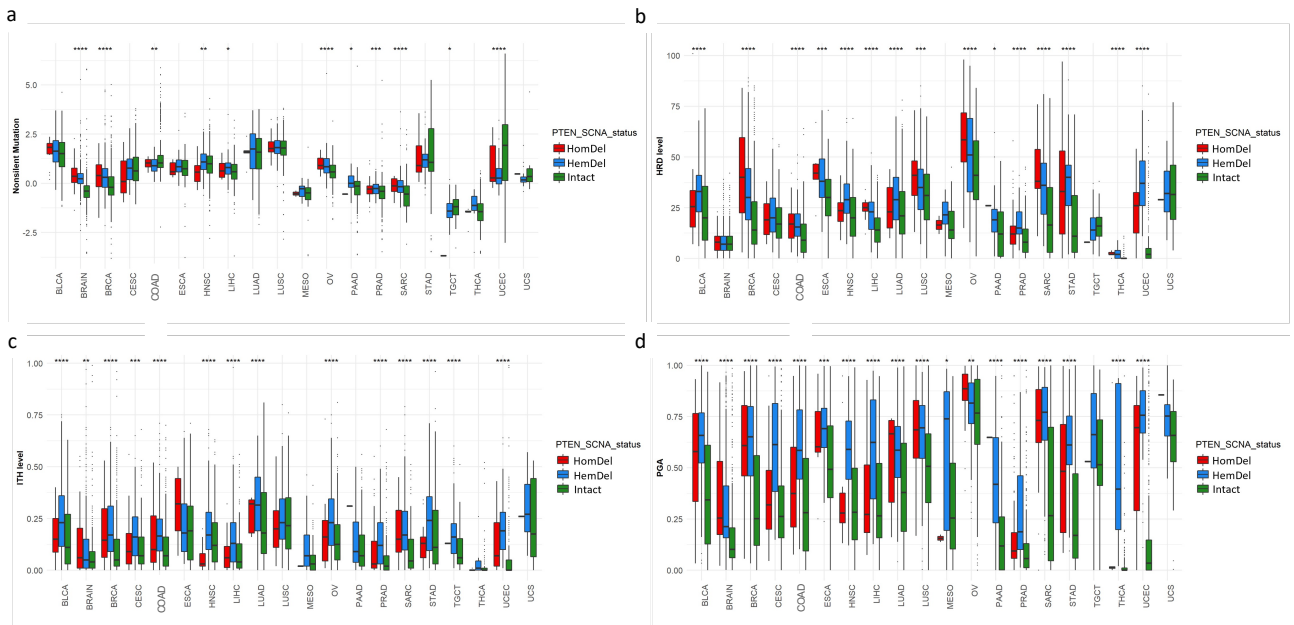
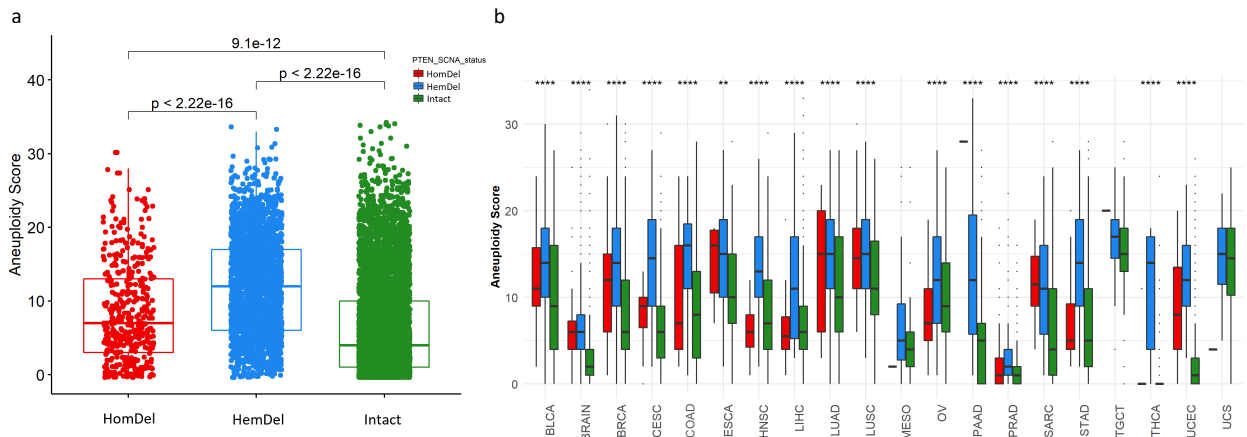


