SUPPLEMENTARY MATERIAL

SUPPLEMENTARY FIGURES

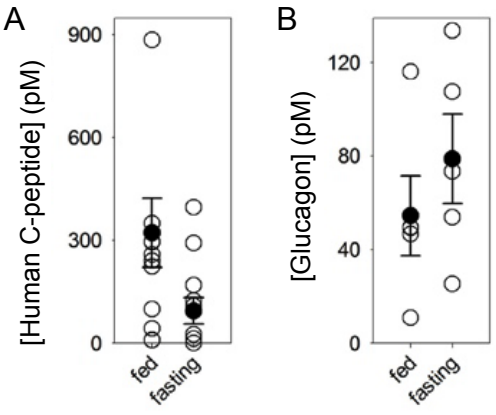

Figure S1. Regulation of hormone secretion from human islet grafts is intact (related to Figure 2)

(A and B) Plasma levels of human C-peptide (A) and glucagon (B) are responsive to changes in glycemia induced by 18 h fasting (*n* = 5-8 mice per group).

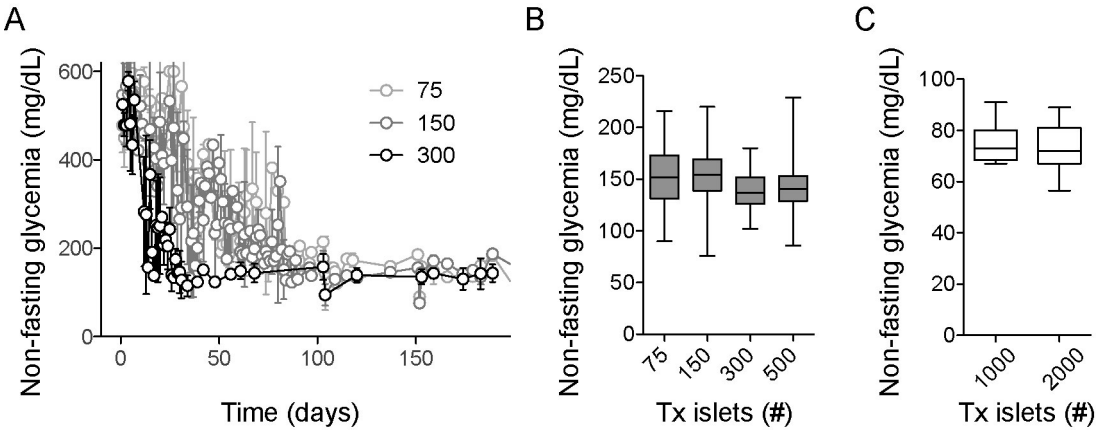

Figure S2. Glycemic levels depend on donor species but are independent of transplanted islet mass (related to Figure 3)

(A and B) Non-fasting glycemic values show that transplanting different numbers of islets from C75Bl6J mice into diabetic C75Bl6J mice reversed diabetes and produced similar levels of glycemia (quantified in B, n = 4-5 mice per group). Note, however, that recipient mice with a smaller mass of transplanted islets needed longer to return to normoglycemia.

(C) Human islet grafts reversed diabetes in diabetic recipient nude mice to human normoglycemic values that were independent of the number of transplanted islets (n = 9-11 recipient mice per group). Experimental groups were not significantly different.

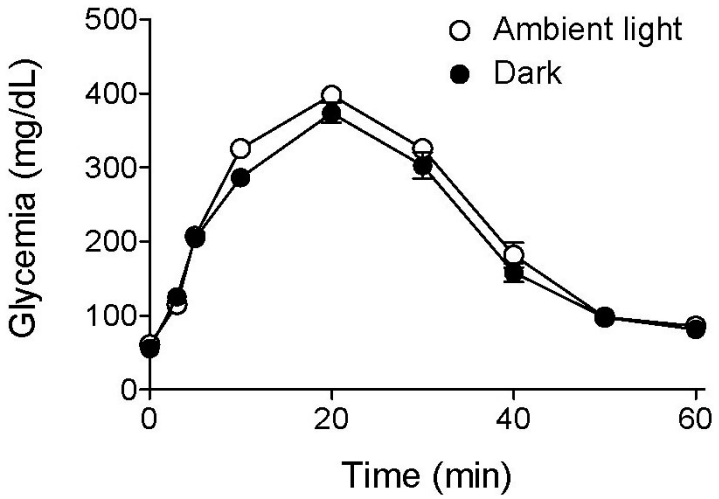

Figure S3. Nervous input does not affect human islets transplanted into the anterior chamber of immunodeficient (nude) mice (related to Figure 4)

