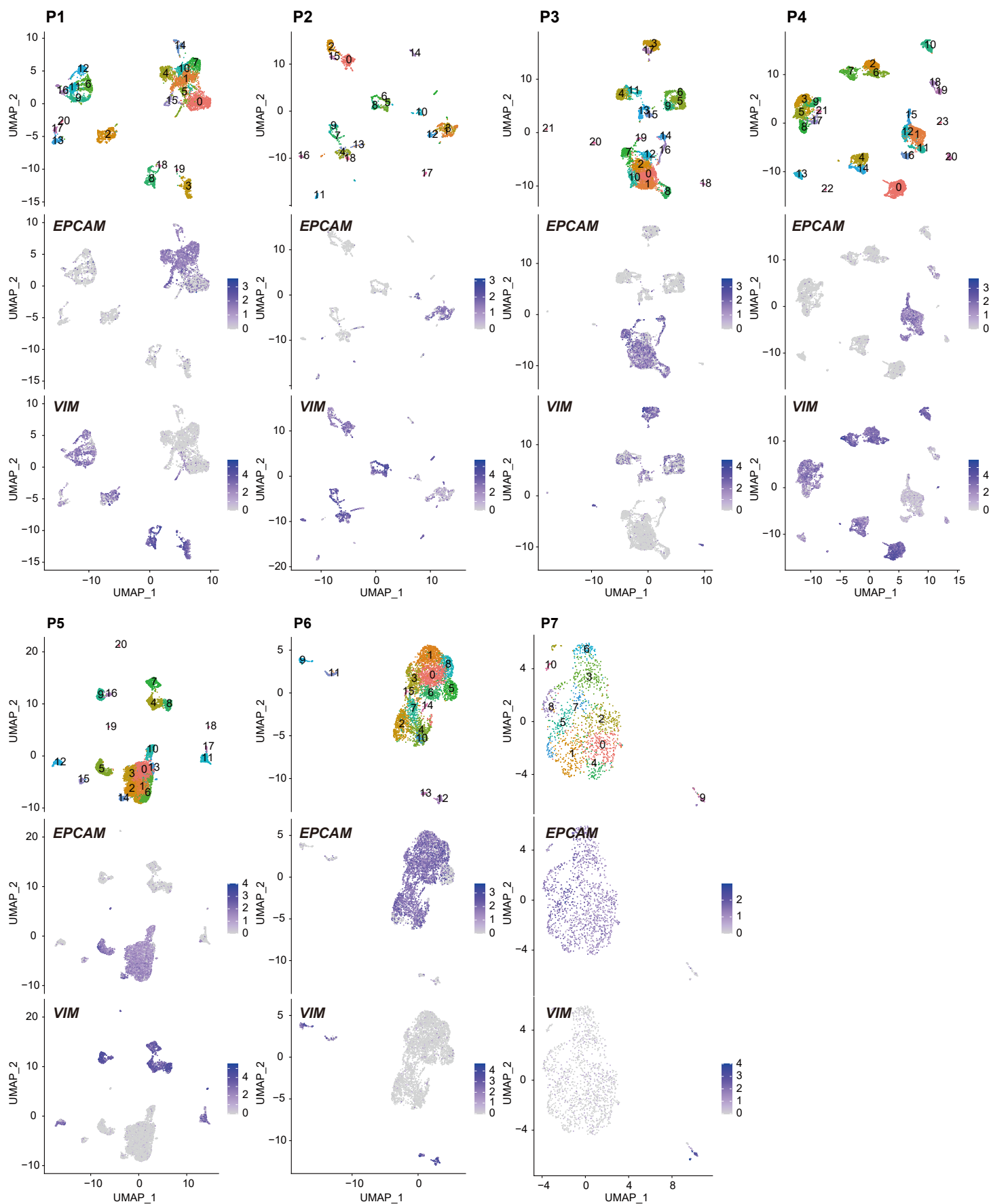


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## **Supplemental information**

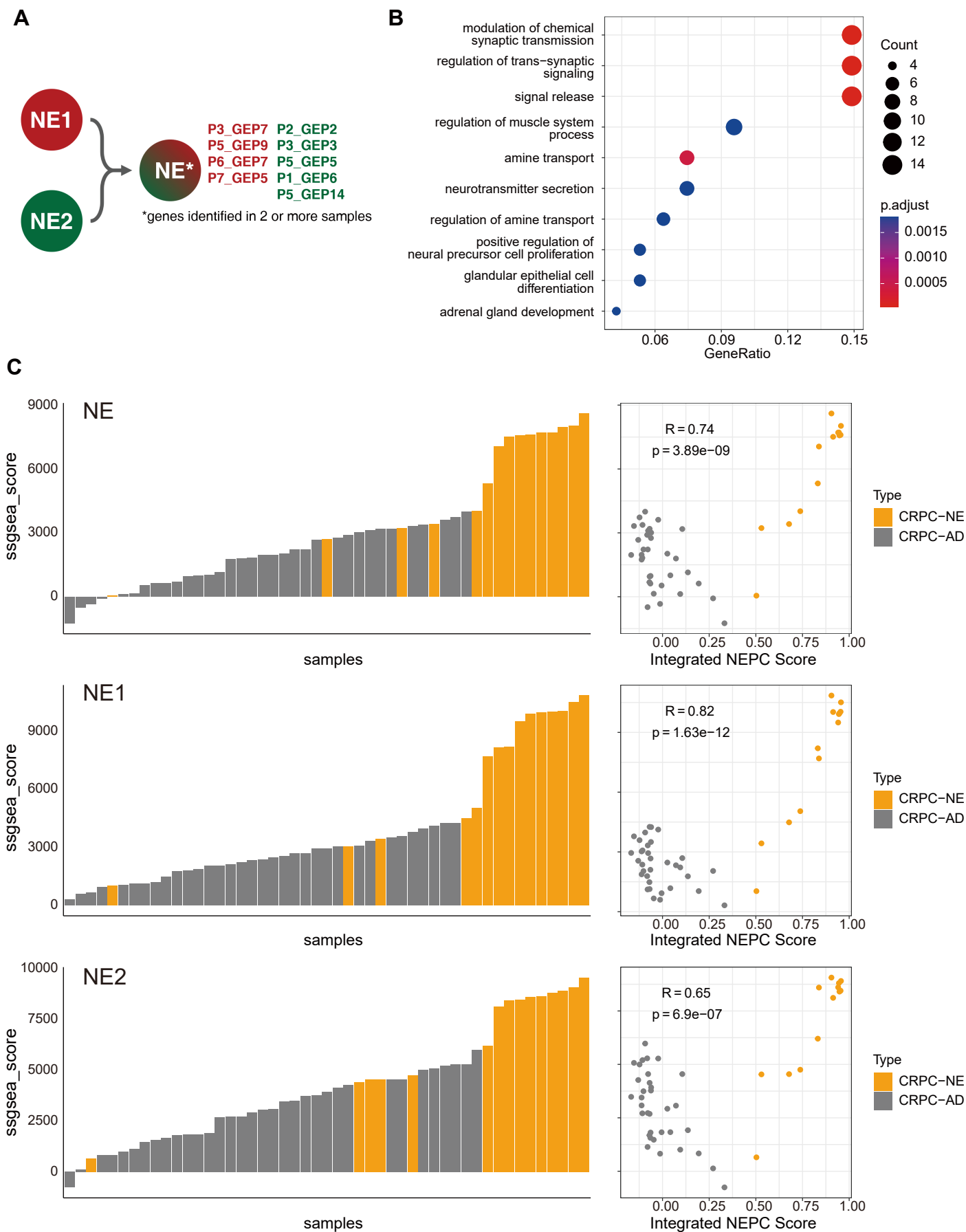
### **Single-cell transcriptional regulation and genetic evolution of neuroendocrine prostate