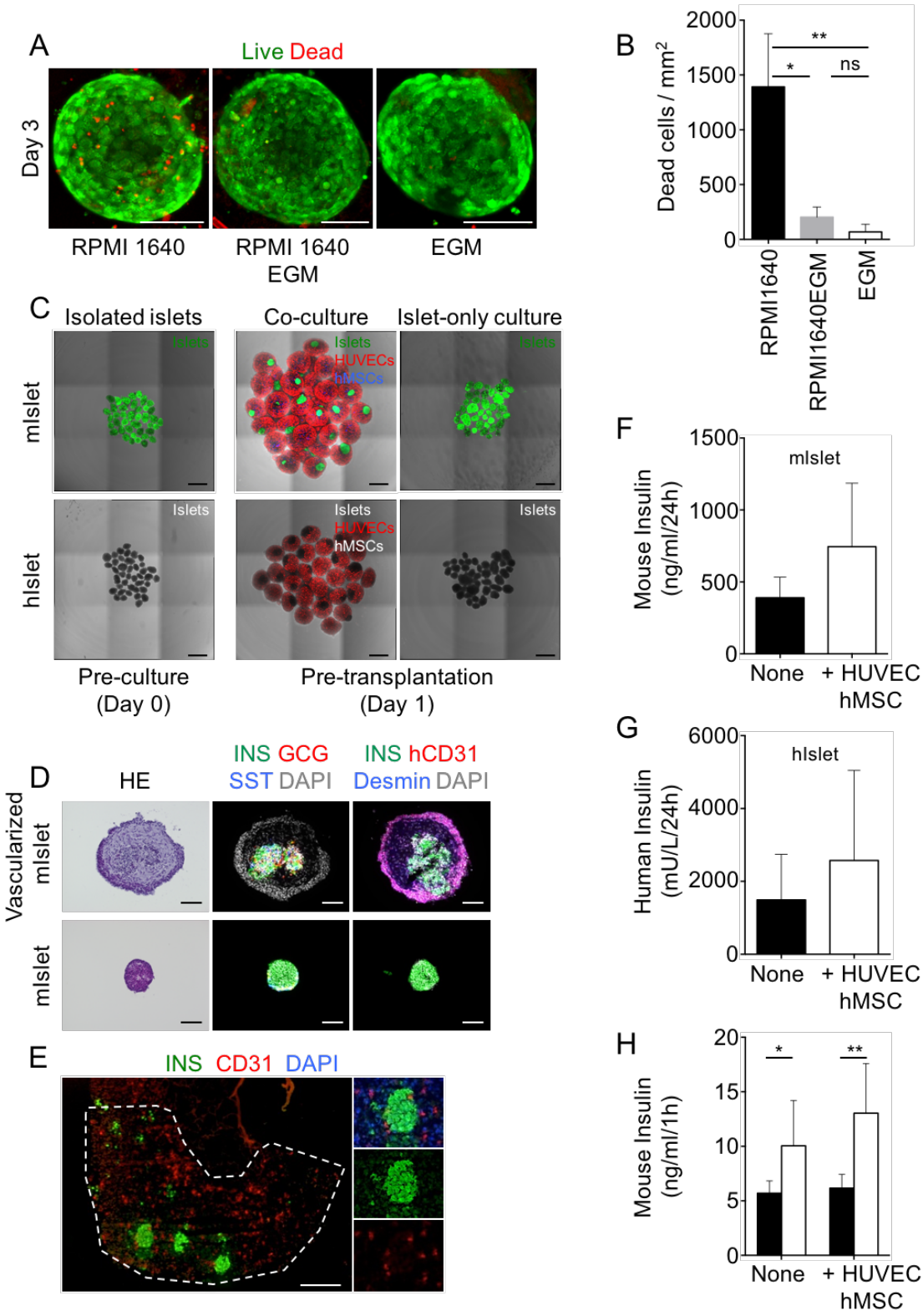

A
Live Dead
Day 3
RPMI 1640
RPMI 1640 EGM
EGM
B
Dead cells / mm²
2000
1500
1000
500
0
**
*
ns
RPMI1640
RPMI1640EGM
EGM
C
Isolated islets
Co-culture
Islet-only culture
mIslet
hIslet
Islets
HUVECs
hMSCs
Pre-culture (Day 0)
Pre-transplantation (Day 1)
D
HE
INS GCG SST DAPI
INS hCD31 Desmin DAPI
Vascularized mIslet
mIslet
E
INS CD31 DAPI
F
Mouse Insulin (ng/ml/24h)
1500
1000
500
0
mIslet
None
+ HUVEC hMSC
G
Human Insulin (mU/L/24h)
6000
4000
2000
0
hIslet
None
+ HUVEC hMSC
H
Mouse Insulin (ng/ml/1h)
20
15
10
5
0
*
**
None
+ HUVEC hMSC

Supplementary Figure 1.