Supplementary Figure 2



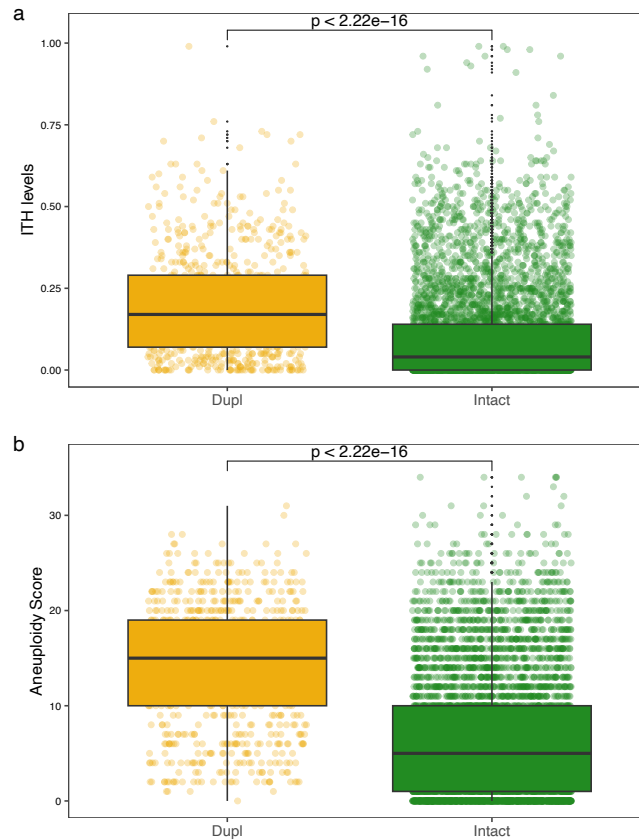
Supplementary Figure 2. *PTEN* deletions are associated with genomic alterations in each tumor type. **(a)** Nonsilent mutations. **(b)** Intratumor heterogeneity. **(c)** Homologous repair defects. **(d)** Percent genome altered. Plotted using *ggplot2* (<https://ggplot2.tidyverse.org/>).

Supplementary Figure 3



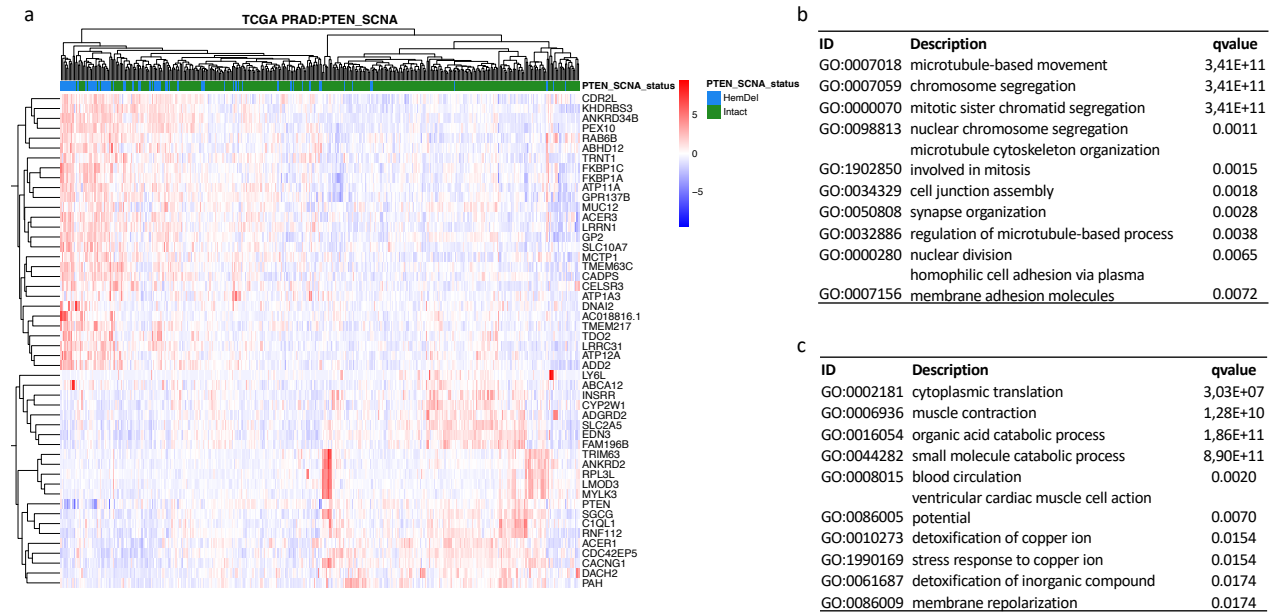
Supplementary Figure 3. Association between aneuploidy levels and *PTEN* inactivation status. **(a)** *PTEN* inactivation is significantly associated with increased levels of aneuploidy. **(b)** Aneuploidy score stratified by tumor type. Prostate and brain tumors showed the lowest levels of aneuploidy across tumor types. Aneuploidy levels were determined based on the length of copy number alterations and normalized by tumor type. The scores range from 0, which indicates low levels of chromosome aberrations (copy number gains and losses). On the other hand, high levels of aneuploidy indicate that the genome of these tumors is highly altered, with larger chromosome gains and losses occurring. Plotted using *ggplot2* (<https://ggplot2.tidyverse.org/>).

