

SUPPLEMENTARY DATA

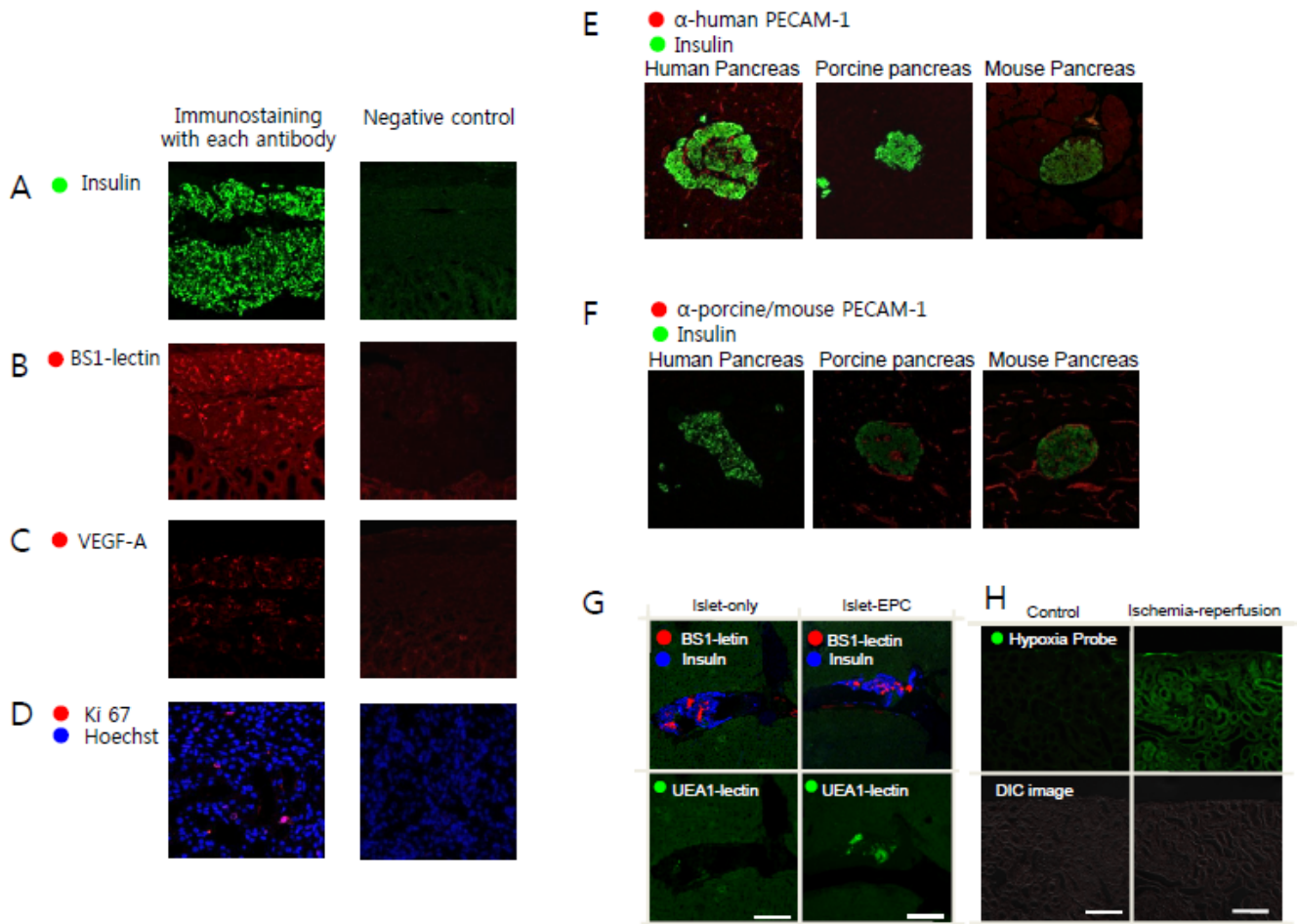
**Supplementary Table 1.** Primers for quantitative RT-PCR

