Supplemental Figure 1

LacZ staining of representative tissue sections from DSCR-1-*lacZ*-Hprt mice. *LacZ* staining was performed on 10 μm tissue sections from adult brain (*A*), heart (*B*), lung (*C*), kidney (*D*), liver (*E*), and thigh skeletal muscle (*F*). Bar = 100 μm.

Supplemental Figure 2

VEGF and LPS administration results in increased DSCR-1s promoter activity. *A and B,* Aorta (*A*) and brain (*B*) were harvested from either control (left), LPS-treated (middle), or VEGF-treated (right) mice. Each cryosection was immunostained with anti-*lacZ* antibody (green, upper column) or anti-PECAM-1 antibody (red, middle column). These were merged with DAPI (blue) (bottom column). White bar = 50 μm. Arrowhead refers to co-localization of *lacZ* and PECAM-1 signals. *C and D,* Lung (*C*) and kidney (*D*) were harvested and stained for *lacZ* in parallel. Lower panel represents merged immunofluorescent images of *lacZ* (green), PECAM-1 (red) and DAPI (blue) obtained from VEGF-treated mice. Bar = 50 μm.

Supplemental Figure 3

DSCR-1 is expressed in the endothelium of VEGF-stimulated mice. 4 h following VEGF administration, heart (*A*) and kidney (*B*) were harvested and cyrosectioned. Immunohistochemical staining was performed using anti-DSCR-1 antibody (green, left) or anti-PECAM1 antibody (red, middle). These were merged with DAPI (blue) (right). Bar = 50 μm.

Supplemental Figure 4

VEGF and LPS administration results in stimulation in multiple organs. *A,* Mice were injected with PBS (-) or VEGF. 10 min later, the heart, lung, liver, spleen, and thigh skeletal muscle were harvested and lysed with RIPA buffer. Whole extracts were immunoprecipitated with anti-Flk-1 antibody. These samples were then immunoblotted with anti-phospho-specific Flk-1 antibody (upper column) or anti-Flk-1 antibody (bottom column). The data show the representative of two independent experiments. *B,* Mice were injected with PBS, VEGF, or LPS. 1 h later, organs were harvested and processed for total RNA. Quantitative real-time PCR was performed using a mouse Egr-1-specific primer pair. The results show the

means and the standard deviations of expression levels relative to cyclophilin A, from three independent experiments. * P<0.001 compared with PBS treatment on each organ.

Supplemental Figure 5

siRNAs against GATA2, NFATc1, NFATc2, and NFATc3 result in significant target inhibition in cultured human endothelial cells. Confluent HMVEC were transfected with siRNAs. Real-time PCR analysis using gene-specific primers for GATA-2 (*A*), NFATc1 (*B*), NFATc2 (*C*), or NFATc3 (*D*) was performed. The results show the means and the standard deviations of expression levels relative to cyclophilin A. * P<0.001, ** P<0.01 compared with si-Control treatment plus VEGF on each experiment. *E,* Western blots were carried out using total cell lysates (50 μg) treated with either si-Control, si-NFATc1, si-NFATc2, or si-NFATc3. To normalize for loading, the membranes were stripped and re-probed with anti-β-actin antibody (bottom).

Supplemental Figure 6

Systemically administered CsA or Ad-miGATA-2 inhibits inducible DSCR-1 promoter activity in *Hprt*-targeted mice. *A,* Mice received 1 mg/kg CsA i.p. every second day. After 14 days, mice were injected with VEGF. 4 h later, the diaphragm and chest wall were removed and stained for *lacZ*. *B,* $1x10^{10}$ pfu Ad-miControl or Ad-miGATA-2 were injected i.v. into DSCR-1-*lacZ*-Hprt mice. The mice received an identical dose of adenovirus on the following day. Three days later, the mice were injected with VEGF. At 4 h, the diaphragm and chest wall were harvested and *lacZ* stained. These results are representative of four (for CsA) and three (for Ad-miGATA-2) independent experiments.

Supplemental Figure 7

Adenovirally expressed miRNA against mGATA-2 reduces GATA2 expression in cultured endothelial cells, aorta and lung. *A,* MS-1 cells were infected with either Ad-miControl or Ad-miGATA-2. Three days later, cell lysates were harvested and subjected to immunoblotting with anti-GATA-2 antibody. *B,* Aortas were harvested after administrated either Ad-miControl or Ad-miGATA-2 (as described in **Figure 7D**), cryosectioned and processed for immunostaining of GATA-2 (red, left and middle) and PECAM-1 (red, right). These images were merged with DAPI (blue). Arrow indicates the endothelial layer. Bar = 50μm. *C,* Following treatment with either Ad-miControl or Ad-miGATA2, the aorta and

lung were harvested and assayed for GATA2 expression by real-time PCR. The results show the means and the standard deviations of expression levels relative to cyclophilin A.

