Supplementary Information

Transplantation of pancreatic beta-cell spheroids in mice via non-swellable hydrogel microwells composed of poly(HEMA-co-GelMA)

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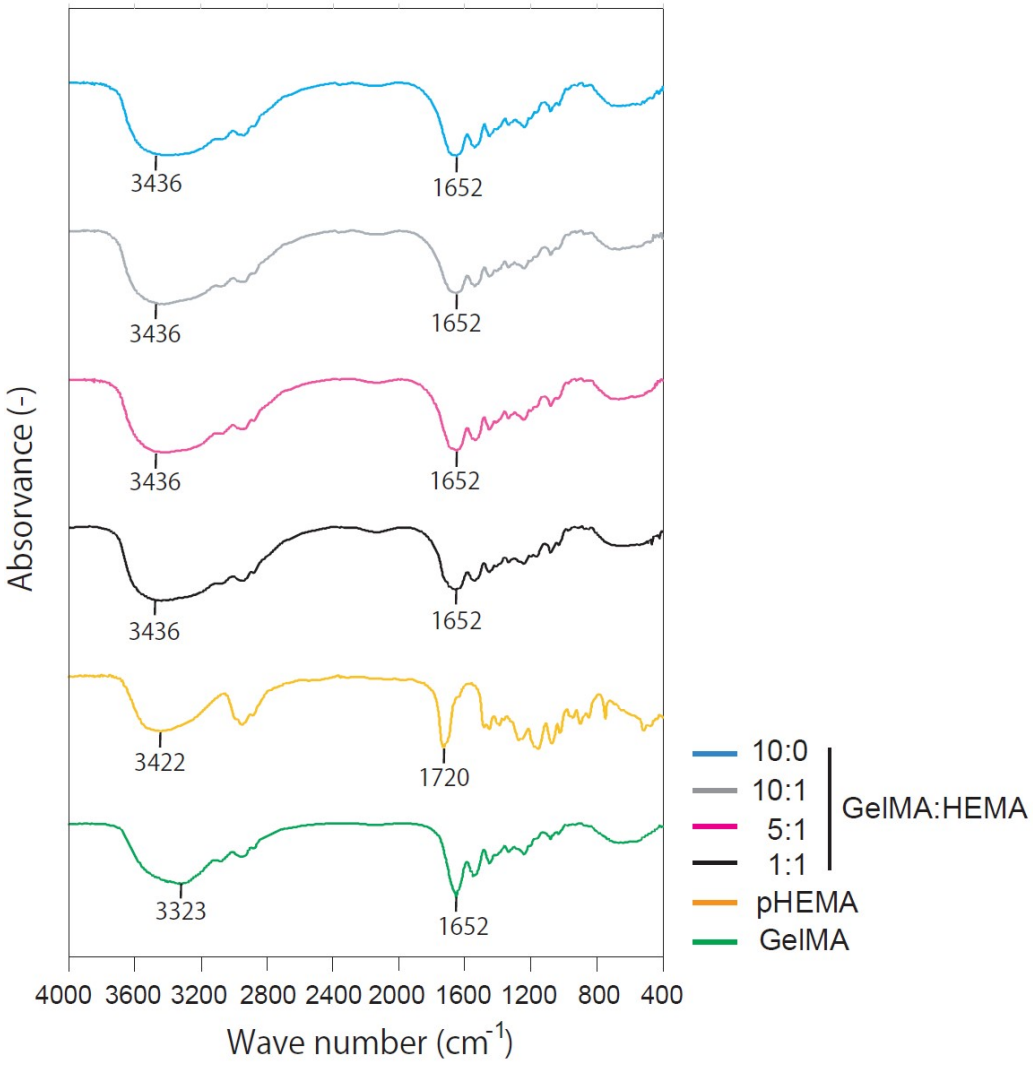

Figure S1. Synthesis of GelMA/HEMA hydrogel consisting of different ratio

FT-IR spectra of GelMA hydrogel, poly HEMA and GelMA/HEMA hydrogel.

