# ESM Methods

*Glucose-induced insulin secretion (GSIS)* Transduced and non-transduced human islet cells were cultured in complete CMRL medium. Insulin secretion assay was performed five days following lentiviral transduction. For each condition, triplicates of 30’000 dispersed human islet cells were attached to laminin covered dishes. For basal secretion, synchronised islet cells were statically incubated with Krebs-Ringer Buffer (KRB) containing 2.8 mmol/l glucose for 1 h at 37°C. Islet cells were stimulated with KRB containing 16.7 mmol/l glucose and 5 mmol/l theophyllin for 1 h at 37°C. Supernatants were collected and analysed by ELISA (Mercodia, 10-1113-01). Normalisation was done on total insulin content of cells lysed over-night in acid-ethanol solution at 4°C.

*Mouse islet isolation and culture* Animal studies were performed according to local ethical committee regulations. Per2::luc reporter mouse pancreases [33] were perfused with type XI collagenase (Sigma, C7657) and then dissected. Islets were isolated by collagenase digestion and Ficoll gradient and were left to recover over-night at 37°C in RPMI 1640 (Gibco) supplemented with 10% FBS, 1% penicillin/streptomycin. Islets were plated on BD Primaria 35 mm dishes (BD Falcon), and were left to attach for 48 h. To synchronise mouse islets, 100 nmol/l dexamethasone or 10 µmol/l forskolin or 50% horse serum was added to the medium. Following incubation of 30 min at 37°C, synchronisation stimuli were replaced by normal culture medium containing 100 µmol/l luciferin, and bioluminescence was monitored in Actimetrics LumiCycler, as previously described [26].

*Indirect immunofluorescence* Human islet cells attached on laminin-covered dishes were washed with PBS and fixed with 2% paraformaldehyde for 30 min at room temperature, five days after transduction. Mouse anti-glucagon (Sigma) and guinea pig anti-insulin (Invitrogen) antibodies were used. Cells were mounted with Dako mounting medium and analysed by fluorescence microscopy.