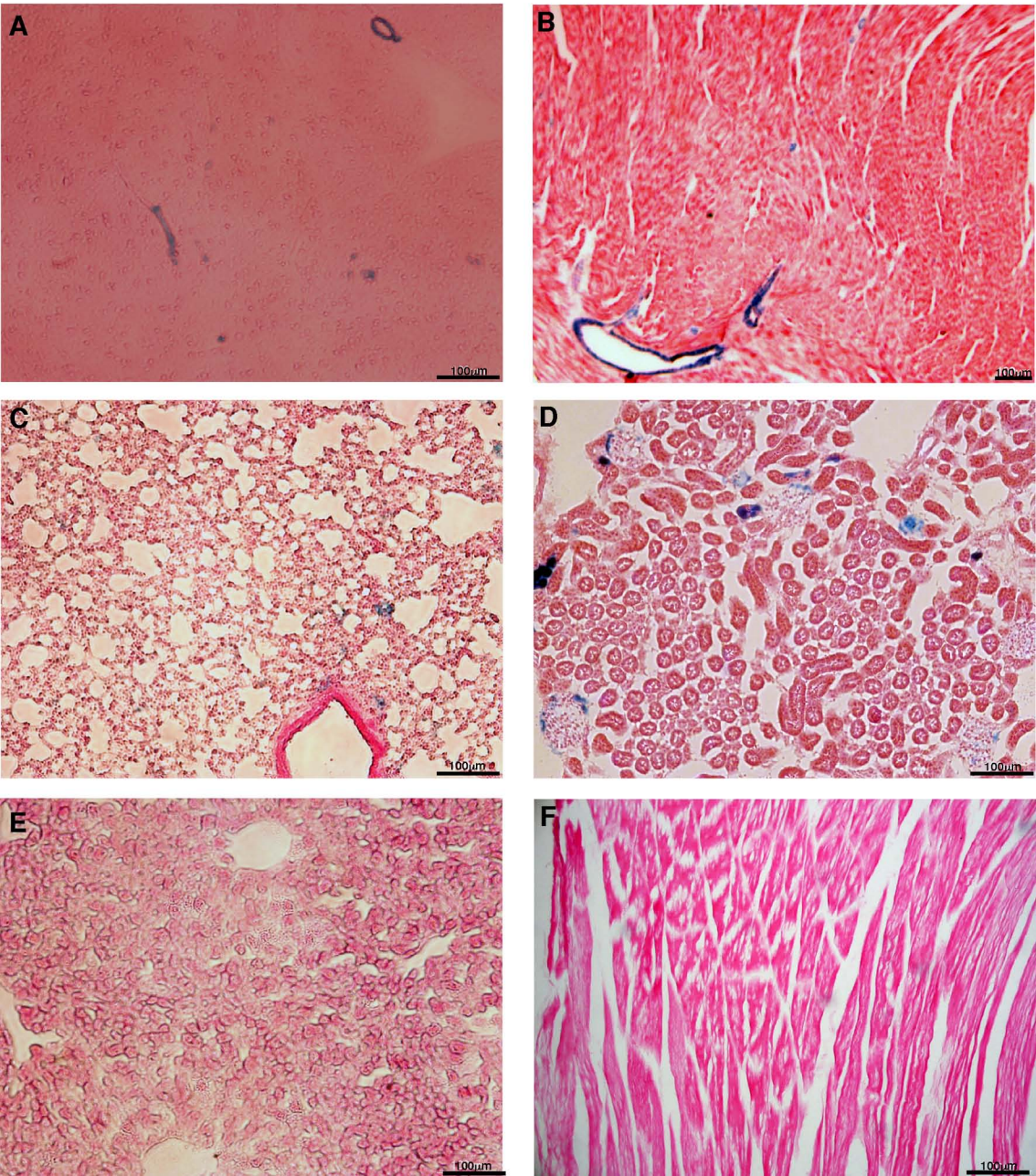
Supplemental Figure 8

DSCR-1 overexpression in endothelium using the Flt-1 promoter. *A,* HMVEC or B16-F1 melanoma was infected adenovirus containing Flt1 promoter plus EGFP alone (Flt1-control) or EGFP and DSCR-1 (Flt1-DSCR-1) for 7 days. Cells were observed under the fluorescent field and bright field. Bar = 200μm. *B,* Total cell lysates derived from HMVEC (lanes 1 and 2) and B16-F1 (lanes 3 and 4) were subjected to immunoblotting using anti-DSCR-1 antibody. β-Actin antibody was used for loading internal control. *C*, Either $5x10^9$ pfu of Ad-Flt1-control or Ad-Flt1-DSCR-1 was injected into C57BL6 mice. After 7 days, organs were removed for real-time PCR analysis with human specific DSCR-1 primer pairs. The results show the means and the standard deviations of expression levels relative to cyclophilin A. * $P<0.001$ compared with expression level from Ad-Flt1-Control. *N.S.*, non-significant. *D,* Lungs were harvested after 10 days following the administration of Ad-Flt1-DSCR-1. Cryo-sections (10 μm) were fixed and observed immuno-stained anti-EGFP (green), or anti-PECAM-1 (red) antibody, or DAPI (blue). Each image was merged and photographed under fluorescent microscopy. Bar = 50μm.

