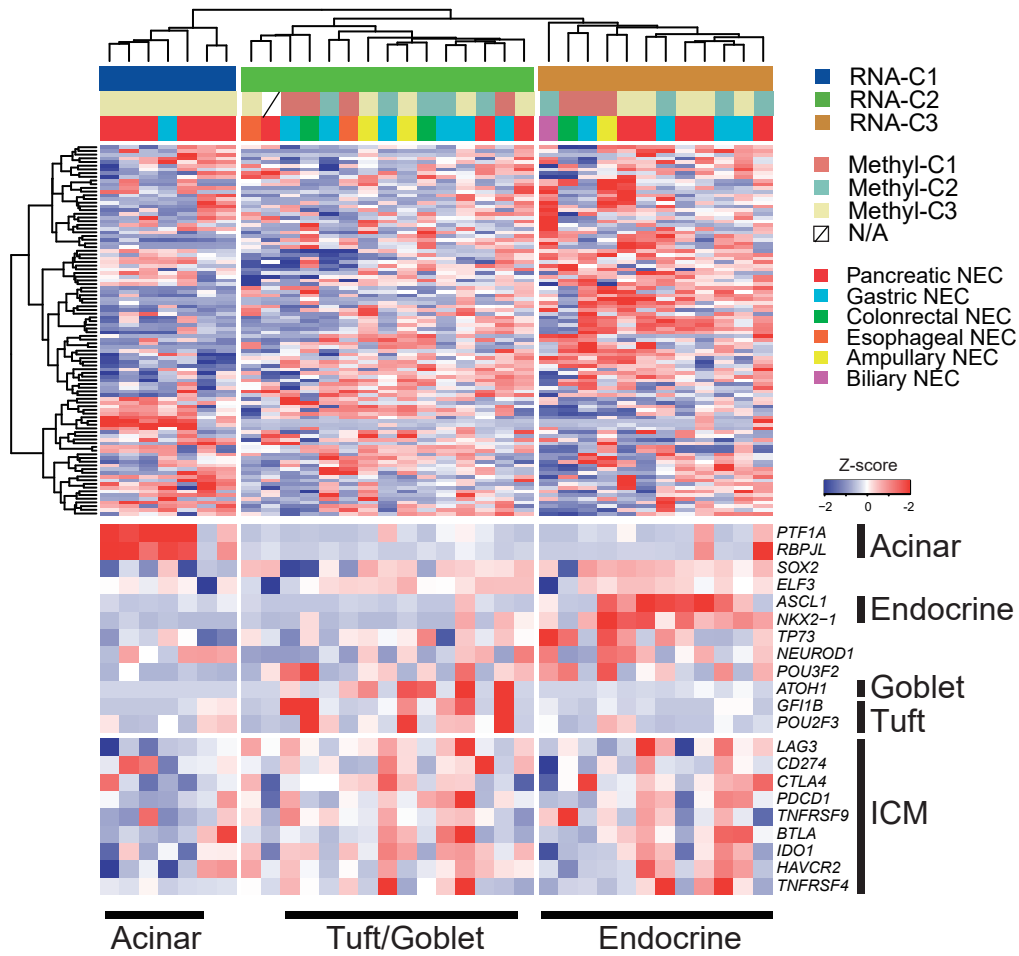
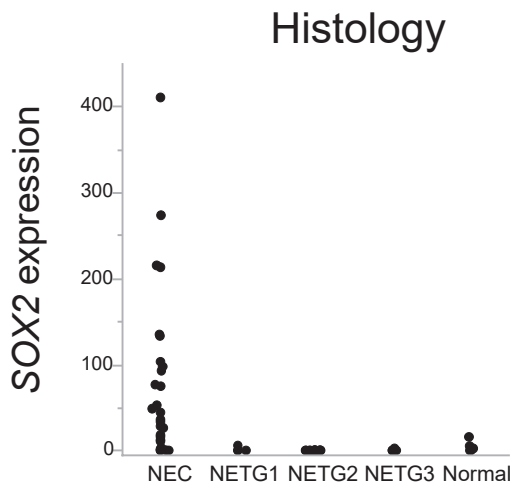


Supplementary Figure S8. Transcriptome profile of GIS-NECs.

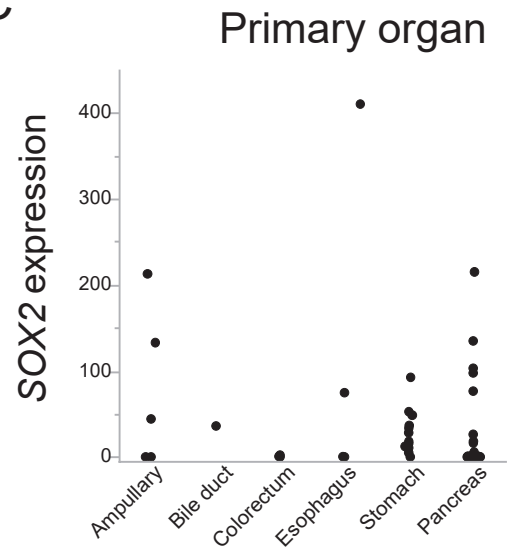
A



B



C



A, Unsupervised clustering with 120 high variant transcriptional factors, resulting in three clusters. The clusters (Methyl-C1, Methyl-C2, and Methyl-C3) based on DNA methylation analysis and the primary organ are indicated at the top. The RNA-C1 cluster, mostly consisting of Panc-NECs, included the cases with high expression of *PTF1A* and *RBPJL*, which are known as acinar differentiation markers (9). All cases in the RNA-C1 cluster belong to the Methyl-C3 group on DNA methylation analysis. The RNA-C2 cluster included cases with high expression of *ATOH1*, which is essential for secretory cell differentiation (Paneth, enteroendocrine, goblet) (10), and *POU2F3* and *GFI1B*, which are tuft cell markers (11). The RNA-C3 cluster showed high expression of *ASCL1*, *SOX2*, and *NKX2-1*, which are known SCLC-lineage markers. ICM, immune checkpoint molecule. **B**, Relationship between *SOX2* expression and histology (WHO classification 2019). A high level of *SOX2* gene expression was not observed in GIS-NETs. **C**, Relationship between *SOX2* gene expression and primary organ of GIS-NECs. Expression is increased across organs.