Specificity	Gene		Sequence
mouse	VEGF-A	Forward	5'CTCCAGGGCTTCATCGTTA3'
		Reverse	5'CAGAAGGAGAGCAGAAGTCC3'
	VEGF-C	Forward	5'TTTAAGGAAGCACTTCTGTGTGT3'
		Reverse	5'GTAAAAACAAACTTTTCCCTAATTC3'
	VEGF-D	Forward	5'GGTGCTGAATGAGATCTCCC3'
		Reverse	5'GCAAGACGAGACTCCACTGC3'
	Ang1	Forward	5'GCAAAGGCTGATAAGGTTATGA3'
		Reverse	5'-AGCTACCAACAACAACAGCA-3'
	Ang2	Forward	5'-TTCTTCTTTACGGATAGCAAC-3'
		Reverse	5'AGCCACGGTCAACAACCTCGC-3'
	VEGFR2	Forward	5'TTCCAGATGCTGGGCAAGTC3'
		Reverse	5'ATGACATCTTGATTGTGGCAT3'
	VEGFR3	Forward	5'TGCATGCTGGGTGGACTATCA3'
		Reverse	5'GCAGGAGGAGGAAGAGGAGC3'
Tie2	Forward	5'GTTGACTCTAGCTCGGACTGT3'	
	Reverse	5'GAAGTCGAGAGGCGATCCC3'	
$\beta$ -actin	Forward	5'-GGAGGAAGAGGATGCGGCA-3'	
	Reverse	5'-GAAGCTGTGCTATGTTGCTCTA-3'	
porcine	Insulin	Forward	5'TCTACACGCCCAAGGCCCGT3'
		Reverse	5'CTCAGGGGCGGCTAGTTGC3'
	VEGF-A	Forward	5'GGCTGCTGCAACGACGAAGGT3'
		Reverse	5'ACCGCCTCGGCTTGTCACATC3'
GAPDH	Forward	5'ACATGGCCTCCAAGGAGTAAGA3'	
	Reverse	5'GATCGAGTTGGGGCTGTGACT3'	
human	HGF	Forward	5'AGGGGCACTGTCAATACCATT3'
		Reverse	5'CGTGAGGATACTGAGAATCCCAA3'
	GAPDH	Forward	5'GGAGTCAACGGATTTGGTCG3'
		Reverse	5'TCCTGGAAGATGGTGATGGG3'
mouse, porcine, human	HGF	Forward	5'ACACAGCTTTTTGCCTTCGAGCT3'
		Reverse	5'CACCAGGGTCCCCCTTCTTCCC3'
	CD31	Forward	5'AGCCAACTTCACCATCCAGAAGG3'
		Reverse	5'GTGGGAATGGCAATTATC3'
	GAPDH	Forward	5'TGATGACATCAAGAAGGTGGTGAAG3'
		Reverse	5'TCTTACTCCTTGAGGCCATG3'

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**Supplementary Figure 1.** Negative controls for each figure

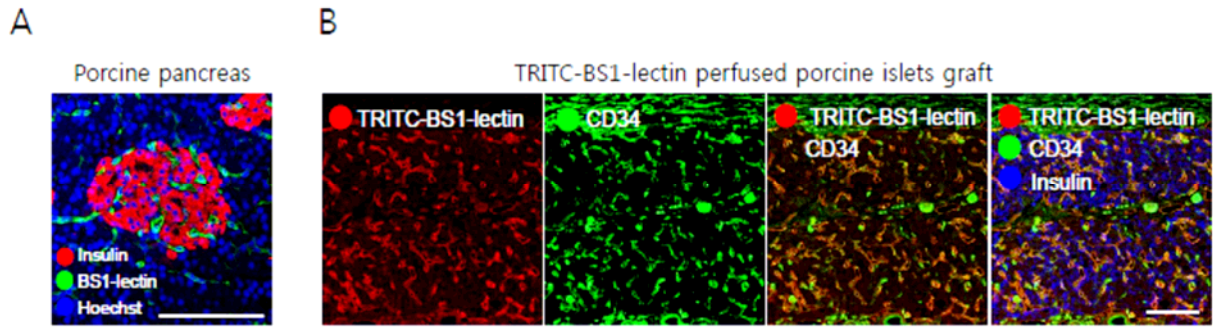
(A-D) As negative control for each immunofluorescence staining, secondary antibody only without primary antibody was incubated and then the images were taken. (A) For insulin staining in figure 1F, 1J, 2G, 3A, 3B, 4C, 4E, 5A, 5B, 6A, (B) for BS1-lectin staining in figure 2A, 2C, 3A, 3B, 4C, 4E, 6A, 6C, (C) for VEGF-A staining in figure 3A, 3B, (D) for Ki67 staining in figure 5A, 5B, all the secondary antibodies used for experiment was tested without primary antibodies. We presented representative figures of each antibodies. (E-F) The species cross-reactivity of various PECAM-1 antibodies was tested with human, porcine, and mouse pancreas tissue. (E) Anti-human PECAM-1 antibody detects human blood vessels only and (F) anti-porcine/mouse antibody detect porcine and mouse blood vessels specifically. Insulin was costained to discriminate the islet boundary. (G) EPCs were cultivated on the surface of porcine islets and infused via the portal vein into the liver of nude mice. The liver was harvested at day 1 post-transplantation and processed for immunostaining. Beta cells were visualized with insulin, and endothelial cells from both porcine islets and recipient mice were visualized with BS1-lectin (Upper panel). The lower panel is the adjacent section of the upper panel. EPCs were visualized with UEA1-lectin. BS1 and UEA1-lectin show no overlapping signals, thus enabling discrimination of human origin EPCs and porcine/mouse origin endothelial cells. (H) The hypoxia probe can adequately detect tissue hypoxia. 60 mg/kg of the hypoxia probe was injected via the tail vein into each mouse 30 min before the tissue harvest. Mice were perfused with 1% paraformaldehyde (PFA) and the grafts were harvested, processed for paraffin section, and visualized for the hypoxia probe-positive area. One kidney of a mouse was ligated for 15 min as a positive control before harvest, (right panel) while the other kidney was sham-ligated as a negative control (left panel). Scale bars, 100  $\mu$ m.