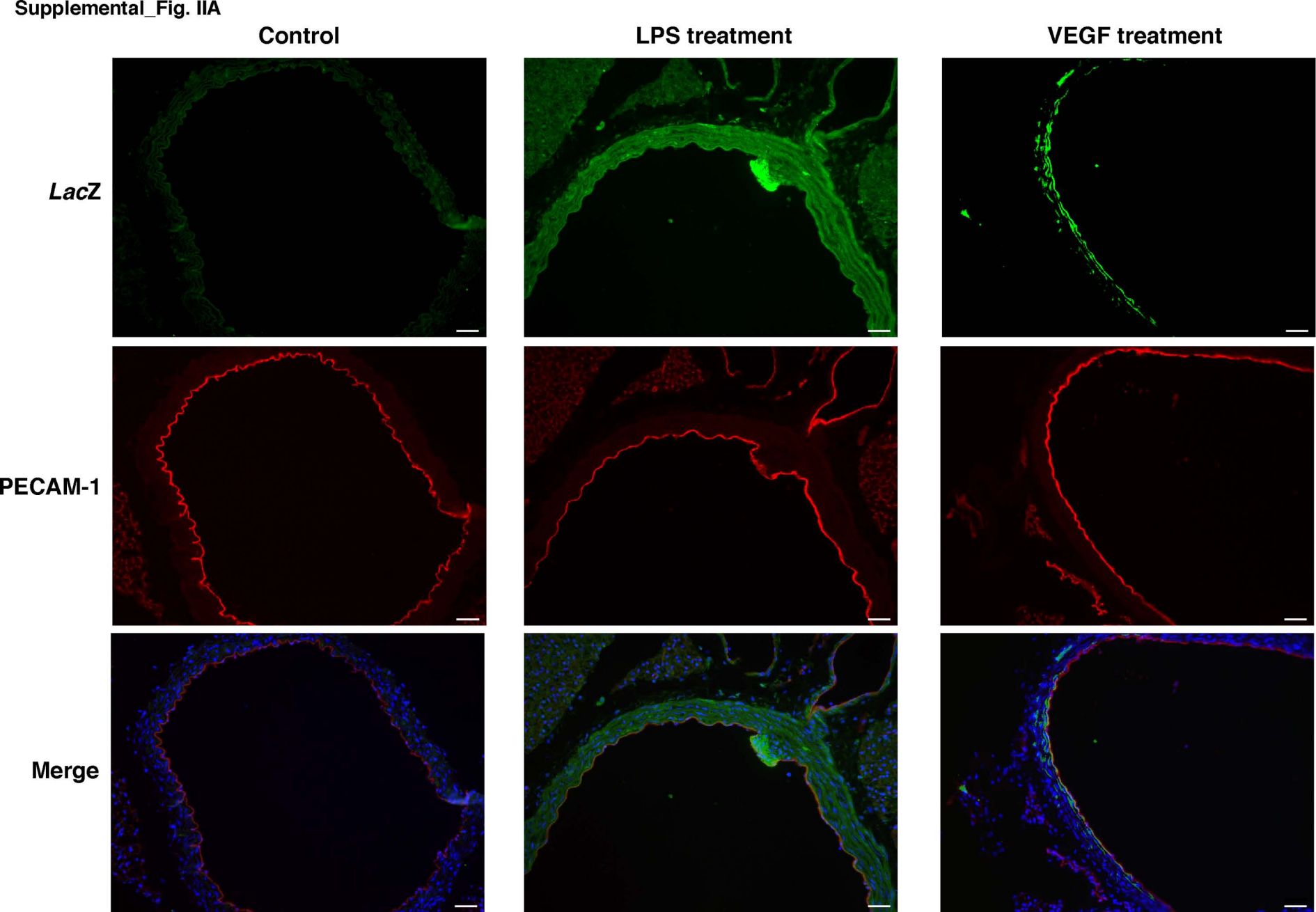
Supplemental Figure 9

DSCR-1 modulates sepsis morbidity. *A,* mice were treated in the absence or presence of 16 mg/kg LPS for 20 h. Plasma samples were harvested and measured IL-6 level by ELISA. Data are expressed as means and the standard deviations, n=10. * $P<0.001$, ** $P<0.01$, *** $P<0.05$ compared with WT or Ad-Flt1-control on each condition. *N.S.*, non-significant. *B,* mice were treated without or with LPS for 24 h. Heart rate and blood pressure were measured. The results show the means and the standard errors of the mean, n=6 (# n=3, due to the mice death or under the detection limit). * $P<0.001$, ** $P<0.05$ compared with WT or Ad-Flt1-control on each condition. *C,* WT (black), DSCR-$1^{-/-}$ (DSCR-1 KO (green)), or mice administrated Ad-Flt1-control (red) or DSCR-1s (blue) were treated 16 mg/kg LPS. Following 0, 2, 4, 6, 13 (WT and DSCR-$1^{-/-}$), 20, and 24 (Ad-Flt1-control and Ad-Flt1-DSCR-1s) h time points, mice body temperature was measured. Data was expressed as means and the standard deviations, n=8, except for DSCR-$1^{-/-}$ as n=6.

