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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Perkin-Elmer IVIS Spectrum CT Living Image 4.0
Data analysis	Graphpad Prism 7.03, Milliplex@ 5.1, Perkin-Elmer IVIS Spectrum CT Living Image 4.0, Becton Dickinson Diva, FlowJo 9.8

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the plots within this paper are available from the corresponding authors upon request.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences

Study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample sizes were selected based on statistical power calculations and previous experience with these metrics.
Data exclusions	Animals that did not achieve primary function (defined as 5 consecutive blood glucose readings <250 mg/dL) were excluded from analysis as this is an effect of poor isolation outcomes and tissue quality and not the experimental groups being evaluated.
Replication	Evaluation of cytocompatibility was performed across two different islet isolations, with 3 individual samples read in triplicates for each analysis. For islet transplants data presented corresponds to >4 different transplants from different islet isolations performed by different users. Results were consistent across independent experimental runs.
Randomization	Animals were randomized among control and treatment groups keeping the initial average weight and blood glucose levels at similar level for all groups.
Blinding	Blood glucose measurements were performed by blinded and nonblinded personnel in a random fashion. Animals were checked in a rotation schedule by 4 different users. All blood glucose measurements were electronically and time-stamped recorded.

Materials & experimental systems

Policy information about availability of materials

n/a	Involved in the study
☐	☒ Unique materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☐	☒ Research animals
☒	☐ Human research participants

Unique materials

Obtaining unique materials	Shirwan has patent on SA-FasL material which is not available commercially. This material is available through a Materials Transfer Agreement upon reasonable request and pending third parties rights.

Antibodies

Antibodies used	glucagon (Abcam, ab 92517 Lot GR293948, 1:50), insulin (DAKO, A0564 Lot 10106406, 1:100), isotype (ab125938, Lot GR3176164-1, 1:100), DAPI (Invitrogen, P36931, 2 drops). Alexa fluor 700 anti-CD4 (clone RM4-5, BD Biosciences cat# 557956, lot# 5156949, 1:200); APC Cy7 anti-CD8 (clone 53-6.7, BD Biosciences cat# 557654 lot# 5351539, 4353542, 1:100); PECy7 anti CD25 (clone PC61.5 eBiosciences cat# 25-0251-82 lot# E07536-1635, 1:100) eFluor 450 anti-CD44 (clone IM7, eBiosciences/ thermofisher cat# 48-0441-82 lot# 4272424, 1:100), PerCpCy5.5 anti-CD62L (clone MEL-14 eBiosciences/thermofisher cat# 45-0621-82 lot# E08348-1632, 1:200), Alexa 488 anti-FoxP3 (clone FJK-16s eBiosciences/thermofisher cat# 11-5773-82 lot# E08870-1635, 1:20), 7AAD (BD Biosciences cat# 51-68981E lot# 5006667-1A, 5006667-1B, 0.5 ul/1x10^6 cells), polyclonal guinea pig anti-insulin (Dako, cat#A0564 lot#10082002, 1:100), goat anti-Guinea Pig IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 555 (Invitrogen/thermofisher cat#A21435 lot#56145A, 1:300), Hoechst 33342 nucleic acid stain (Molecular Probes/thermofisher cat#H3570 lot#7241, 1:25), glucagon (D16G10) XP® Rabbit mAb (Cat#8233S, Cell Signaling Technology 1:200), Goat anti-Rabbit IgG (H+L)-Alexa Fluor 647 (Life Technologies, Cat#A21244, 1:100).
Validation	Antibodies were validated for use in this system using positive and negative control samples using dilutions and conditions based on the manufacturer's recommendation or our previous experience. Omission of the primary antibody was used for validating staining for all antibodies tested for IHC. For monoclonal antibodies, an isotype matched was used as a control for IHC staining. For flow, all antibodies were titrated using cells positive for the antibody marker. Isotype controls were implemented for FOXP3 and CD25 staining.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	murine A20 B-lymphoma cell line (ATCC)
Authentication	validated by flow cytometry for FasL-induced apoptosis
Mycoplasma contamination	Cells were not tested in house for Mycoplasma contamination but ATCC certified them free of contamination.
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Research animals

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Animals/animal-derived materials	For isolations for allogeneic transplants in EFP: Balb/C females were used as donors (age between 7-9 weeks). Recipients of allo tranplants in EFP are B6 male mice from 8-9 weeks in age. For in vitro compatibility islets were isolated from male Lewis Rat from 250-300 g (9-11 weeks). For kidney capsule transplants, male and female Balb/c were used for isolations between (5-9 weeks).

Method-specific reporting

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ Magnetic resonance imaging

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Spleen, kidney draining lymph nodes and graft bearing kidney were harvested. Spleen and Kidney draining lymph nodes were processed using frosted slides ends. Single cells from spleen were treated with RBC lysis buffer. For graft infiltrating lymphocytes, kidney capsule was torn apart using forceps in sterile PBS to release islet mass. Islet mass along with kidney capsule were then processed using frosted slides and enzymatic digestion were performed when needed. Cells were counted then processed for flow cytometry analysis.
Instrument	BD LSR II (serial number: H55100034, H47100051)
Software	BD Facs Diva and FlowJo 9.8
Cell population abundance	NA
Gating strategy	For immunophenotyping, cell populations were gated based on forward and side scatter followed by doublet exclusion . The single cells were subjected to CD4 and CD8 gating. CD4 and CD8 positive cells were then subjected to CD44 vs CD62L gating. CD44hi CD62Llo were defined as effector T cells, CD44hi CD62Lhi were defined as central memory T cells where as CD44lo CD62Lhi as naive T cells. CD4 positive cells were further subjected to FoxP3 vs CD25. Isotype control was used against CD25 and FoxP3 to separate positive and negative populations. For immune cells proliferation assay, live cells were gated as 7AAD negative population followed by SSC-A vs FSC-A gating. The resulting population was then subjected to CD4 vs CD8 gating. Each CD4 or CD8 positive population were then subjected to FSC-A vs CFSE gating.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.