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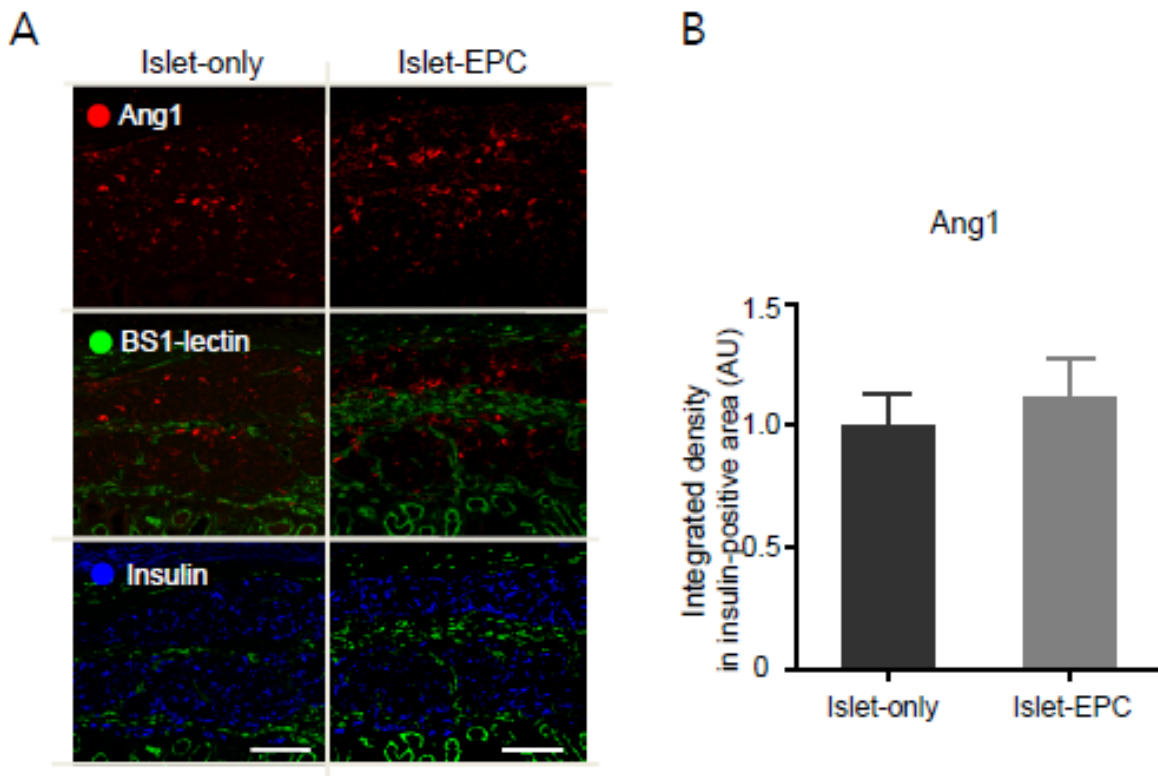
**Supplementary Figure 2.** BS1-lectin detects the microvessels inside the islets in both endogenous and transplanted porcine islets

(A) Porcine pancreas was harvested and immunostained with BS1-lectin, insulin, and Hoechst. (B) TRITC-BS1-lectin perfused graft from the islet-only group was harvested and immunostained with CD34 and insulin at day 35 post-transplantation. Scale bars, 100  $\mu$ m.