Supplemental_Fig. I



Supplemental_Fig. IIA



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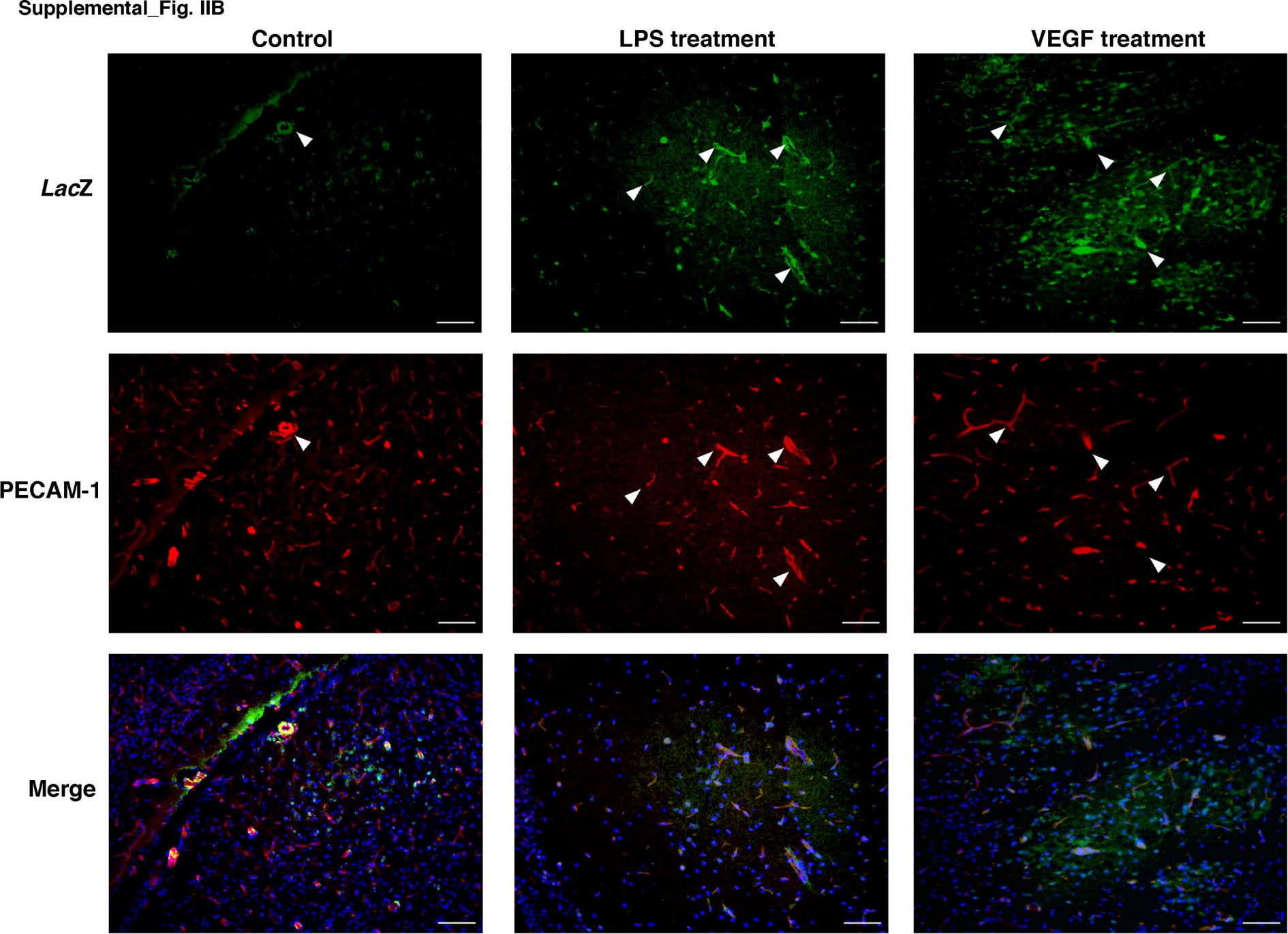

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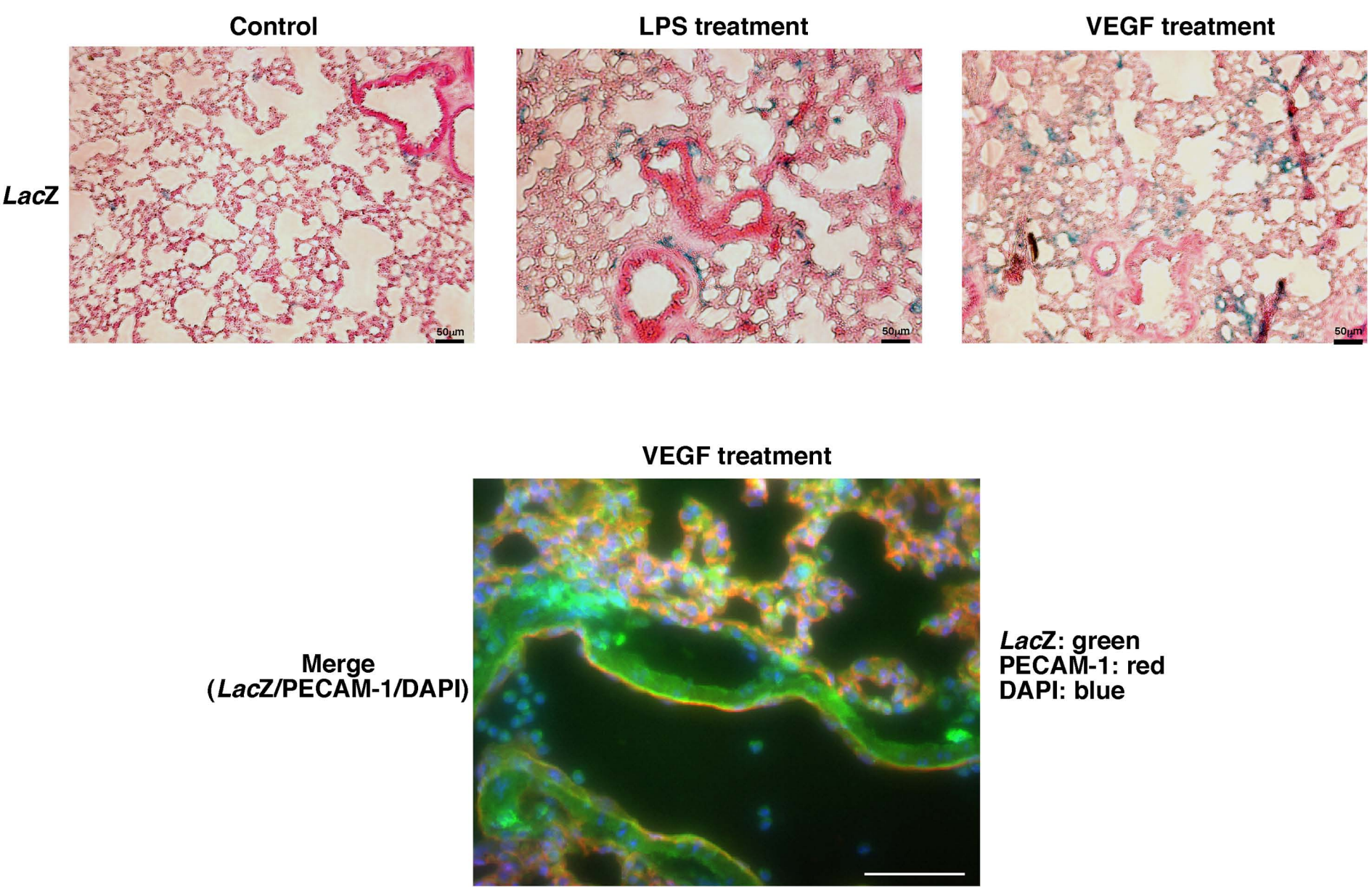