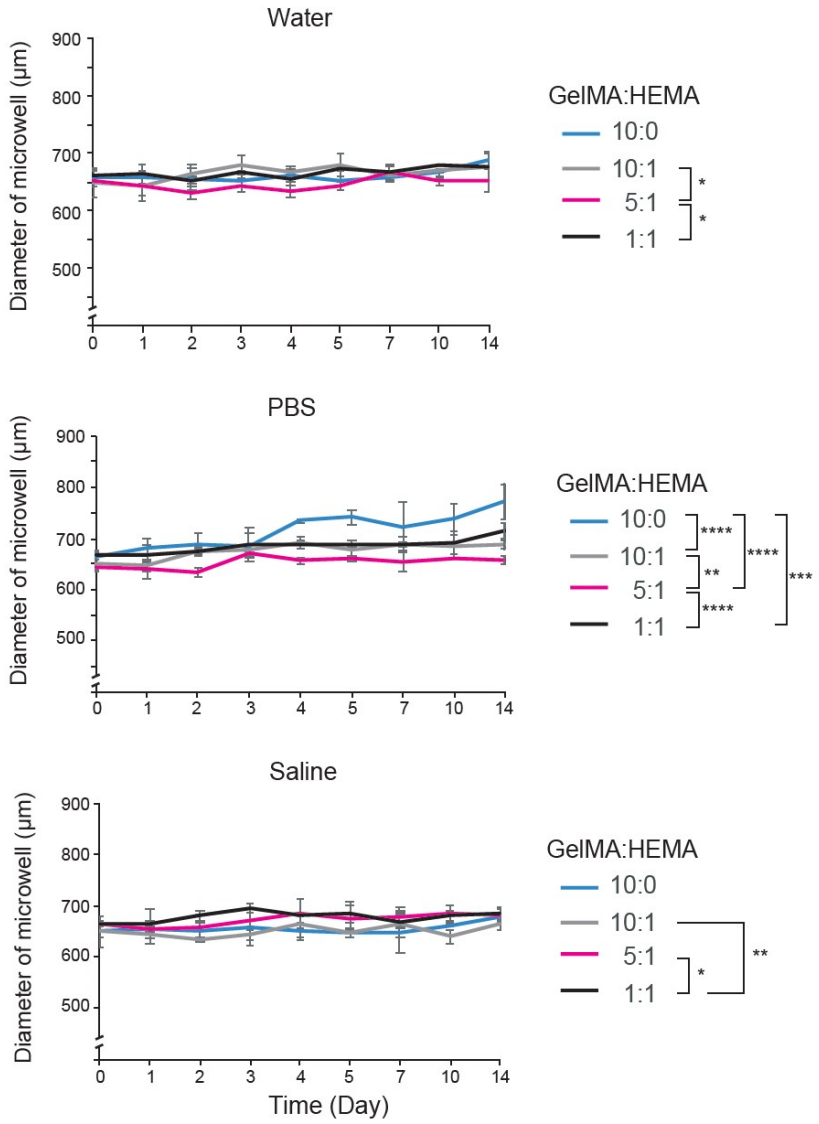

Figure S2. Change the diameter of GelMa/HEMA hydrogel microwell devices consisting of different ratio

Change in the diameter of GelMa/HEMA hydrogel microwells during the incubation in water (Upper panel), PBS (Middle panel) and saline (Downer panel). Microwells fabricated from 500 μm templates were used. Data are presented as average ± standard deviation (n = 3, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$).

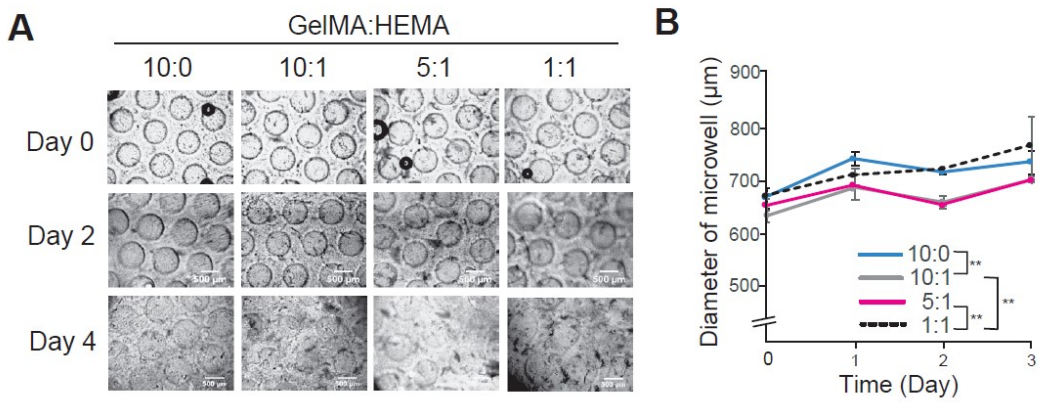

Figure S3. Characterization of GelMA/HEMA hydrogel microwell devices consisting of different ratio in collagenase

(A)Microscopic images of GelMA/HEMA hydrogel microwell device incubated in 1 μg/ml collagenase. Scale bar, 500 μm. (B) Quantification of changes in microwell diameter. Data are presented as average ± standard deviation (n = 3, $^{**}p < 0.01$).