Supplementary Figure 4



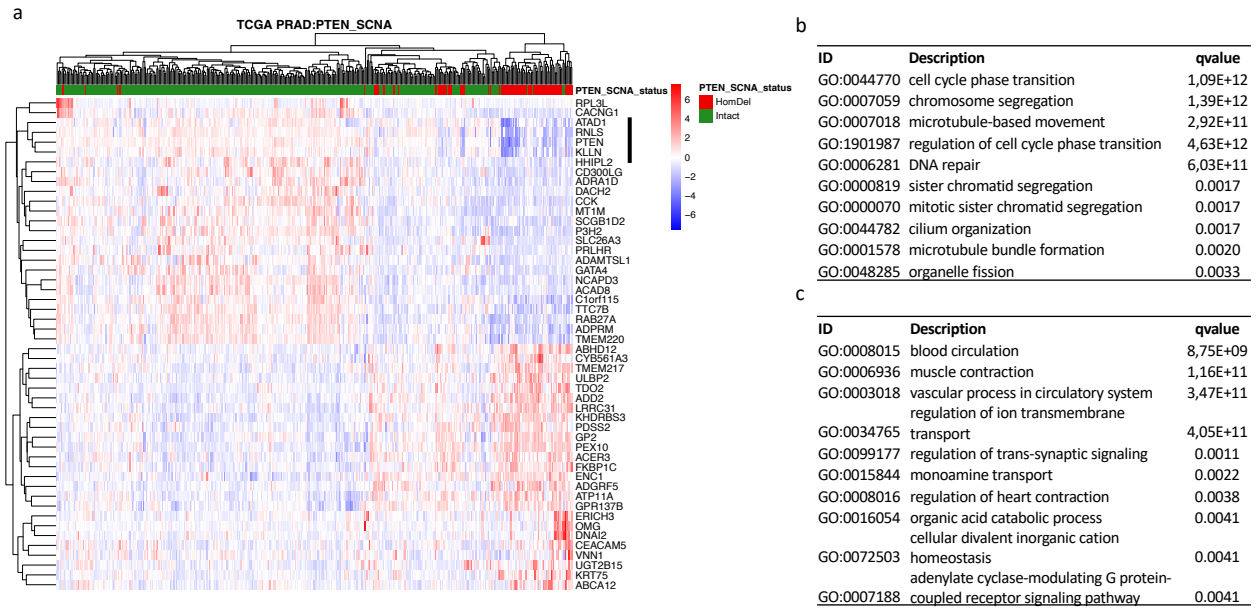
Supplementary Figure 4. *PTEN* duplication is associated with genomic alterations. **(a)** *PTEN* Duplication is associated with elevated levels of Intratumor heterogeneity and **(b)** Aneuploidy score. Aneuploidy levels were determined based on the length of copy number alterations and normalized by tumor type. The scores range from 0, which indicates low levels of chromosome aberrations (copy number gains and losses). On the other hand, high levels of aneuploidy indicate that the genome of these tumors is highly altered, with larger chromosome gains and losses occurring. Plotted using *ggplot2* (<https://ggplot2.tidyverse.org/>).

Supplementary Figure 5



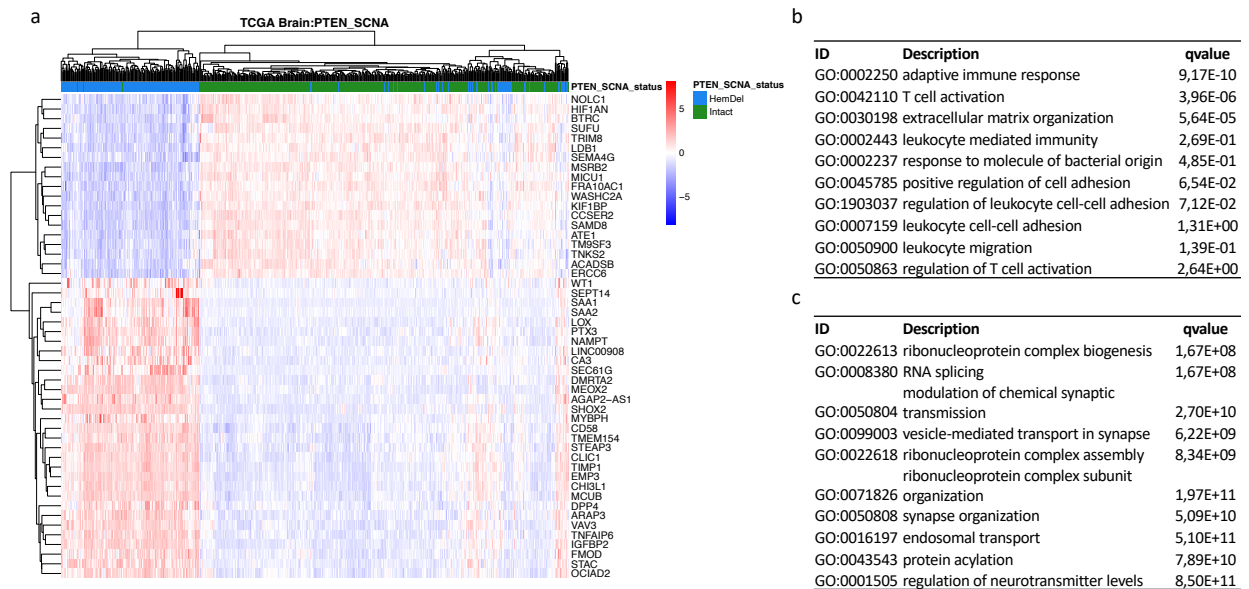
Supplementary Figure 5. *PTEN* HemDel PRAD showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). **(b)** Enriched GO (BP) pathways of the upregulated genes. **(c)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 6



