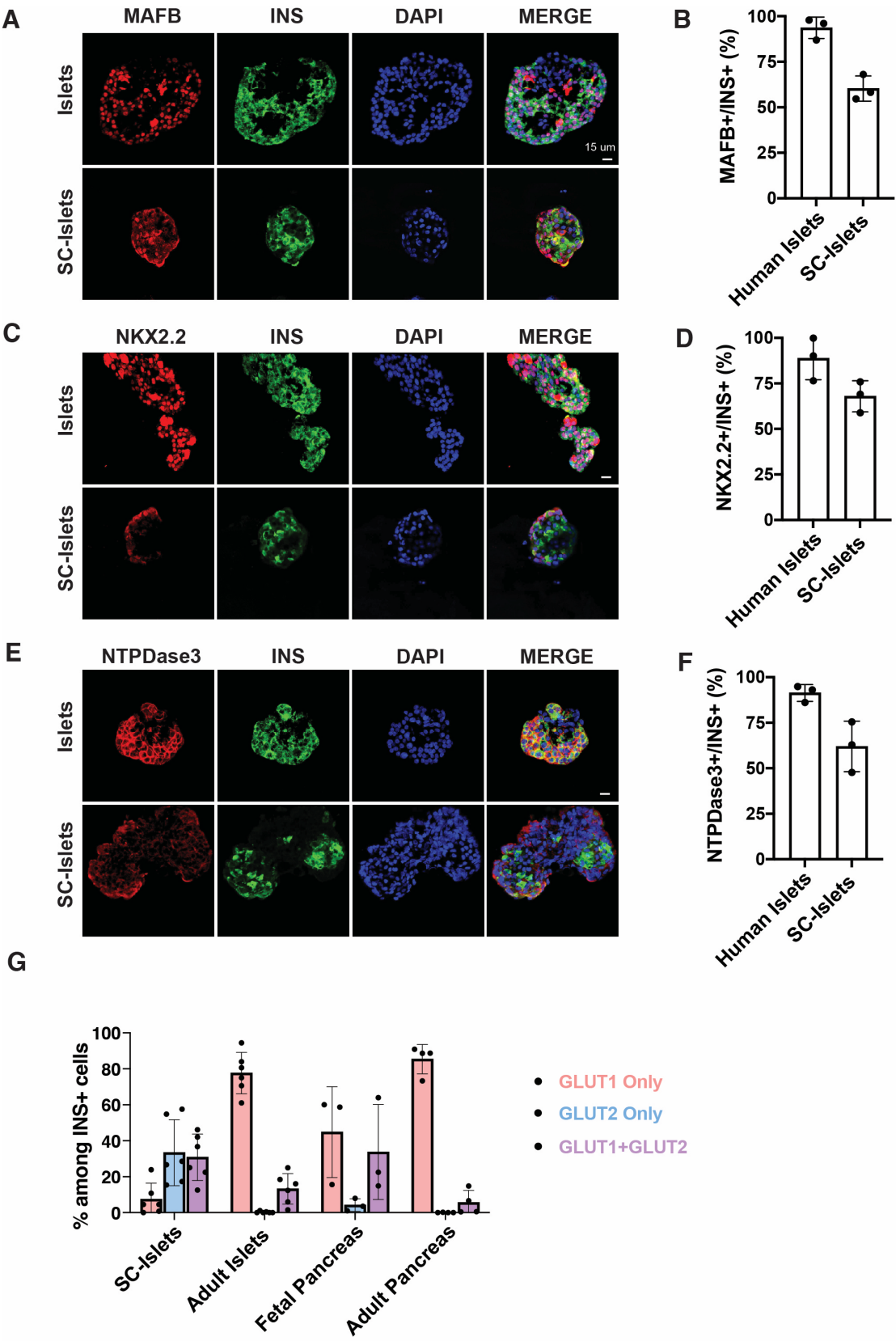