**Supplementary Figure 3.** No significant difference of Ang1 expression between the islet-only and islet-EPC groups

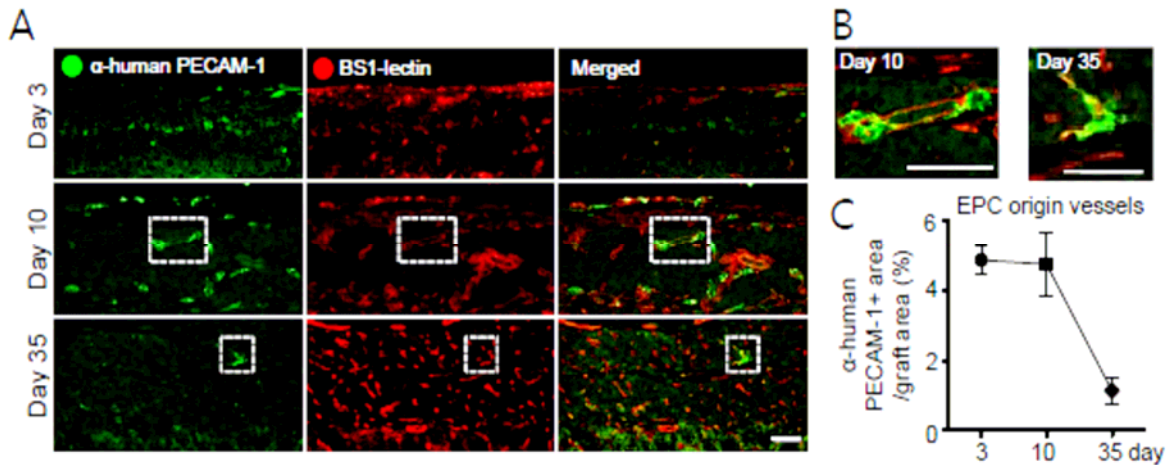
At day 14 post-transplantation, the graft-bearing kidney was visualized with Ang1, BS1-lectin, and insulin immunostaining. (A) A representative image is shown. Scale bars, 100  $\mu$ m. (B) Integrated densities of Ang1 expression in the islet-EPC group were measured in the given area and presented as arbitrary units (AU) compared to the value of the islet-only group, which was set as 1 (n=3).



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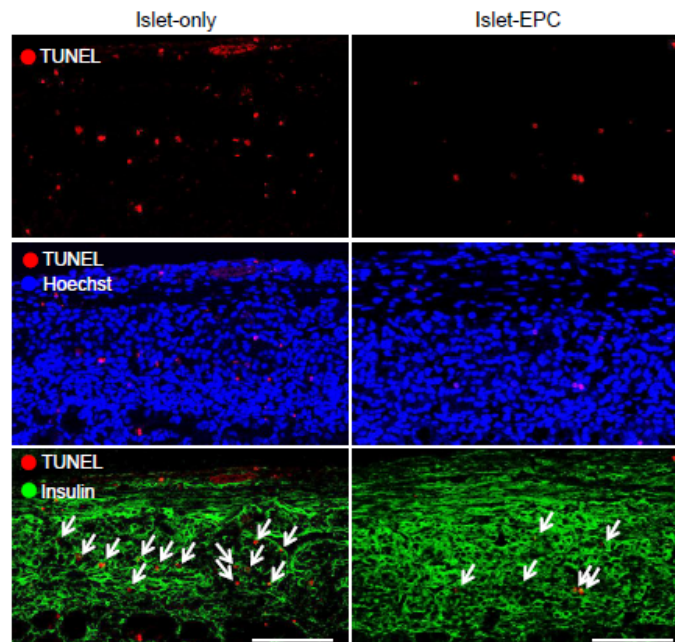
**Supplementary Figure 4.** A few of EPC origin blood vessels decreasing by time

(A-C) Blood vessels of the graft site in islet-EPC group were visualized at day 3, 10, and 35 post-transplantation with BS1-lectin for porcine and mouse origin endothelial cells, and with human specific PECAM-1 antibody for EPC origin cells, respectively. (B) The areas in the white dotted rectangle at day 10 and 35 are shown as magnification view. Scale bars, 50  $\mu$ m. (C) The area of EPC origin vessels which are positive for human-specific PECAM-1 was measured in the graft site and presented as percentage of total graft area.



**Supplementary Figure 5.** Fewer apoptotic beta cells by EPC co-transplantation

At day 10 post-transplantation, the graft-bearing kidney was harvested, sectioned, and analyzed for apoptosis with TUNEL and also, insulin immunostaining. TUNEL/insulin double positive apoptotic beta cells are indicated with arrow. Representative images are presented. Scale bars, 100  $\mu$ m.



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**Supplementary Figure 6.** Basement protein ColIV is mainly expressed in the vicinity of endothelial cells

The porcine pancreas was visualized for intra-islet basement membrane with ColIV staining and co-stained with BS1-lectin for blood vessels and insulin for beta cells. The right lower panel is a magnified view of the insert in the left lower image. Scale bars, 100  $\mu$ m.