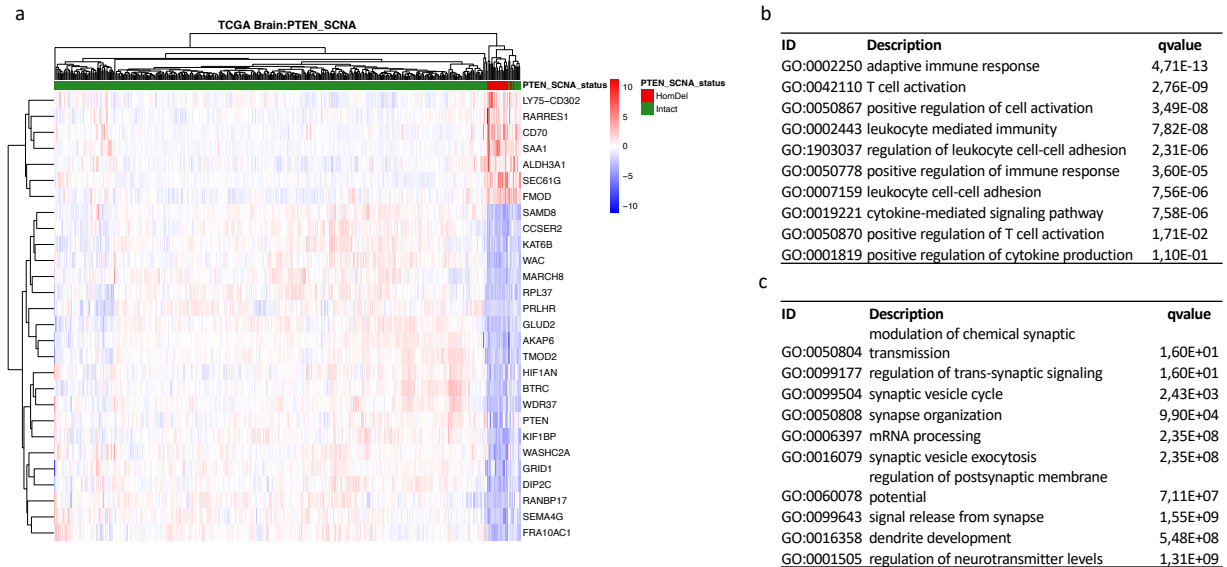
Supplementary Figure 6. *PTEN* HomDel PRAD showed distinct transcriptome activity. **a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log₂Fold change >0.58). **b)** Enriched GO (BP) pathways of the upregulated genes. **c)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Vertical bar indicates the closely linked passenger genes (*ATAD1*, *RNL5* and *KLLN*) that are concurrently down-regulated when *PTEN* is lost by a large deletion of chromosome 10. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 7



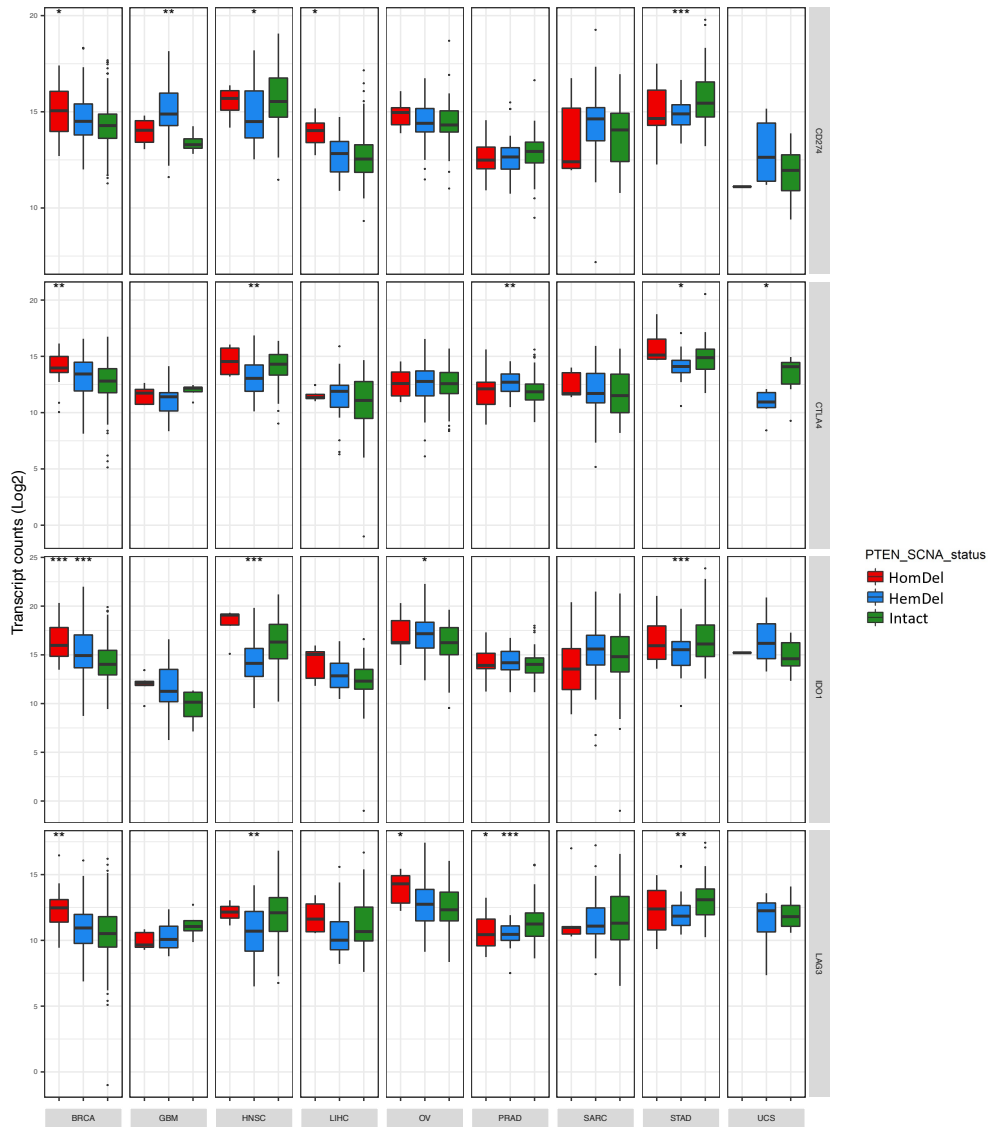
Supplementary Figure 7. *PTEN* HemDel Brain (GBM + LGG) showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). **(b)** Enriched GO (BP) pathways of the upregulated genes. **(c)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 8