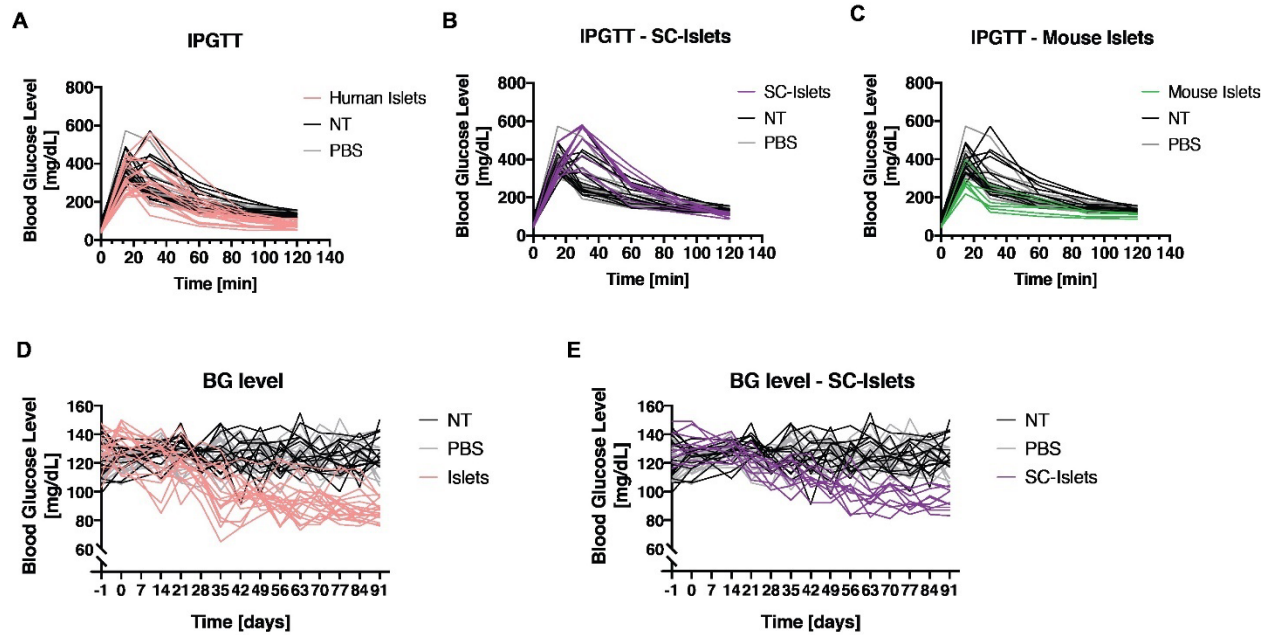


