Supplementary Information

**Improvement of the therapeutic capacity of insulin-producing cells trans-differentiated from human liver cells using engineered cell sheet**

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Table S1. Characteristics of donors from whom liver cells were isolated

|  |  |  |
| --- | --- | --- |
| Donor | Age | Sex |
| #1 | 66 | F |
| #2 | 61 | M |
| #3 | 50 | M |
| #4 | 69 | F |
| #5 | 53 | M |
| #6 | 69 | M |
| #7 | 54 | F |
| #8 | 67 | M |
| #9 | 53 | F |
| #10 | 53 | M |
| #11 | 42 | M |
| #12 | 74 | M |
| #13 | 79 | F |
| #14 | 71 | M |
| #15 | 43 | M |
| #16 | 32 | F |
| #17 | 39 | M |
| #18 | 77 | F |
| #19 | 36 | F |
| #20 | 34 | F |
| #21 | 55 | F |
| #22 | 31 | F |
| #23 | 17 | F |
| #24 | 38 | F |
| #25 | 52 | M |
| #26 | 50 | F |
| #27 | 73 | F |
| #28 | 38 | F |
| #29 | 54 | F |
| #30 | 34 | F |
| #31 | 62 | M |
| #32 | 55 | M |
| #33 | 60 | F |
| #34 | 39 | F |
| #35 | 30 | F |
| #36 (D1) \* | 45 | F |
| #37 (D2) \* | 20 | F |
| #38 (D3) \* | 33 | F |
| Average ±SD | 50.2 ± 16.1 | M:F=14:24 |

Sex: M, male; F, female\* Type I diabetics patients

Table S2. Expression of surface antigens and albumin on liver cells analyzed by flow cytometry

|  |  |  |  |
| --- | --- | --- | --- |
| Passage | Early | Mid | Late |
| Isotype control | 2.5±2.2 | 1.6±0.5 | 1.2±1.5 |
| CD29 | 99.1±1.7 | 98.5±2.6 | 98.9±0.9 |
| CD31 | 1.4±1.3 | 0.9±0.6 | 0.1±0.2 |
| CD45 | 1.8±1.9 | 1.0±0.4 | 0.1±0.1 |
| CD73 | 92.8±2.9 | 95.0±4.1 | 99.1±1.1 |
| CD90 | 99.6±0.4 | 99.3±1.1 | 99.1±1.1 |
| CD105 | 99.4±0.8 | 99.9±0.1 | 99.5±0.1 |
| Albumin | 19.8±10.5 | 5.2±1.3 | 0.5±0.2 |

Liver cells at early (1-2), mid (6-7), and late (12-14) passages were used. (n=4)

Figure S1. Immunofluorescence for checking the expression of PDX1, NEUROD1, and MAFA in human liver cells. Human liver cells (passage 6) were treated with Ad-CMV-PDX1, Ad-CMV-NEUROD1, and Ad-CMV MAFA with various multiplicities of infection (MOIs) for 2 days.Scale bars denote 200 µm.



Figure S2. BrdU ELISA cell proliferation assay of liver cells and IPCs on day 2 and day 5 after initial virus transduction. Cells (5×10^3) were plated and allowed to attach for 12 h. BrdU incorporation in cells measured through ELISA (Roche Diagnostics) following 24 h of treatment according to the manufacturer’s directions. There was greater incorporation of BrdU in liver cells and IPCs on day 2 after transduction of initial transcription factor than that in IPCs on day 5. Proliferation was occurring not only in liver cells but also in IPCs in the early stages (day 2) of differentiation, but it was delayed in IPCs on day 5 of insulin production and maturation process.