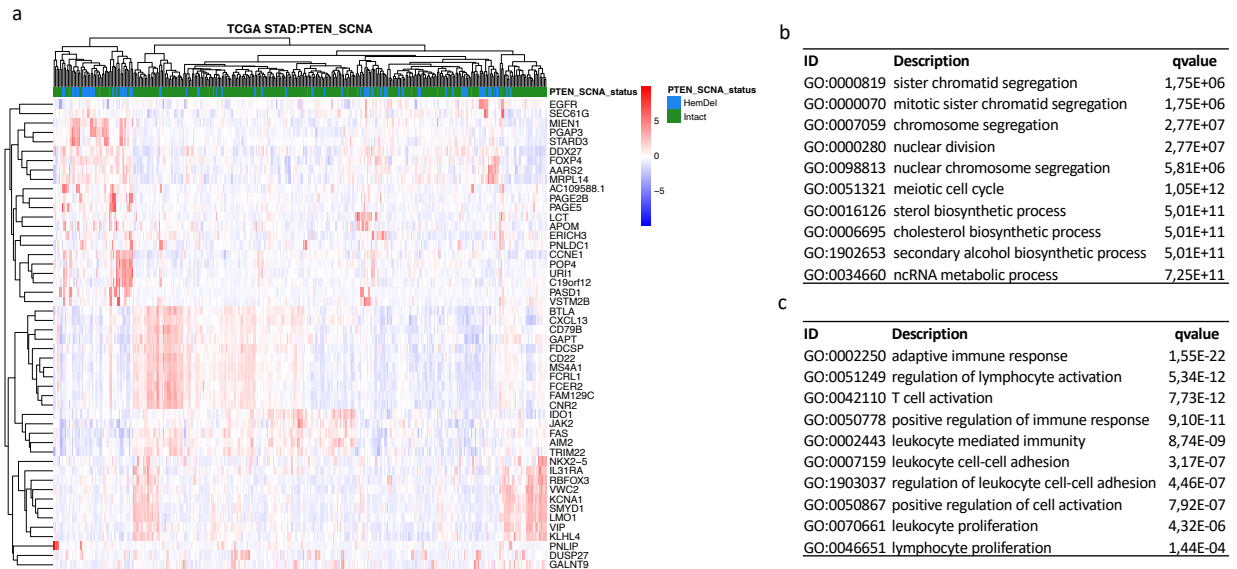
Supplementary Figure 8. *PTEN* HomDel Brain (GBM + LGG) showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). Of the 4106 overexpressed genes in the HomDel tumors 66.7% were also overexpressed in the 3562 HemDel tumors. Similarly, of the 7332 underexpressed genes in the HomDel tumors 59.9% were also underexpressed in the 10902 underexpressed genes in the HemDel tumors **(b)** Enriched GO (BP) pathways of the upregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 9



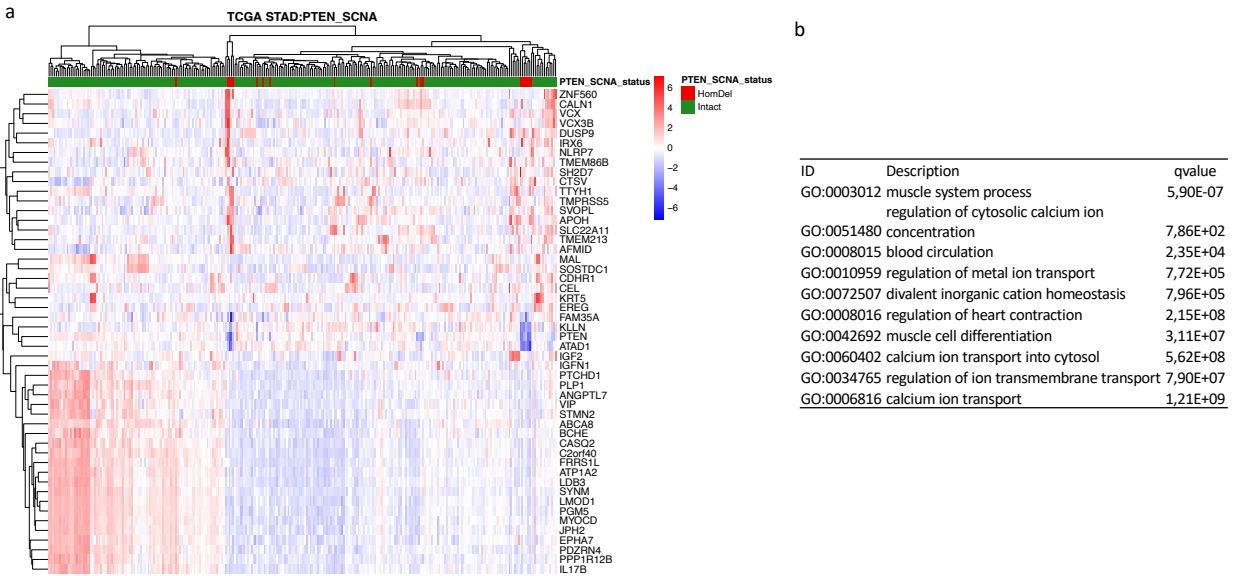
Supplementary Figure 9. The RNA-sequencing expression level of immunomodulatory genes *CD274* (*PD-L1*), *CTLA4*, *IDO1*, and *LAG3* in BRCA, GBM, HNSC, LIHC, OV, PRAD, SARC, STAD, and UCS. *: p -value < 0.05; **: p -value < 0.01, by Mann-Whitney test. *CD274* (*PD-L1*), Programmed Cell Death 1 Ligand 1; *CTLA4*, Cytotoxic T-Lymphocyte Associated Protein 4; *IDO1*, Indoleamine 2,3-Dioxygenase 1; *LAG3*, Lymphocyte Activating 3. Plotted using *ggplot2* (<https://ggplot2.tidyverse.org/>).