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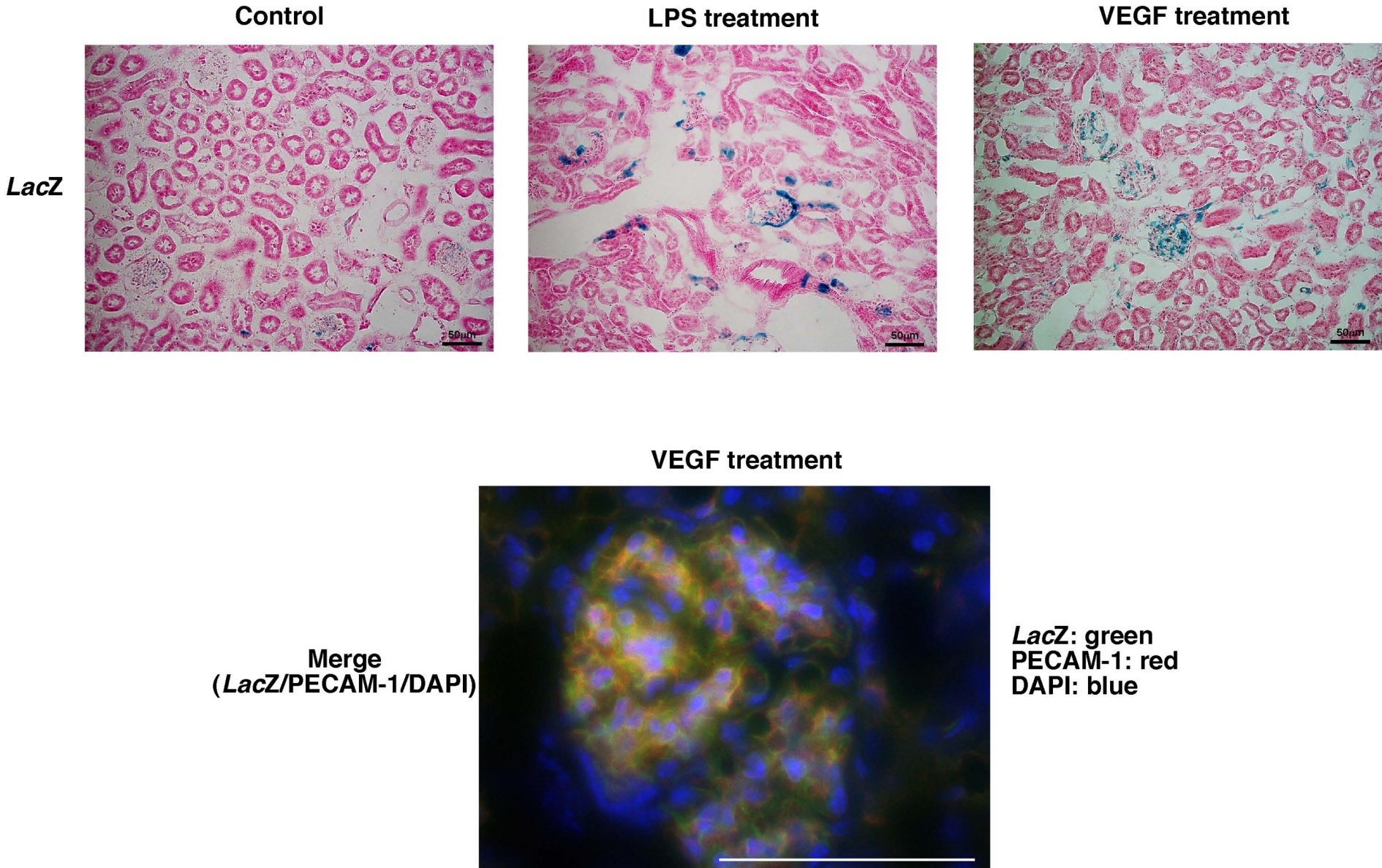

