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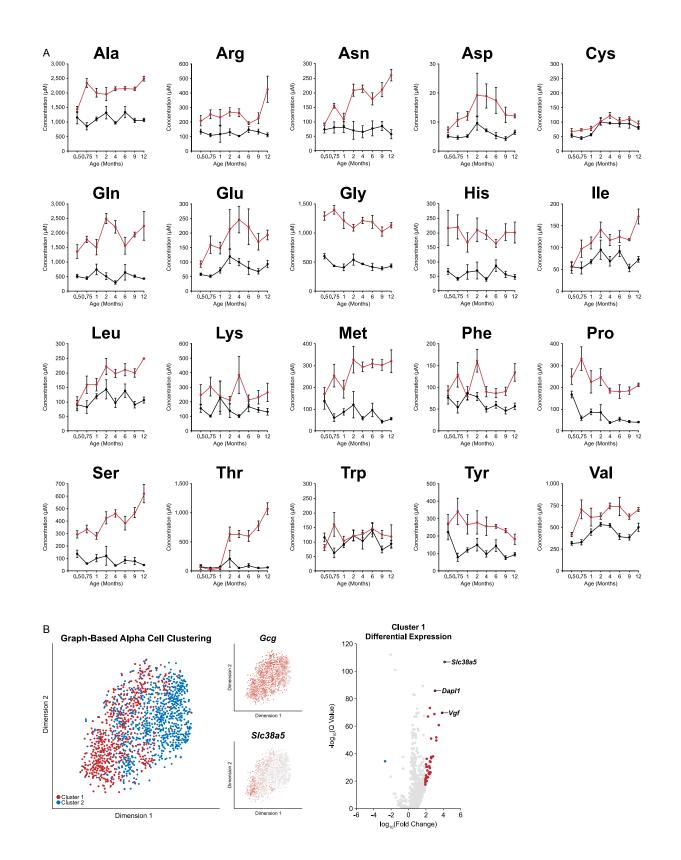
Supplemental Information

Elevated Serum Amino Acids Induce a Subpopulation

of Alpha Cells to Initiate Pancreatic

Neuroendocrine Tumor Formation

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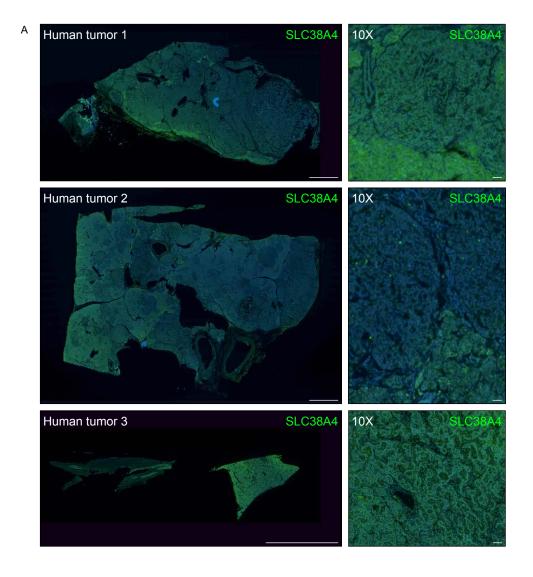


Supplemental Figure 1. Individual plasma amino acid concentrations and graph-based clustering identifies alpha cell subpopulation in *Gcgr* knockout islets

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 μm