Supplementary Figure 10



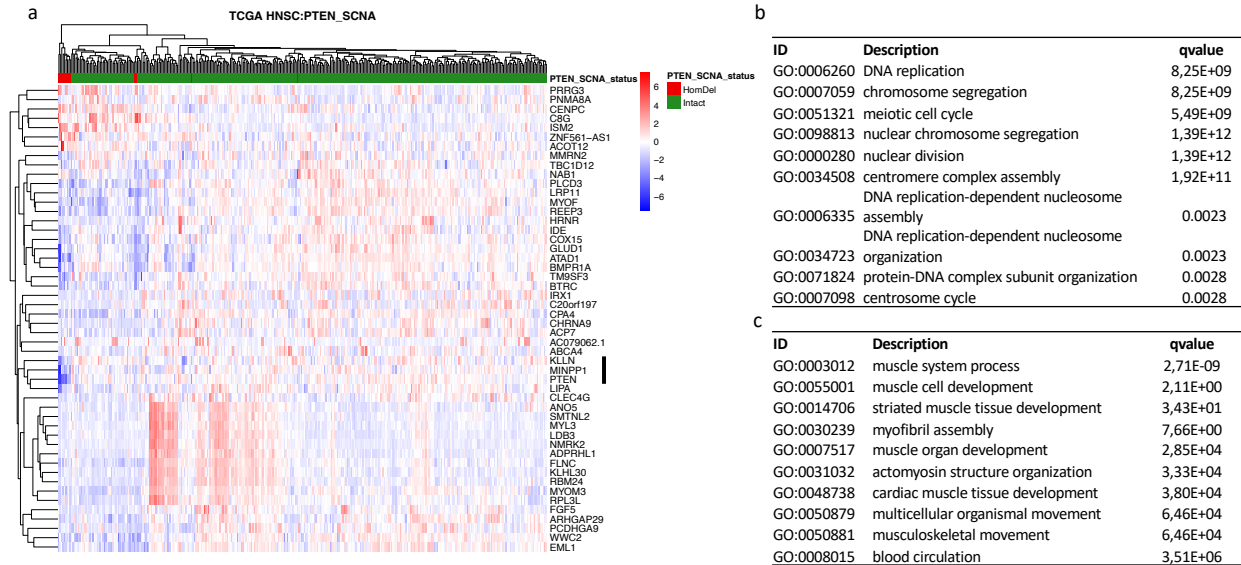
Supplementary Figure 10. *PTEN* HemDel STAD showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log₂Fold change >0.58). **(b)** Enriched GO (BP) pathways of the upregulated genes. **(c)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 11