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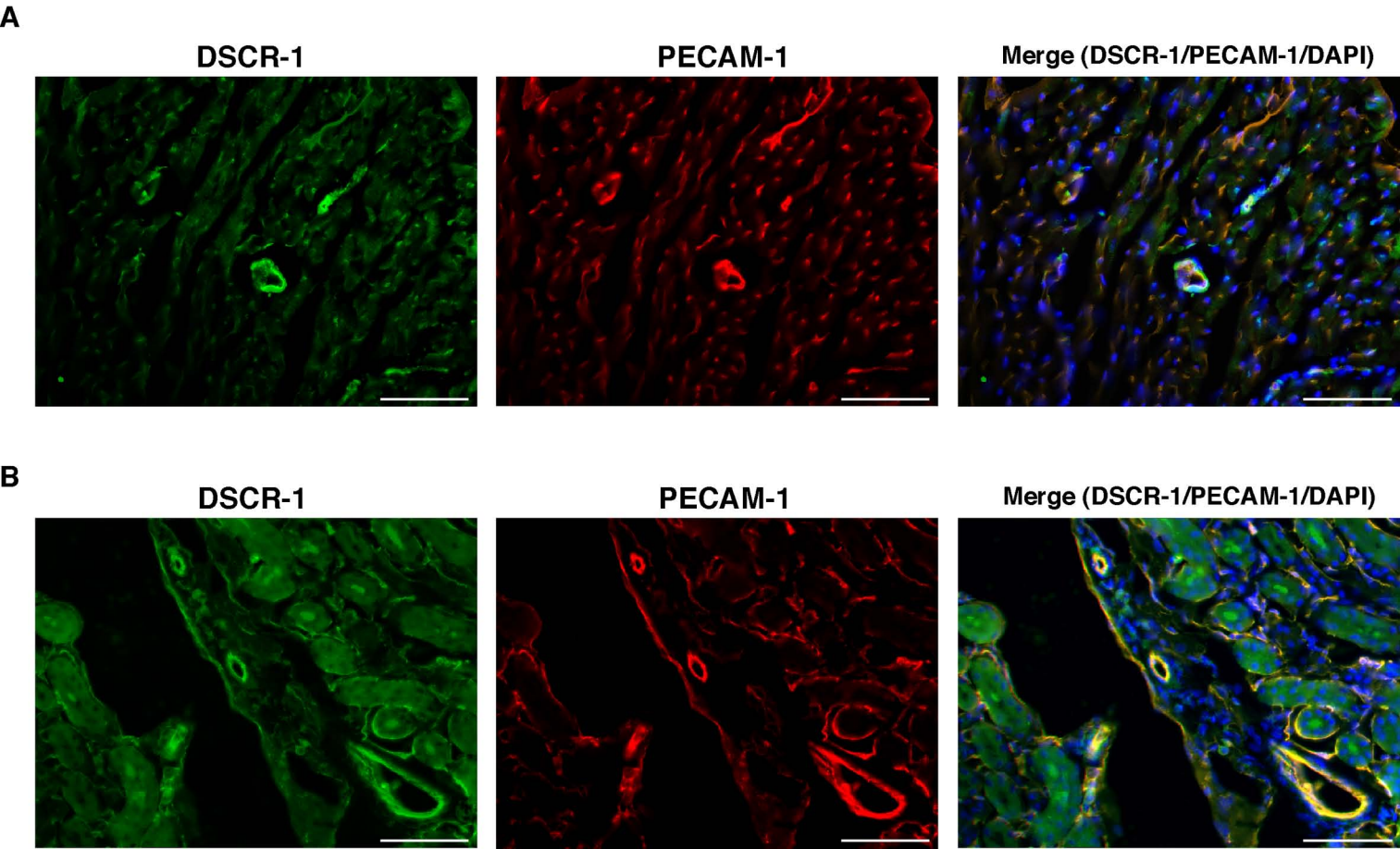
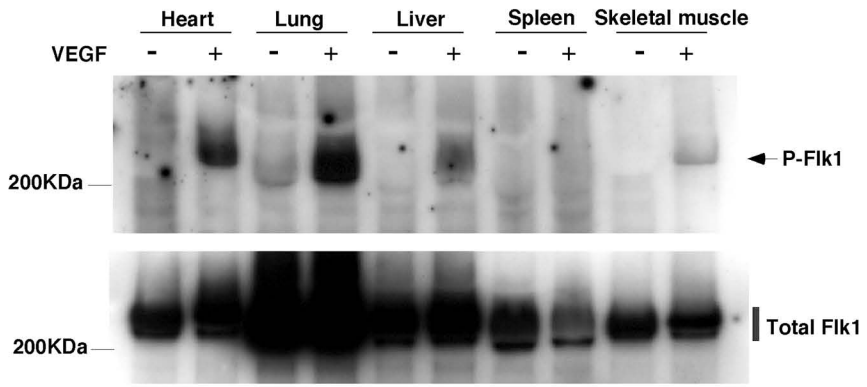