Supplemental figure 1.



Supplemental Figure 1. β cell maturation markers. Representative image of MAFA (A) NKX2.2 (C) and NTPDase3 (E) expression in human islets and SC-islets. Quantification of MAFA (B) NKX2.2 (D) and NTPDase3 (F) positive population within INS⁺ cell population. Human islets and SC-islets data was quantified based on images taken from n=3 sperate human islet donors and n=3 SC-islets differentiations. Scale bar is 15 μ m. Data are mean \pm SD. (G) GLUT1 and GLUT2 expression distribution in INS⁺ cells of SC-islets differentiations (n=6), human adult islet donor (n=6), fetal pancreas donors (n=3) and adult pancreas donors (n=4). Data are mean \pm SD. This data is represented in Figure 1C,D,F,G.

Supplemental figure 2.



Supplemental Figure 2. BG levels of human islets and SC-islet transplanted mice. (A)

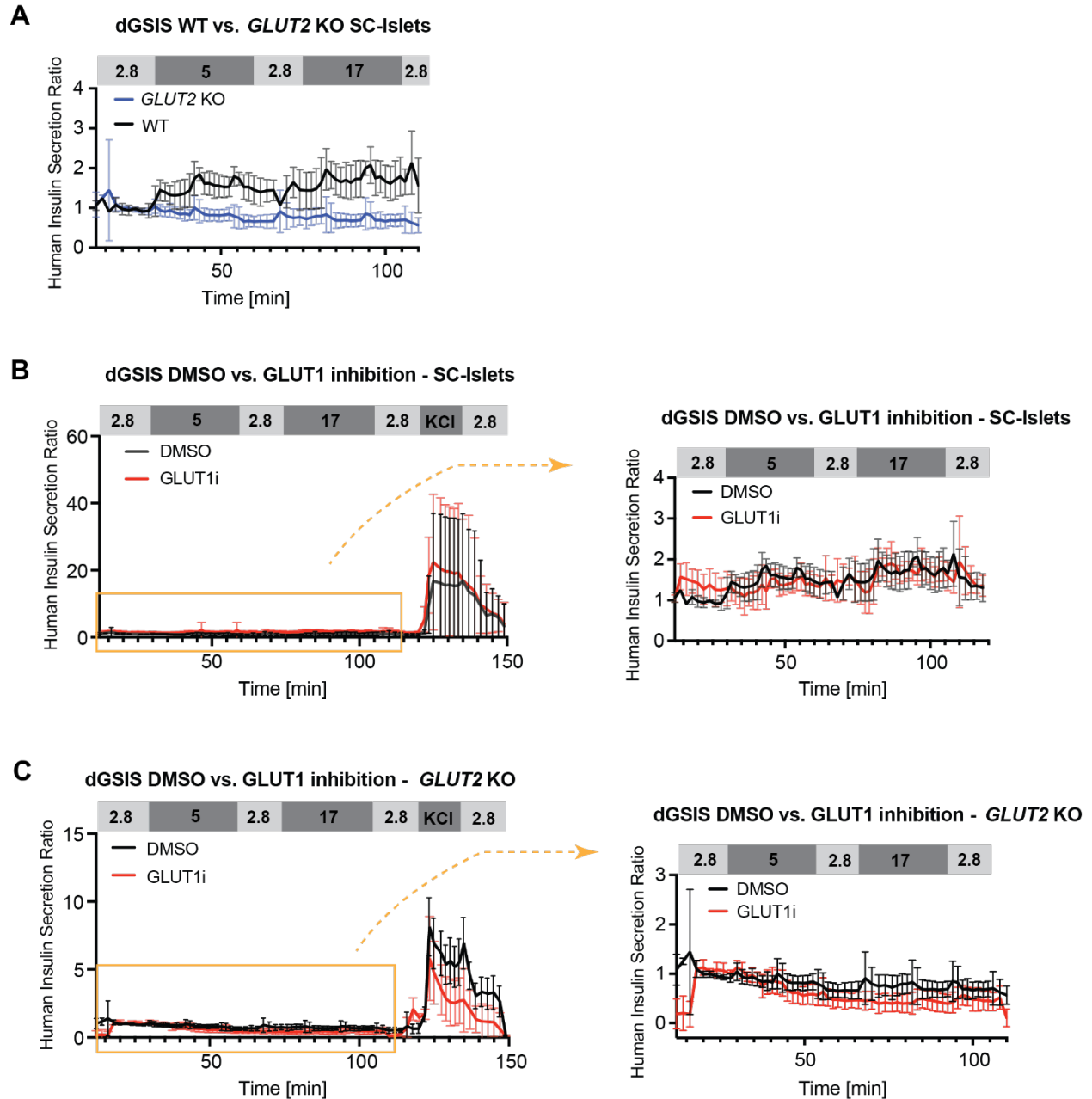
Individual traces of IPGTT BG levels of NT, PBS, and human islets transplanted mice. (B)

Individual traces of IPGTT BG levels of NT, PBS, and SC-islets transplanted mice. (C)

Individual traces of IPGTT BG levels of NT, PBS, and mouse islets transplanted mice. (D)