Modulating nervous input to human islet grafts via the pupillary light reflex with ambient illumination did not change glucose excursions in intraperitoneal glucose tolerance tests. Values were obtained and tests were performed > 2 months after transplanting 1,000 human islets into both eyes of diabetic nude mice ($n \geq 12$ mice per group. These results are in contrast with those obtained in mice transplanted with mouse islets (Rodriguez-Diaz et al., 2012).

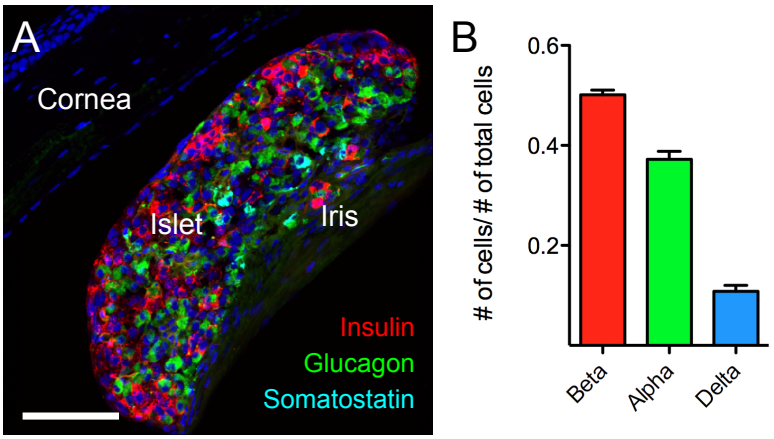

Figure S4. The structure of human islet grafts is preserved after transplantation into the eye of nude mice. (related to Figure 5)

(A) Confocal image of an eye section containing a human islet immunostained for insulin (red), glucagon (green), and somatostatin (light blue).

(B) Quantitative enumeration of the contribution of beta, alpha, and delta cells to the composition of human islet grafts (n = 8 islet grafts from 3 transplanted mice).

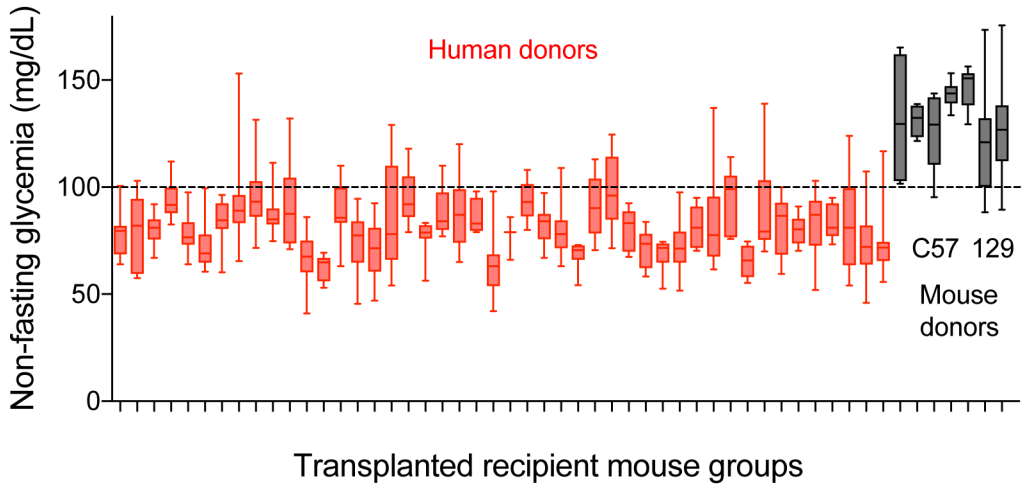

Figure S5. Glycemic outcomes of individual islet preparations from > 30 human donors (red symbols) and 7 mouse donors (grey symbols) after transplantation into the eye or under the kidney capsule of recipient mice (related to Figure 5)

Notice that mice transplanted with human islet show variability in their glycemia but did not reach mouse glycemic levels.