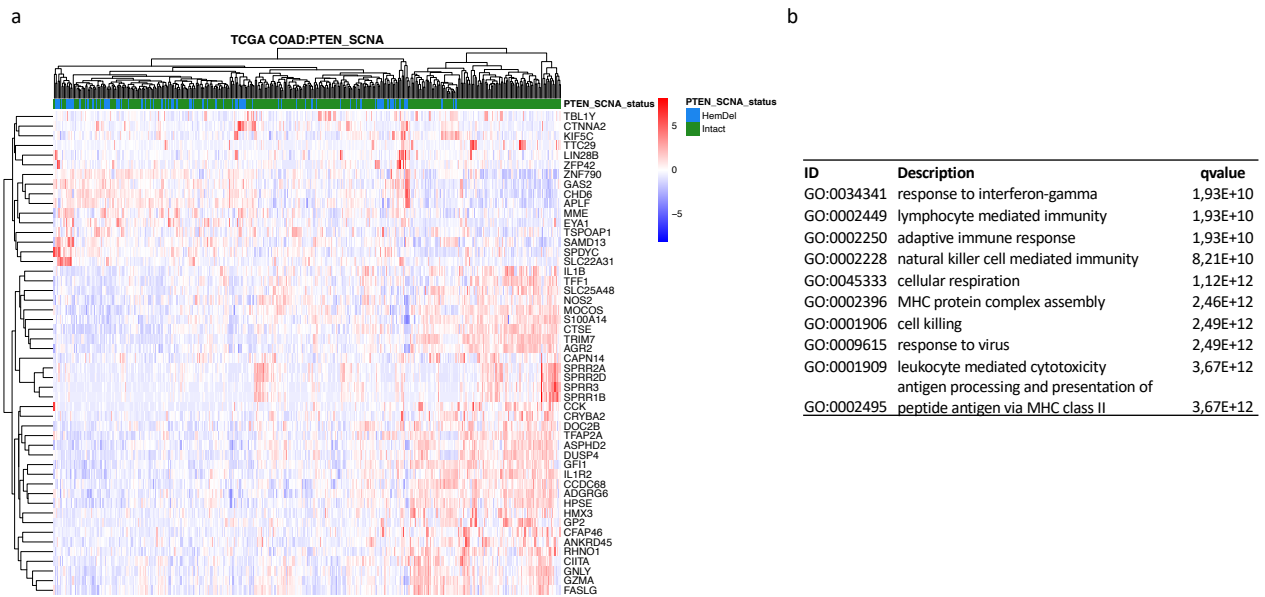
Supplementary Figure 11. *PTEN* HomDel STAD showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). **(b)** Enriched GO (BP) pathways of the upregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 12



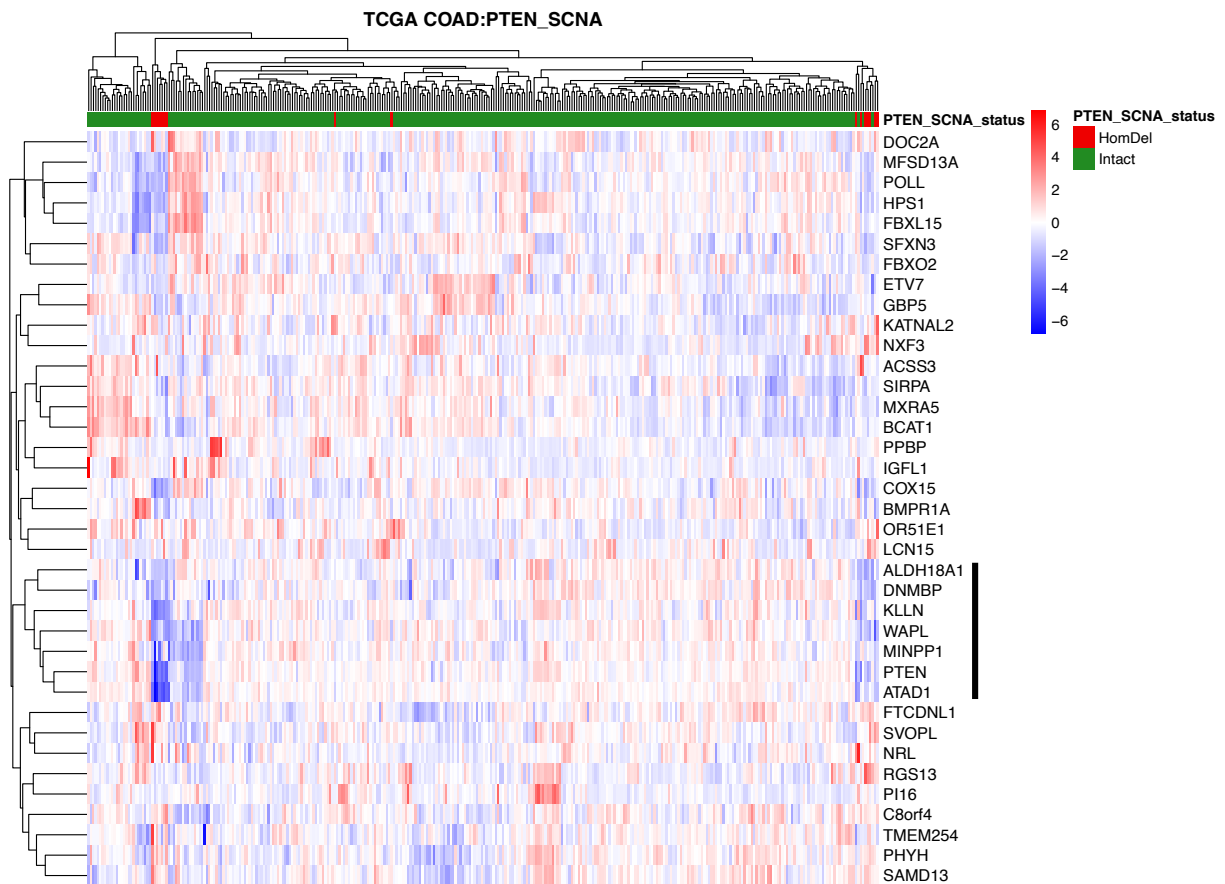
Supplementary Figure 12. *PTEN* HomDel HNSC showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). **(b)** Enriched GO (BP) pathways of the upregulated genes. **(c)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the *Z*-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Vertical bar indicates the two closely linked passenger genes (*MINPP1* and *KLLN*) that are concurrently down-regulated when *PTEN* is lost by a large deletion of chromosome 10. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 13