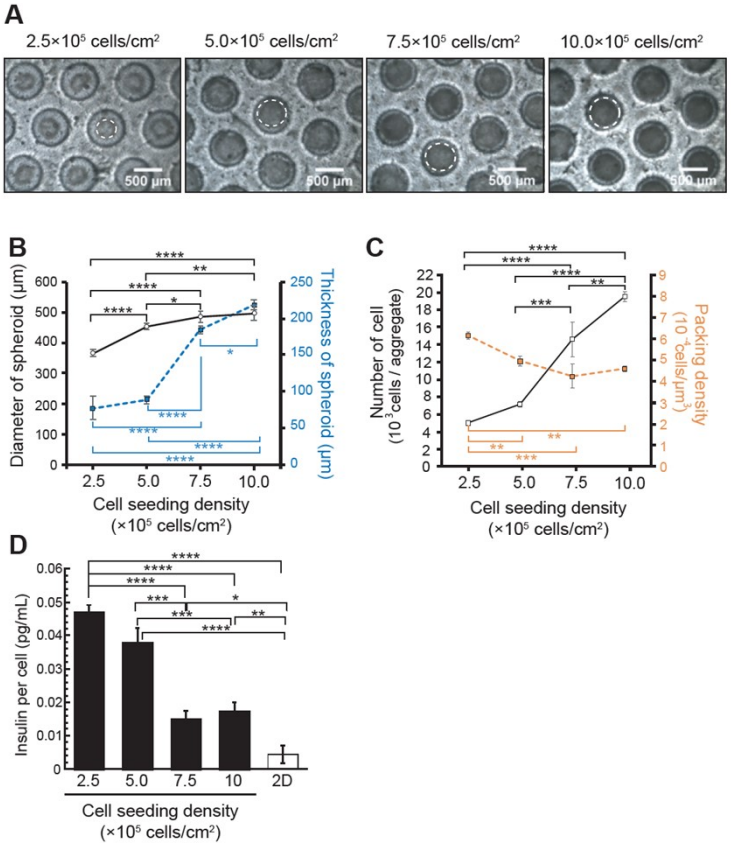

Figure S4. Spheroid formation of iGL and insulin secretion in GelMA/HEMA hydrogel microwell device

(A) Optical microscopic images of iGL aggregates formed on GelMA/HEMA hydrogel microwells with different seeding densities. The outline of spheroids are indicated by dotted line, respectively. (B)(C) Effect of cell seeding density on diameter, thickness, cell number, and packing density of iGL aggregates formed on GelMa/HEMA hydrogel microwells. Data are presented as average ± standard deviation (n = 3-5, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$). (D) Insulin secretion from iGL aggregates formed on GelMa/HEMA hydrogel microwells with different seeding densities. Results of the 2D-cultured cells on a TCPS culture dish is also shown for comparison. Data are presented as average ± standard deviation (n =3, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$).