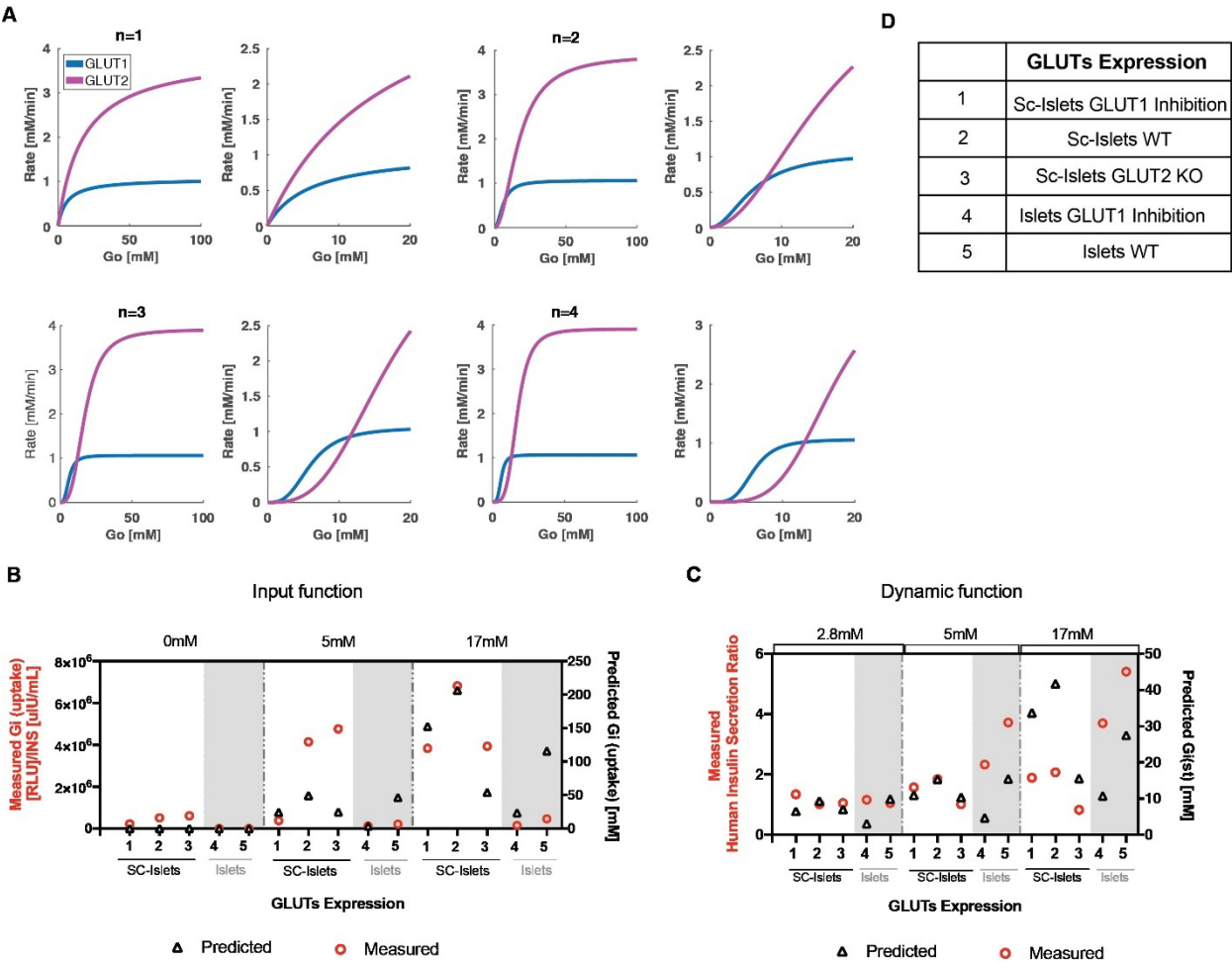
Individual traces of non-fasting BG levels of NT, PBS and human islets transplanted mice. Day 0 indicates day of surgery. (E) Individual traces of non-fasting BG levels of NT, PBS and SC-islets cells transplanted mice. Day 0 indicates day of surgery.

Supplemental figure 3.



Supplemental Figure 3. dGSIS of SC-Islets. (A) dGSIS plots of WT and *GLUT2* KO SC-islets. (B-C) dGSIS plots of (B) WT SC-islets and (C) *GLUT2* KO SC-islets with and without *GLUT1* inhibitor *GLUT2* KO SC-islets. Left plot displays the full dGSIS sequence. Orange box marks area of zoom-in shown on the right. (n=6 for both WT and *GLUT2* KO cells, from 3 different differentiations). Protocol of glucose concentration and exposure duration is indicated in the grey bar above each plot. Numbers indicate glucose concentration use in the specified time.

Supplemental figure 4.



Supplemental Figure 4. Mathematical model validation. (A) Rate prediction based on different values of the Hill coefficient (n) between the values of 1-4. G_o is the extracellular concentration of glucose. Left plot displays a wide range of G_o between 0 to 100 mM. Box indicates the zoom-in area of the right plot at a narrower G_o range (0-20 mM). (B-C) Individual values of predicted vs. measured results of (B) human islets and (C) SC-islets. Numbers legend in D. (D) GLUT1 and GLUT2 disruption states legend for B and C.