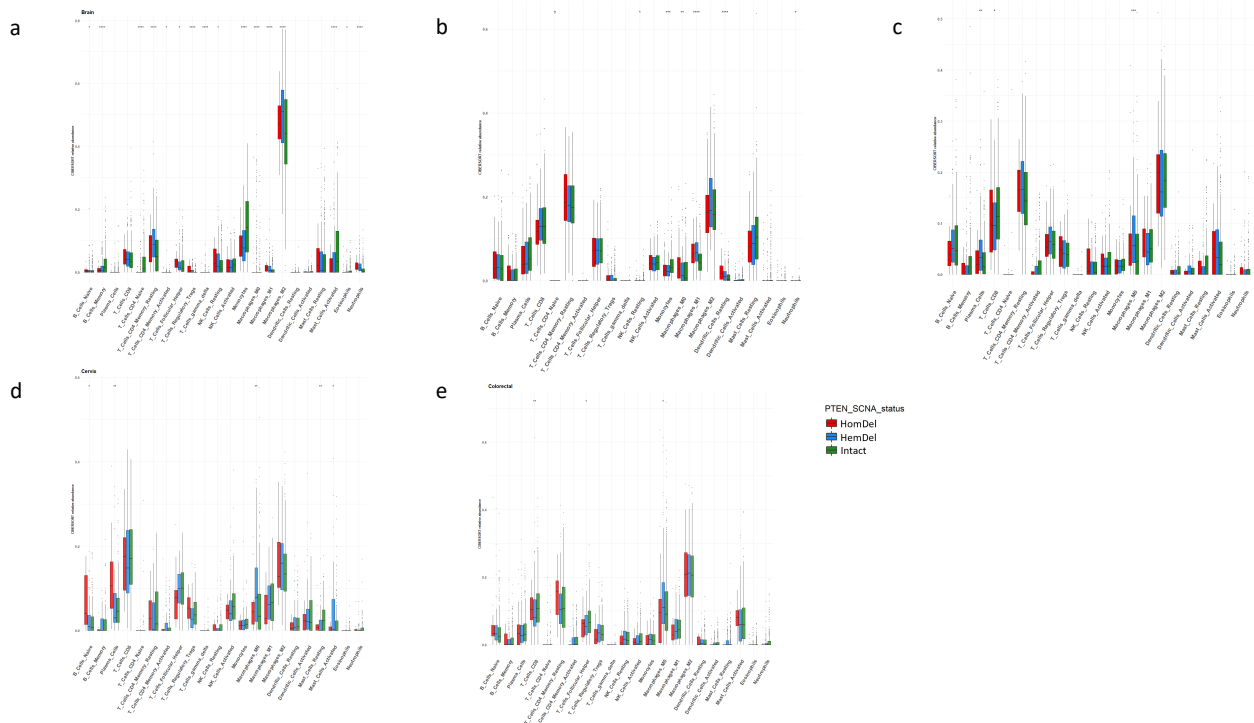
Supplementary Figure 13. *PTEN* HemDel COAD showed distinct transcriptome activity. **(a)** Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). **(b)** Enriched GO (BP) pathways of the downregulated genes. The color scale in the heatmap represents the Z-score of the normalized read counts for each gene, where the red scale color indicates upregulated and blue low-expressed genes. Enrichment analyses were performed using *clusterProfiler* and *p*-adjusted value = 0.05 as the cutoff. Tables show the top 10 most significant Gene Ontology (BP) terms. Plotted using *pheatmap* (<https://rdocumentation.org/packages/pheatmap/versions/1.0.12>).

Supplementary Figure 14



Supplementary Figure 14. *PTEN* HomDel COAD showed distinct transcriptome activity. Transcriptome heatmap exhibiting clustering of top 50 DEGs (Log2Fold change >0.58). Vertical bar indicates the closely linked passenger genes (*ALDH18A1*, *DNMBP*, *KLLN*, *WAPL*, *MINPP1*, *ATAD1*) that are concurrently down-regulated when *PTEN* is lost by a large deletion of chromosome 10. Plotted using *pheatmap* ([https://rdocumentation.org/packages/pheatmap/versions/1.0.12](https://rddocumentation.org/packages/pheatmap/versions/1.0.12)).

Supplementary Figure 15



Supplementary Figure 15. CIBERSORT-derived immune-cell abundance of 22 distinct cell subsets based on *PTEN* status and tumor type. Y-axis shows CIBERSORT relative scores. **(a)** *PTEN* HemDel in brain tumors was linked to higher CD4 T memory cells and M2 macrophage abundance and lower M1 macrophages, monocytes, and CD8 T cells. **(b)** Prostate tumors with *PTEN* HemDel showed increased M1 macrophages and decreased M0 macrophages and monocytes. **(c)** Stomach tumors with *PTEN* HemDel showed increased plasma and M0 macrophages and decreased in CD8 T cells. **(d)** Cervical tumors with *PTEN* HemDel were linked to higher M0 macrophages and mast cells activated. **(e)** Colorectal tumors with *PTEN* HemDel were linked to higher M0 macrophages and lower CD8 T cells. *: p -value < 0.05; **: p -value < 0.01, by Mann-Whitney test. DC, dendritic cell; NK, natural-killer cell; PCa, prostate cancer; Treg, regulatory T cell; M0, M0 macrophage; M1, M1 macrophage; M2, M2 macrophage. Plotted using *ggplot2* (<https://ggplot2.tidyverse.org/>).