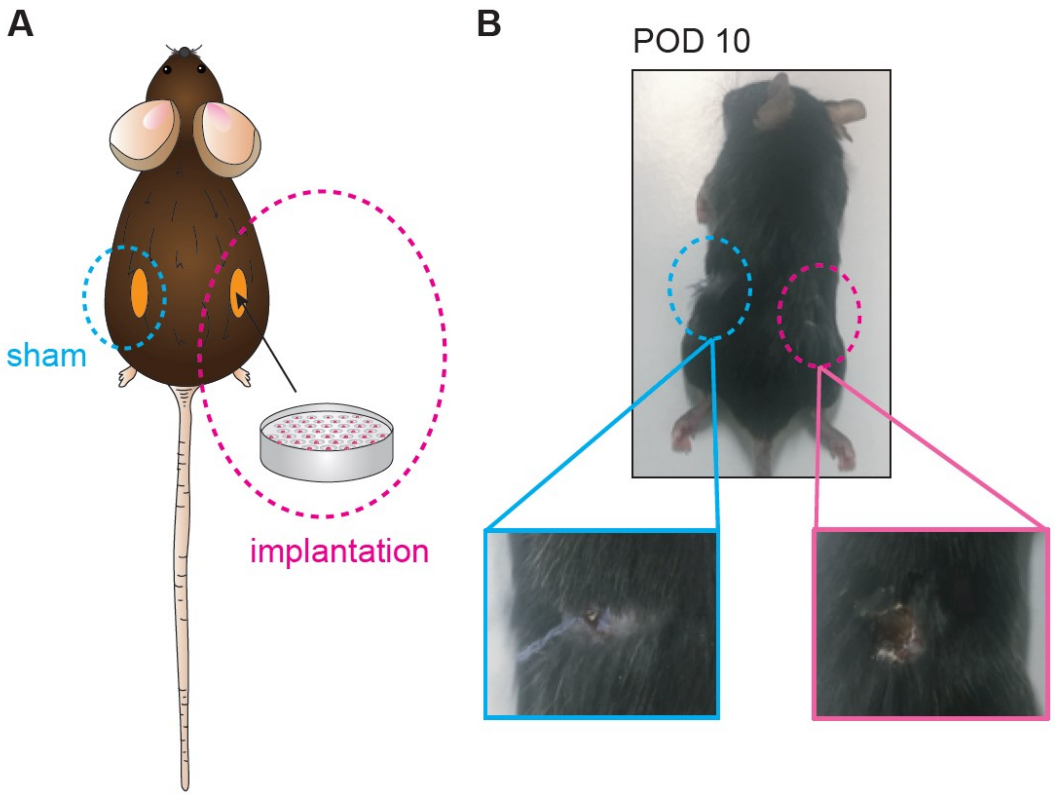

Figure S5 Subcutaneous implantation of the GelMA/HEMA hydrogel microwell device in C57BL/6J mice.

(A) Scheme for how to implant the GelMA/HEMA hydrogel microwell device subcutaneously in the C57BL/6J mouse. MIN6-m9 cells were cultured in the device for 3 days prior to implantation. On the opposite side of implantation site, sham operation was performed. (B) Wound conditions 10 days after implantation. The left panel shows wound conditions 10 days after sham operation. The right panel shows wound conditions 10 days after implantation.

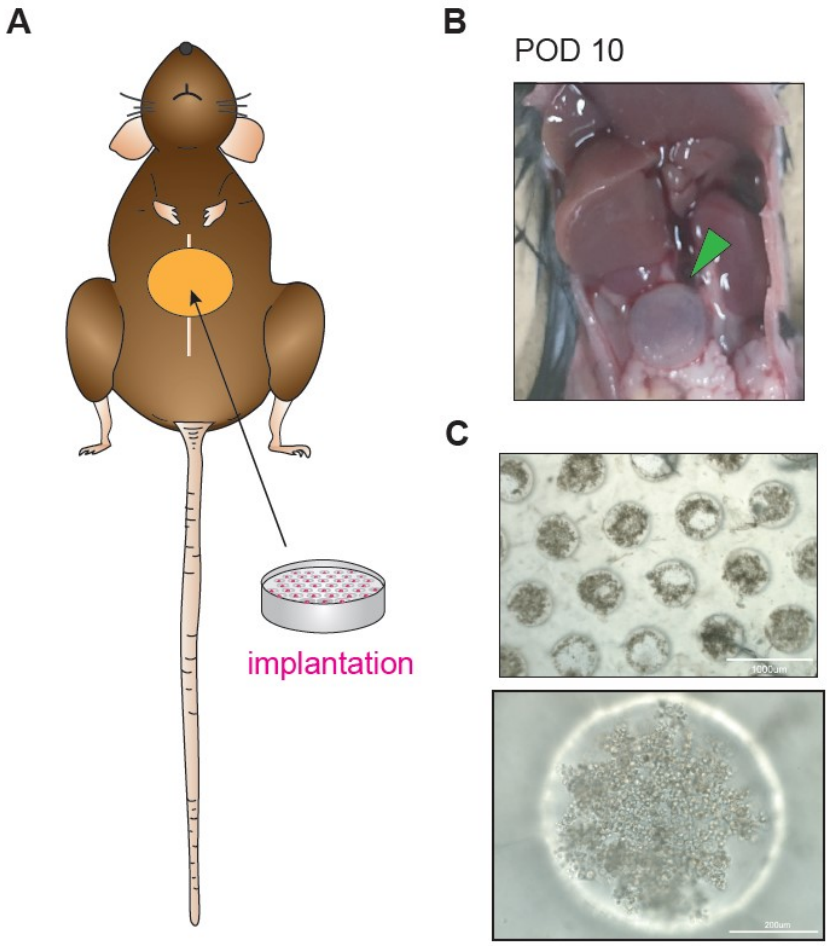

Figure S6 Intraperitoneal implantation of the GelMA/HEMA hydrogel microwell device in C57BL/6J mice.

(A) Scheme for how to implant the GelMA/HEMA hydrogel microwell device in the C57BL/6J mouse. MIN6-m9 cells were cultured in the device for 3 days prior to implantation. (B) 10 days after implantation, C57BL/6J mice were laparotomized. A white arrowhead indicates the location of the implanted microwell device. (C) Microscopic images of MIN6-m9 cells seeded in the GelMA/HEMA hydrogel microwell device. MIN6-m9 cell aggregates were partially maintained 10 days after implantation. The downer panel is a higher-magnification image of the upper panel.

Supplementary movie

Immunofluorescent staining for insulin (magenta) of MIN6-m9 cell aggregates in the GelMA/HEMA hydrogel microwell device 12 days after transplantation . Nuclei (blue). Scale bar, 30 μm.