cancer**

**Ziwei Wang, Tao Wang, Danni Hong, Baijun Dong, Yan Wang, Huaqiang Huang, Wenhui Zhang, Bijun Lian, Boyao Ji, Haoqing Shi, Min Qu, Xu Gao, Daofeng Li, Colin Collins, Gonghong Wei, Chuanliang Xu, Hyung Joo Lee, Jialiang Huang, and Jing Li**

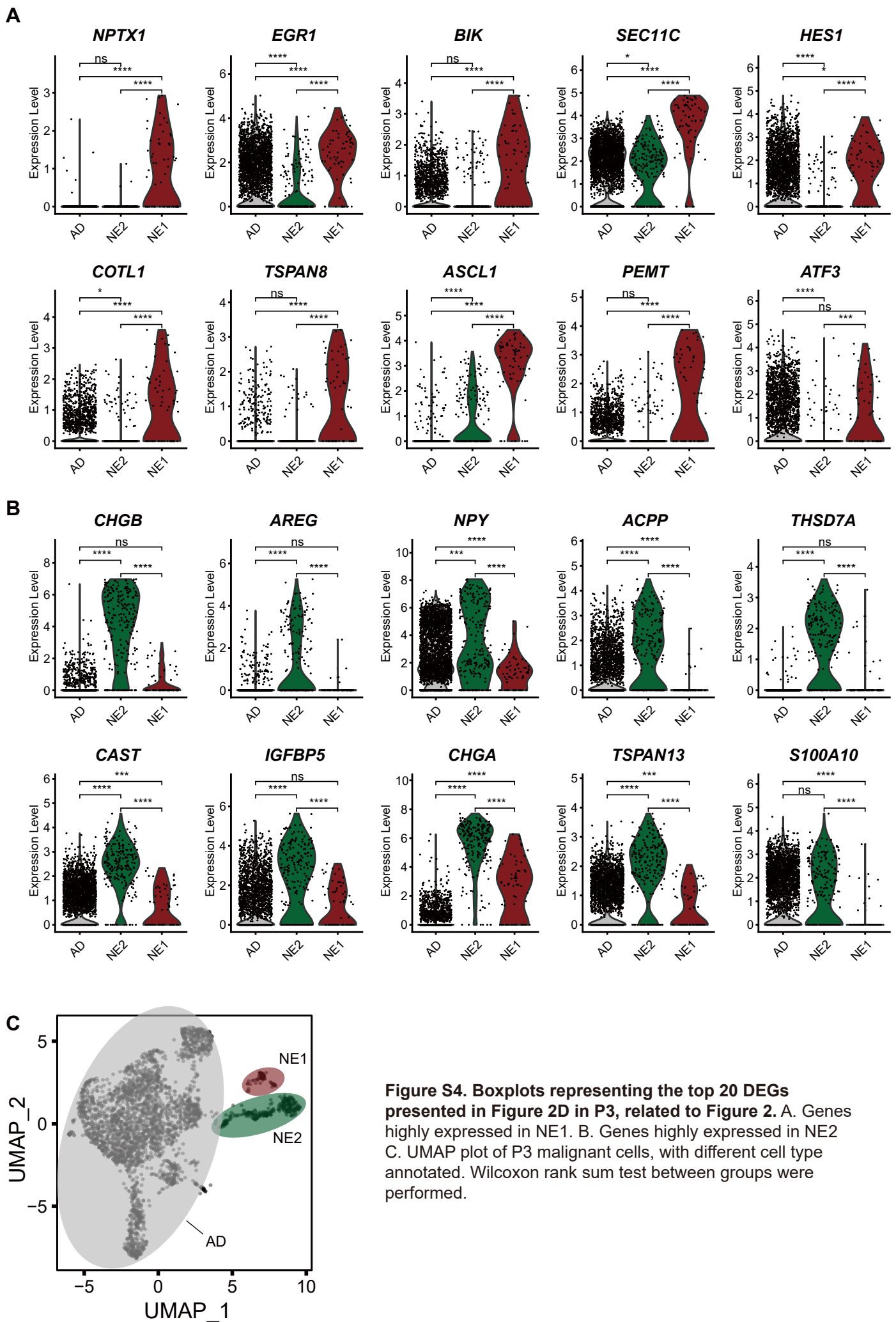