Supplemental_Fig. IV

A



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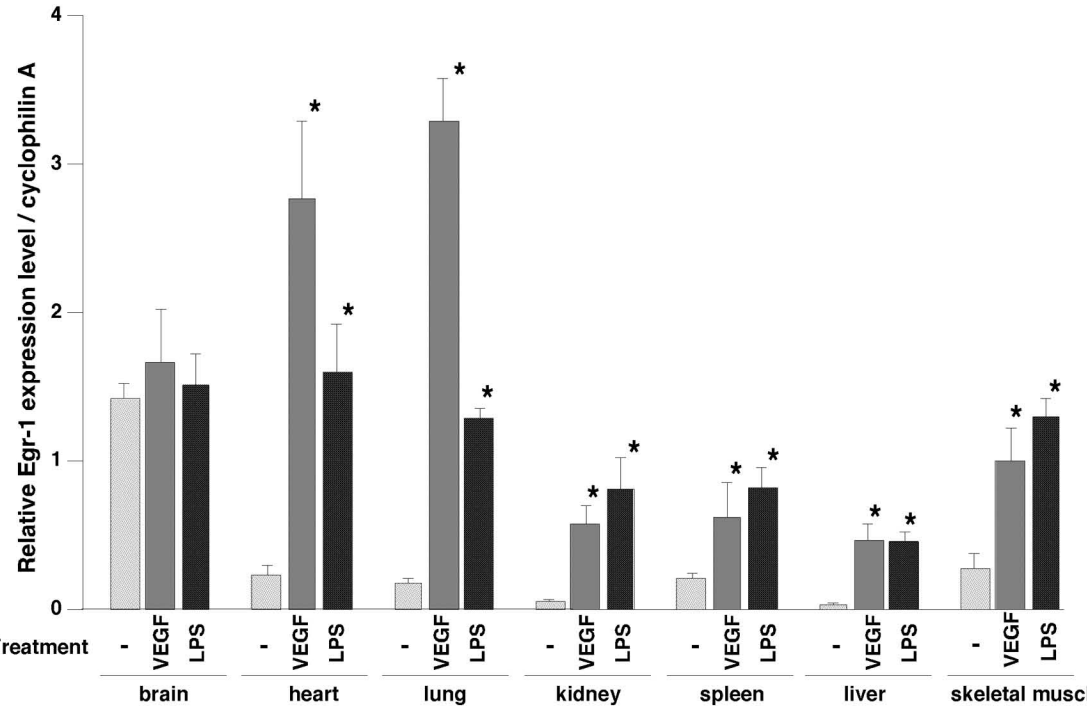

