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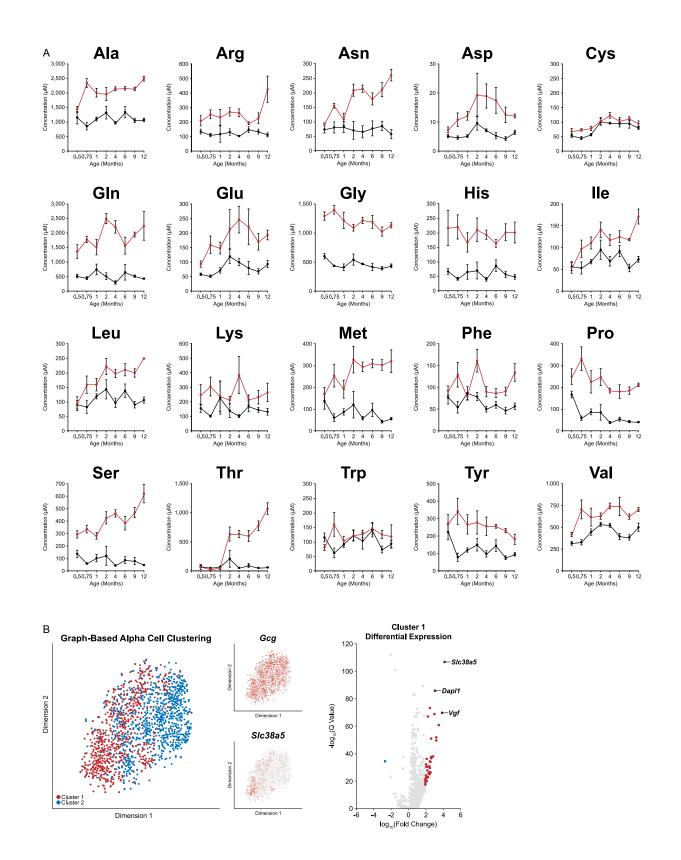
## **Supplemental Information**

## **Elevated Serum Amino Acids Induce a Subpopulation**

## of Alpha Cells to Initiate Pancreatic

## **Neuroendocrine Tumor Formation**

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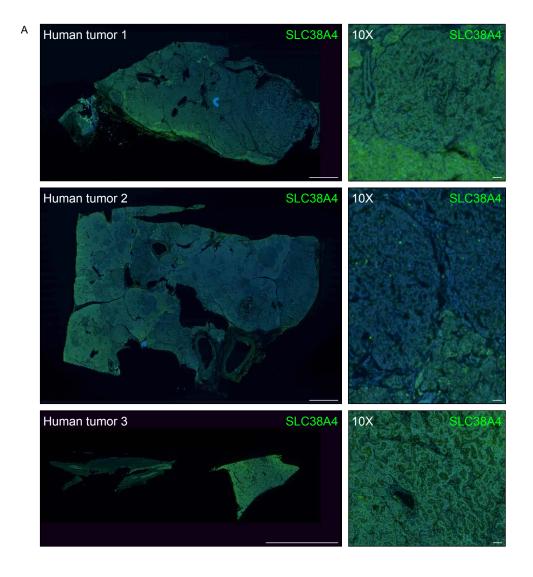


# Supplemental Figure 1. Individual plasma amino acid concentrations and graph-based clustering identifies alpha cell subpopulation in *Gcgr* knockout islets

#### Related to Figure 1.

(A) Time-course analysis of individual blood amino acid concentrations in heterozygous and homozygous *Gcgr* knockout mice. SLC38A5 is a neutral amino acid transporter that primarily transports Ala, Asn, Gln, Gly, His, and Ser.

(B) tSNE visualization of graph-based alpha cell clustering from *Gcgr* homozygous knockout mice with alpha cell-specific *Gcg* and *Slc38a5* expression plots. Differential expression analysis was performed using two groups identified from graph-based clustering and this highlights the multiple genes that contribute to each cluster.



### Supplemental Figure 2. SLC38A4 expression in human tumor tissues.

### Related to Figure 4.

(A) Human tumor tissues stained for SLC38A4 immunofluorescence exhibit minimal signal-to-noise by

whole slide scanning and confocal microscopy. Scale bar: 2.5 mm and 250  $\mu m$