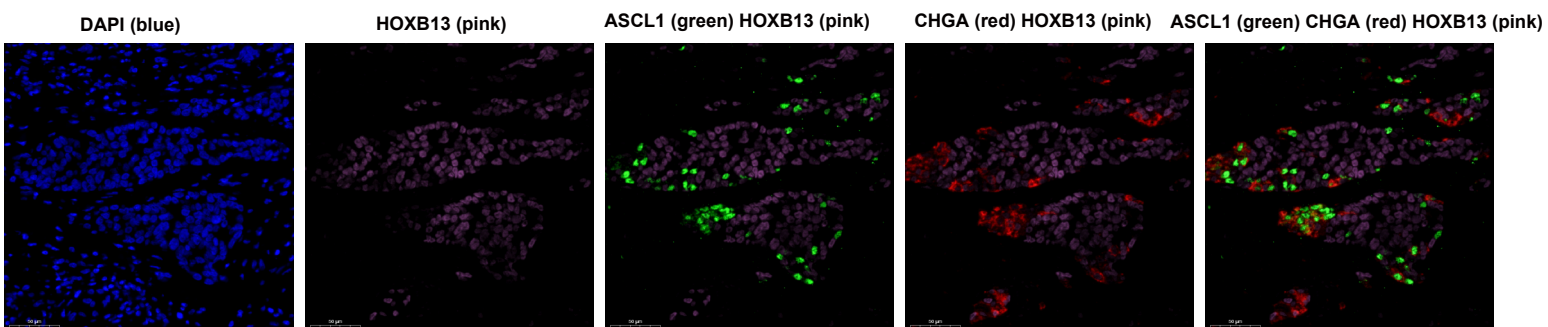
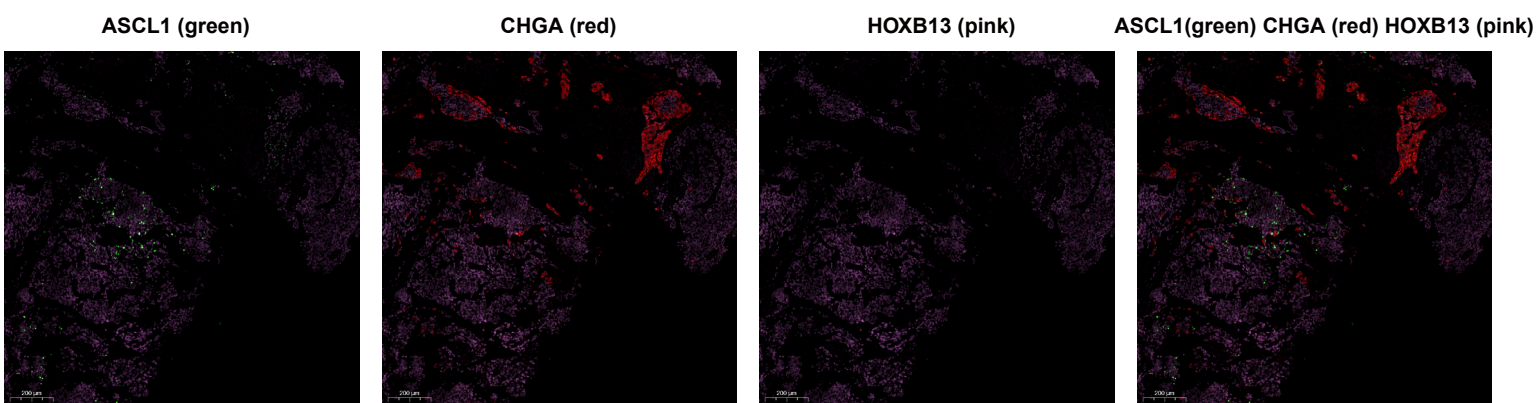
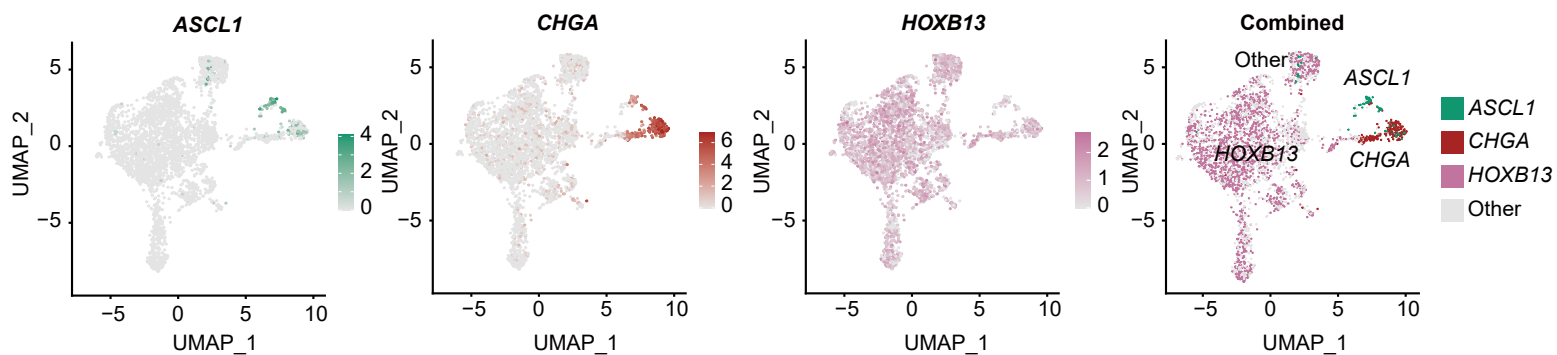
**Figure S1. Discerning being epithelial- or mesenchymal-like, related to Figure 1.