The culture conditions for the vascularization of functional primary pancreatic islets, Related to Figure 1.

(A) LIVE/DEAD cell viability assay. Green, live cell; red, dead cell. Bars, 75 μm.

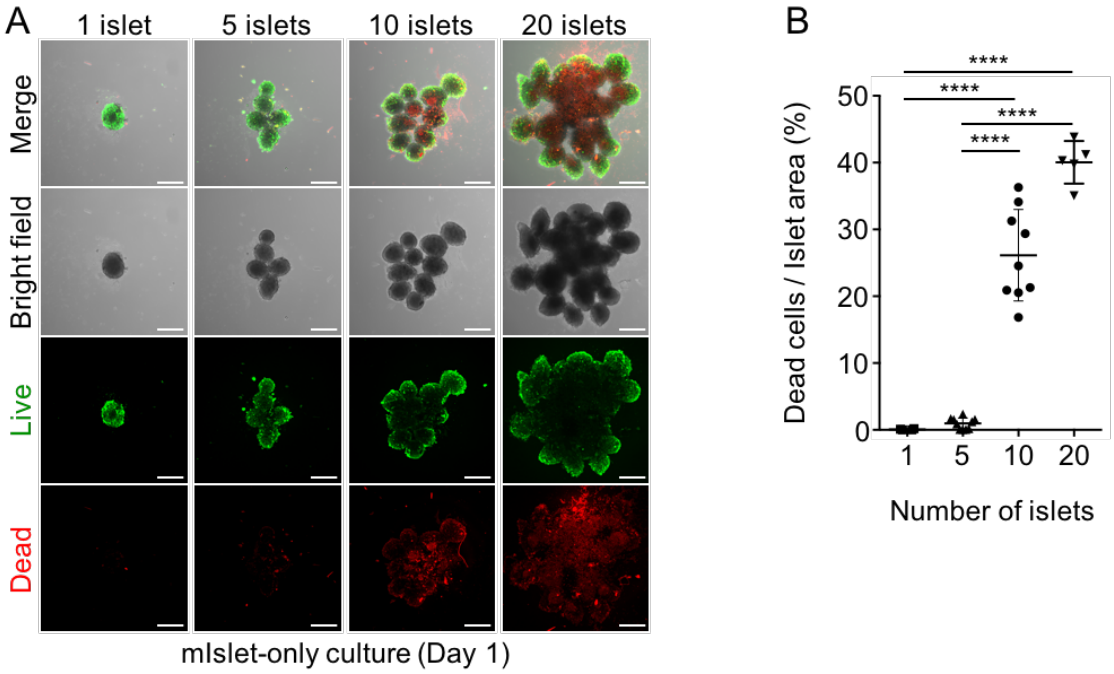
(B) Quantification of (A). The data represent the mean ± SD, $n = 3$, $^{**}P < 0.01$, $^{*}P < 0.05$, ns: not significant.

(C) Confocal microscopy imaging of the pre-transplantation islet alone (right), mini-sized vascularized islet (middle) and pre-culture islet alone (left). Islet, green or unlabeled; HUVECs, red; human MSCs, blue or unlabeled. Bars, 500 μm.

