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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

Sample size was chosen on the basis of previous experience with NHP cohort sizes, and by choosing a minimum number of NHPs per experimental group, owing to ethical concerns in sacrificing an excessive number of NHPs. We determined that reproducible results can be achieved by using 2 or 3 NHPs for material biocompatibility studies. For experiments with allogeneic islets, we increased the number to 3 or 4 NHPs per time-point group due to the presence of allogeneic tissue and to the higher potential for an immune response.

2. Data exclusions

Describe any data exclusions.

No animals were excluded from the analyses.

3. Replication

Describe whether the experimental findings were reliably reproduced.

Experimental findings were reliably reproduced. Six out of seven encapsulated-islet preparations demonstrated significantly higher viability than 75%, from pre-encapsulation (naked) to post-encapsulation (pretx) to post retrieval from NHPs. Encapsulated islets from one primate (CN8800) were retrieved at 4 months and presented with fibrosis and non-viable islets. At the time of transplantation, this same lot of encapsulated islets was also transplanted into a separate primate (CN8801) that yielded viable islets without fibrosis when retrieved at 4 months. These distinct results using the same lot of material/islets lead us to hypothesize that the cause of fibrosis in the one primate may be related to undocumented differences in the transplant procedure or to natural animal variability when using non-inbred NHP models.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

NHPs were randomly assigned to groups.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Surgeons were blinded during the implantation/transplantation and retrievals of empty spheres and of spheres containing allogeneic islets. This was to ensure that the same procedure/samples were collected for analysis. Viability assessments were performed by the same operator to reduce inter-operator error.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	Prism vs 6 was used to make figures and to analyse numerical data for statistical significance. ImageJ was used to process inverted-phase contrast images by converting colors to black and white, and then by inverting in order to better visualize the presence of islets within retrieved spheres without fibrosis. All stained tissue sections were processed using the Qcapture Pro5.1 program to set appropriate gains and exposure times. HCImage software was used for image acquisition and analysis, for the microfluidic-based dynamic-glucose-challenge assay to monitor intracellular coupling factors/fluorescent intensity changes in islets post stimulation with high glucose.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	No unique materials were used to generate the chemically modified alginate derivatives for the study.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

Description of the antibodies used in the study are given in Methods. For validation of histology antibodies, isotype controls (Isotype-same as primary Ab + secondary Ab), negative control (diluent only+ secondary ab) and positive tissue control (cyno spleen and or lymph nodes for CD11b) were used. The antibodies were tittered against the positive tissue control and adjusted when necessary to the specimen of interest. Initially, all isotype and negative controls were applied to both the tissue of interest and to the positive tissue control to see the background the tissue may elicit. The CD11b stain was controlled against both human and cyno spleen. For flow cytometry validation of antibodies, proper background and laser intensity settings were determined using, unstained, single antibody, and IgG controls.

Histology:
Primary antibodies mouse IgG1 against
CD11b (1:100 clone ICRF44; Cat#: ab34216, Abcam)
SMA (1:100 clone IA4; Cat # ab7817; Abcam)
Secondary Antibody
Alexa Fluor 594 anti-mouse (1:200, Cat# A-11032; Invitrogen)

Flow cytometry:
CD68: CD68-Alexa647, Clone KPI, Cat. no. sc-20060, Santa Cruz Biotechnology, 1:100)
CD11b: CD11b-Alexa-488, Clone M1/70, Cat. #101217, BioLegend, 1:250)

For proper background and laser intensity settings, unstained, single antibody, and IgG (labeled with either Alexa-488 (CA# 400625, BioLegend) or Alexa-647 (CA# 400526, BioLegend) were run as controls.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

No eukaryotic cell lines were used.

b. Describe the method of cell line authentication used.

No eukaryotic cell lines were used.

c. Report whether the cell lines were tested for mycoplasma contamination.

No eukaryotic cell lines were used.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

No eukaryotic cell lines were used.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Non-human primates (Baboons (papio anubis), Cynomolgus Macaques (macaca fascicularis) and mice (C57Bl/6J, 8 wks, male) were used in this study. All transplant procedures were performed under the guidelines of the National Institute of Health, and protocols were approved by the animal care committee at UIC. Baboons were used as recipients for biocompatibility studies of alginates tested in clinical trials. The vendor stopped selling these animals so studies were switched to cynomolgus macaques. The clinical alginate spheres (UPMVG-Ca2+/Ba2+) were transplanted into both baboons and cynomolgus macaques to verify that both NHP species yielded similar biocompatibility results. Subsequent experiments with allogeneic islets were all completed with cynomolgus macaques as donors and recipients. Cynomolgus macaques males and females were used in the study.

Recipient (cynomolgus) CN8700 Z1-Y15 1 mo 6 yrs 6.0 kg male; Donor (cynomolgus) CN8705 male 5 yrs 5.6 kg
Recipient (cynomolgus) CN8708 Z1-Y15 1 mo 6 yrs 7.2 kg male; Donor (cynomolgus) CN8706 male 6 yrs 5.4 kg
Recipient (cynomolgus) CN8798 Z1-Y15 1 mo 5 yrs 7.5 kg male; Donor (cynomolgus) CN8806 male 6 yrs 7.3 kg
Recipient (cynomolgus) CN8802 Z1-Y15 1 mo 5 yrs 7.1 kg male; Donor (cynomolgus) CN8806 female 5 yrs 5.4 kg
Recipient (cynomolgus) CN8799 Z1-Y15 4 mo 5 yrs 9.4 kg male; Donor (cynomolgus) CN8572 male 6 yrs 7.3 kg
Recipient (cynomolgus) CN8800 Z1-Y15 4 mo 5 yrs 8.3 kg male; Donor (cynomolgus) CN8572 female 11 yrs 4.7 kg
Recipient (cynomolgus) CN8801 Z1-Y15 4 mo 5 yrs 7.8 kg male; Donor (cynomolgus)CN8632 female 11 yrs 4.7 kg

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

The study did not involve human research participants.