** For each patient, non-supervised clustering, expression levels of EPCAM and VIM were displayed from top to bottom.



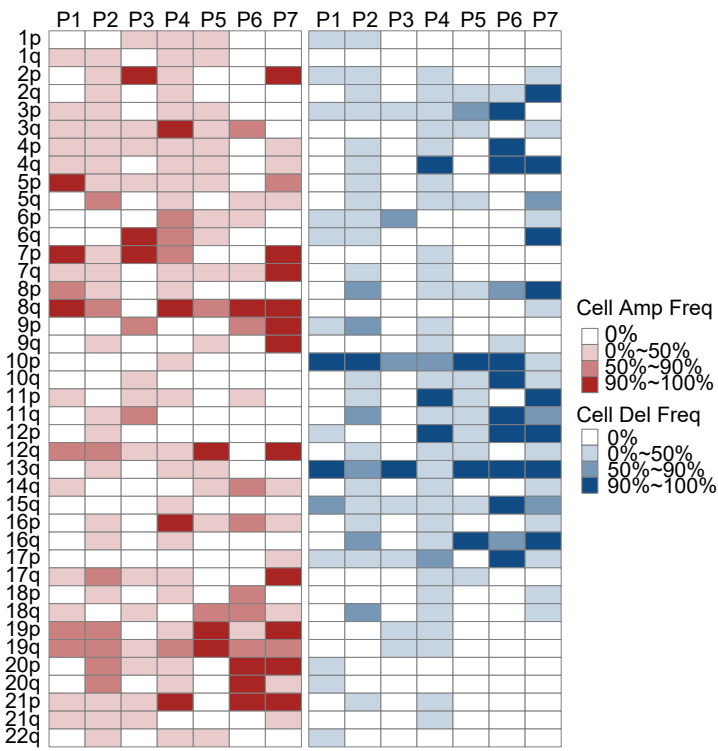
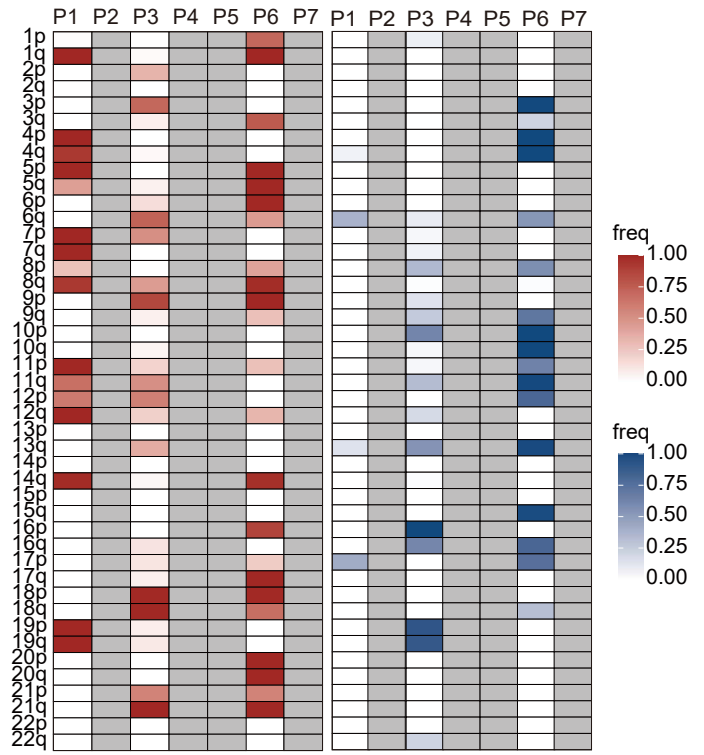
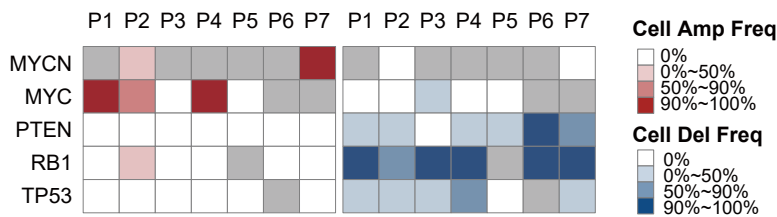
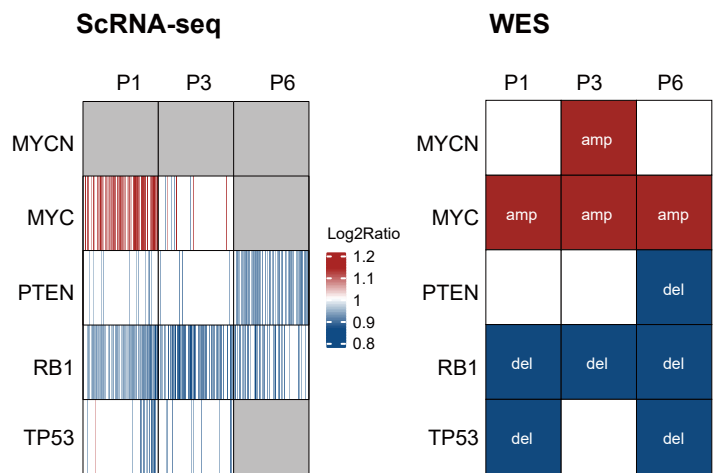


**Figure S3. External validation of the NE module genes, related to Figure 2.** A. We applied the same approach and defined a combined NE-module. The corresponding module genes were summarized in Supplementary Table S7. B. GO enrichment analysis of the combine NE module. C. (Left column) The ssGSEA scoring using NE, NE1, and NE2 module genes in the external bulk RNAseq dataset ( $n = 49$ ). (Right column) The scatterplot showing the relationship between the ssGSEA score and the 'integrated NEPC score' in the original research.