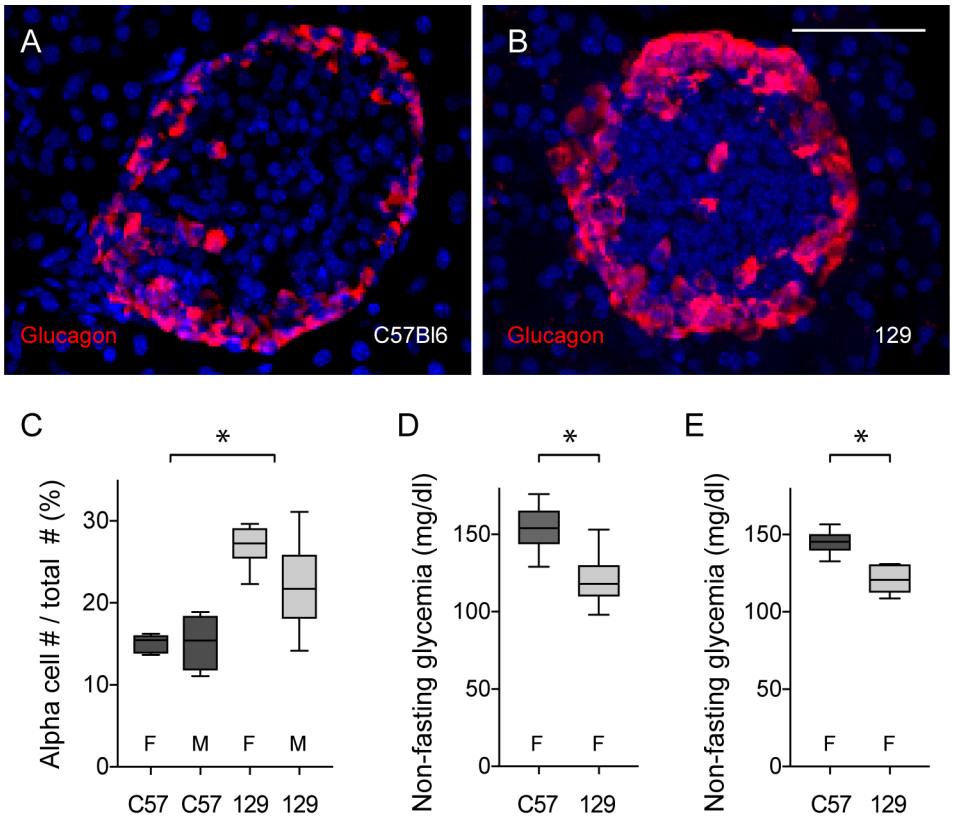

Figure S6. Proportion of alpha cells in islets in the mouse strains C57Bl6J and 129X1/SvJ and respective glycemic levels before and after transplantation under the kidney of nude mice (related to Figure 5)

(A and B) Maximal projections of Z-stacks of confocal images of pancreatic islet of C57Bl6J (A) and 129X1/SvJ (B) immunostained for glucagon (red).

(C) Quantification enumeration of the contribution of glucagon-containing cells (alpha cells) to the composition of islets in male (M) and female (F) C57Bl6J (dark grey symbols) and 129X1/SvJ mice (light grey symbols). Asterisk denotes statistical significance between C57Bl6J and 129X1/SvJ groups (n = 3 mice per group, $P < 0.05$; ANOVA followed by multiple comparisons).

(D) Non-fasting glycemic levels of female C57Bl6J (dark grey symbols) and 129X1/SvJ mice (light grey symbols). Asterisk denotes statistical significance between the groups (n = 20 per group, $P < 0.05$, Student's t-test).

(E) Non-fasting glycemia of diabetic nude mice transplanted under the kidney capsule with islets from female C57Bl6J (dark grey symbols) and 129X1/SvJ mice (light grey symbols). The glycemic levels were similar to those of the donor mice shown in (D). Asterisk denotes statistical significance between the groups (n = 4-8 per group, $P < 0.05$, Student's t-test).