(D, E) Hematoxylin and eosin and immunofluorescence staining of the pre-transplantation vascularized islet (upper), islet alone (lower). INS, insulin; GCG, glucagon; SST, somatostatin; hCD31, human CD31. Bars, 100 μm.

(F, G) *In vitro* insulin secretion. The data represent the mean ± SD, ns: not significant, $n = 7$ and 4 mouse and human islet, respectively.

(H) *In vitro* glucose stimulated insulin secretion. The data represent the mean ± SD, $n = 5$ mouse islet alone and mouse islet + HUVECs and human MSCs, $^{**}P < 0.01$, $^{*}P < 0.05$.


A
1 islet
5 islets
10 islets
20 islets
Merge
Bright field
Live
Dead
mIslet-only culture (Day 1)
B
Dead cells / Islet area (%)
Number of islets
****
C
Co-culture
Day 0
Day 1
5 mIslets
D
Merge
Bright field
Live
Dead
Co-culture
mIslet-only culture
Day 1
5 mIslets
E
Blood glucose (mg/dl)
0
300
600
Vascularized mIslet (10 islets/well × 20)
Vascularized mIslet (5 islets/well × 40)
*
10 days after transplantation

Supplementary Figure 2.

Optimization of pancreatic islets number in vascularized islet, Related to Figure 2.

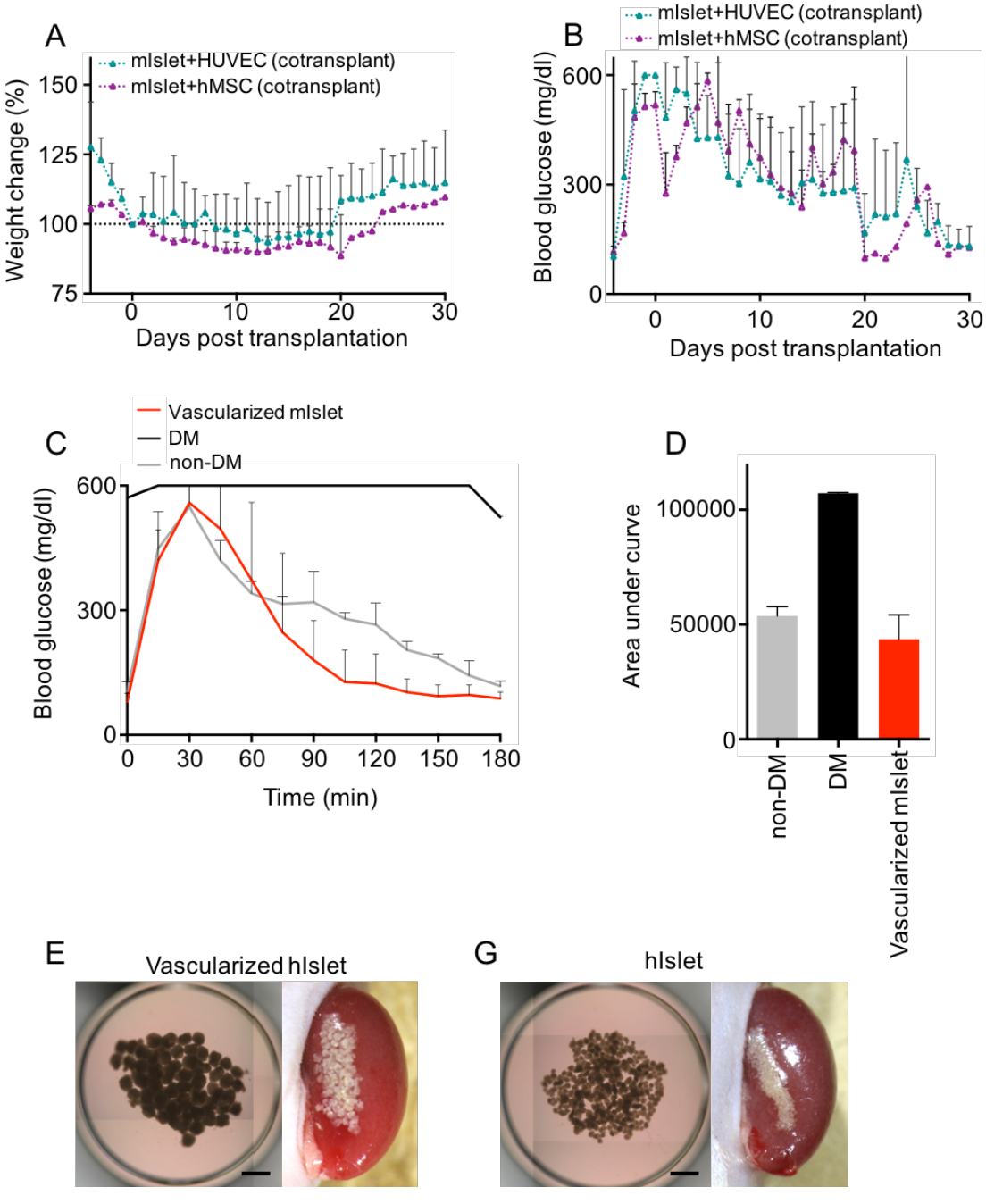
(A) LIVE/DEAD cell viability assay. Green, live cell; red, dead cell. Bars, 250 μm.