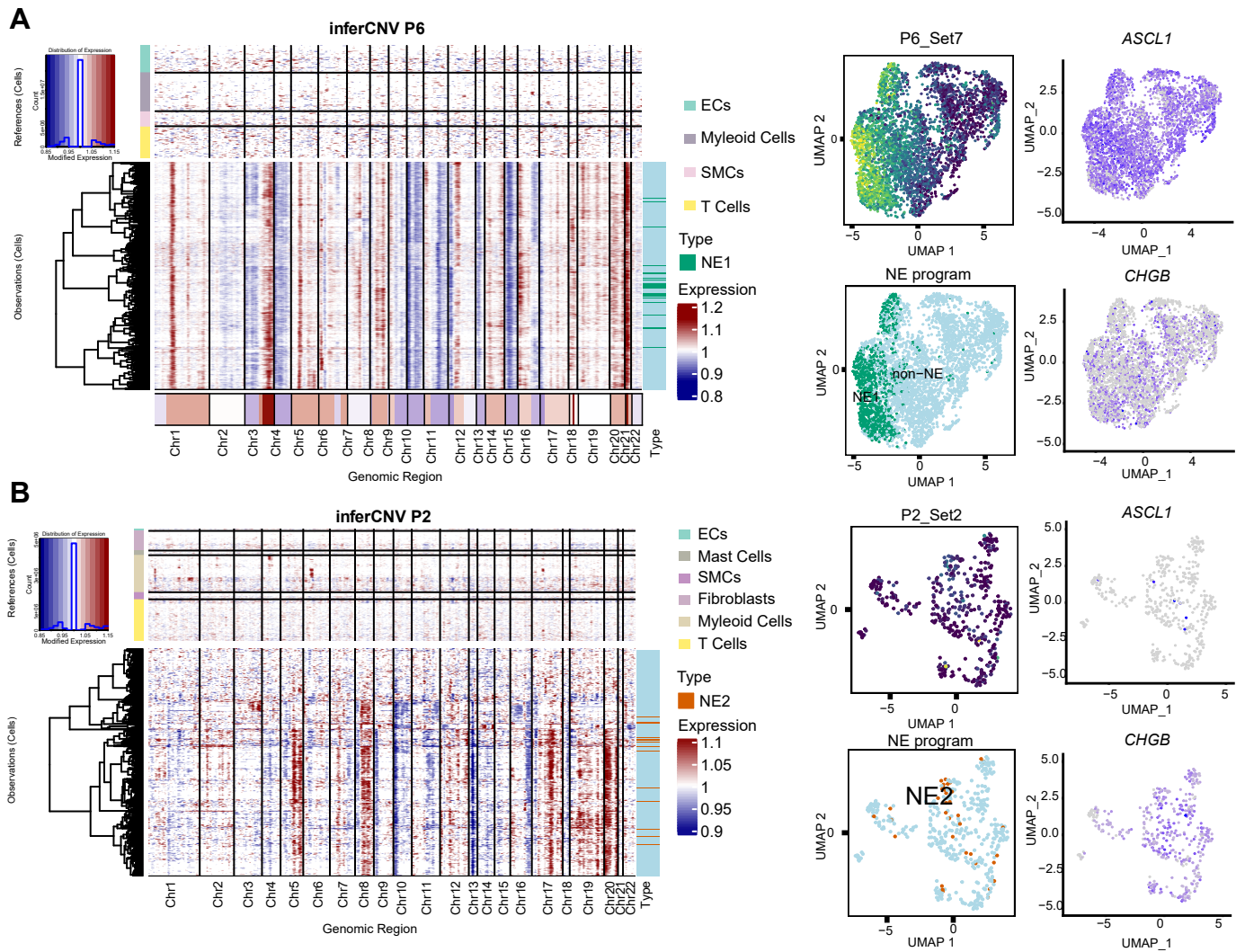




**Figure S5. Immunofluorescence co-staining validation of cluster-specific genes, related to Figure 4.** Immunofluorescence of ASCL1, CHGA, and HOXB13 in P3 sample slices (bottom) and corresponding gene level at UMAP embedding.

**A****ScRNA-seq****B****WES****C****D**

**Figure S6. Parallel bulk WES validation, related to Figure 4 and 5.** (A) CNV alteration frequency of samples at chromosome arm level. For a single cell, arms with >40% of genes gained or lost were considered having CNV. (B) CNA alteration of P1, P3, and P6 inferred from parallel bulk WES. (C) CNV alteration of NEPC-related genes inferred from scRNA-seq. (D) CNV alteration of NEPC-related validated by bulk WES.



**Figure S7. inferCNV analysis and NE programs visualization for P6 (A) and P2 (B), related to Figure 3-5. WES validation for P6 was also available (A).**