(B) Quantification of (A). *n* = 4 (1 islet/well), 10 (5 islets/well), 9 (10 islets/well) and 5 (20 islets/well), respectively. The data represent the mean ± SD, ****$P < 0.0001$.

(C) Optimization of the number of pancreatic islets in the mouse vascularized islet. Isolated mouse Islets were aggregated in culture medium using low-cell-adhesion 96-well plates with U-bottomed conical wells. 24 h later mini-sized vascularized mouse islet autonomously formed. Bars, 500 μm.

(D) LIVE/DEAD cell viability assay. Green, live cell; red, dead cell. Bars, 100 μm.

(E) Blood glucose measurements of the progressively diabetic mice. The blood glucose level of the diabetic mice were monitored 10 days after transplantation. The data represent the mean ± SD, *n* = 3 vascularized mouse islet (5 islets/well × 40), *n* = 3 vascularized mouse islet (10 islets/well × 20). The data represent the mean ± SD, *$P < 0.05$.


A
mIslet+HUVEC (cotransplant)
mIslet+hMSC (cotransplant)
Weight change (%)
150
125
100
75
0
10
20
30
Days post transplantation
B
mIslet+HUVEC (cotransplant)
mIslet+hMSC (cotransplant)
Blood glucose (mg/dl)
600
300
0
0
10
20
30
Days post transplantation
C
Vascularized mIslet
DM
non-DM
Blood glucose (mg/dl)
600
300
0
0
30
60
90
120
150
180
Time (min)
D
Area under curve
100000
50000
0
non-DM
DM
Vascularized mIslet
E
Vascularized hIslet
G
hIslet

Supplementary Figure 3.

Vascularized islet transplantation normalized blood glucose levels in diabetic mice, Related to Figure 2.

(A) Percentage of body weight variations in the diabetic mice. The data represent the mean ± SD, *n* = 4 mouse islet + HUVECs, *n* = 2 mouse islet + human MSCs.

(B) Blood glucose measurements of the progressively diabetic mice. The glucose measurements were saturated at 600 mg/dl. The data represent the mean ± SD, *n* = 4 mouse islet + HUVECs, *n* = 2 mouse islet + human MSC.

(C) Glucose tolerance testing 35 days after transplantation. The data represent the mean ± SD, *n* = 3 vascularized mouse islet, *n* = 2 DM mice, *n* = 2 non-DM mice.

(D) Area under the curve for (A). Data represent the means ± SD.

(E, F) Brightfield image of the collected human islets (left) and recipient kidneys after transplantation (right). Bars, 500 μm. Images are a montage created by merging views at 4X objective lens using powerpoint.