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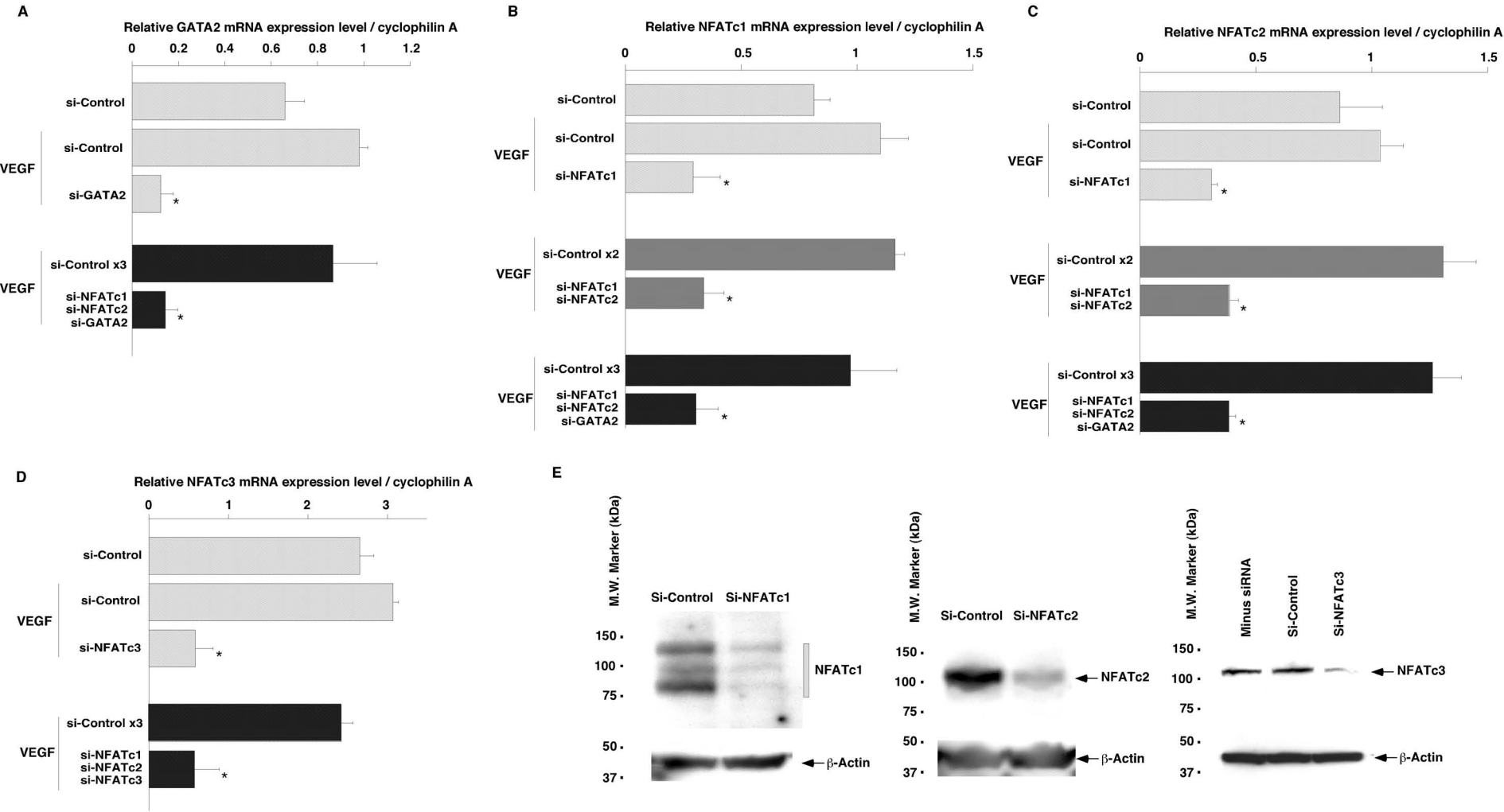
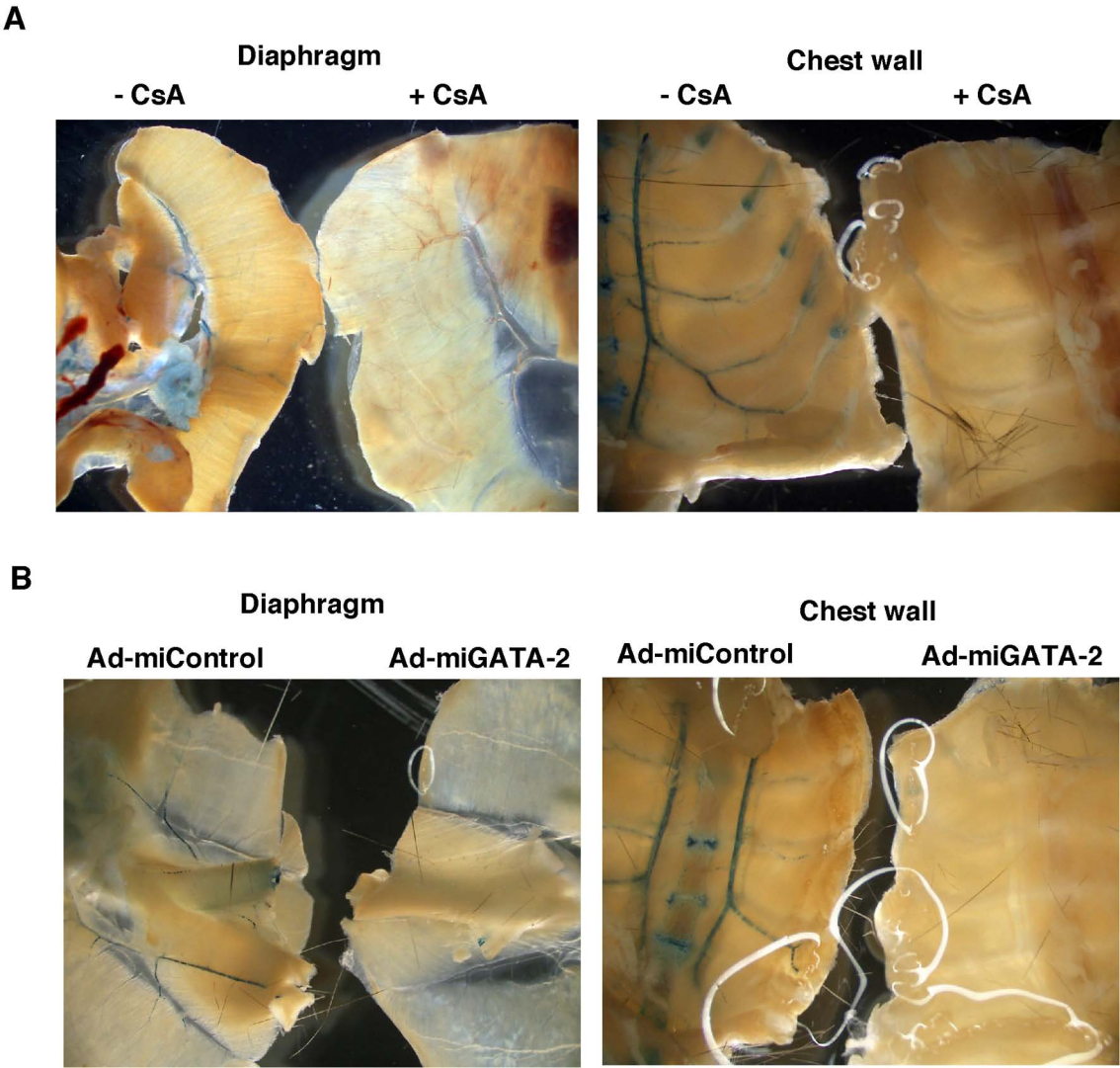
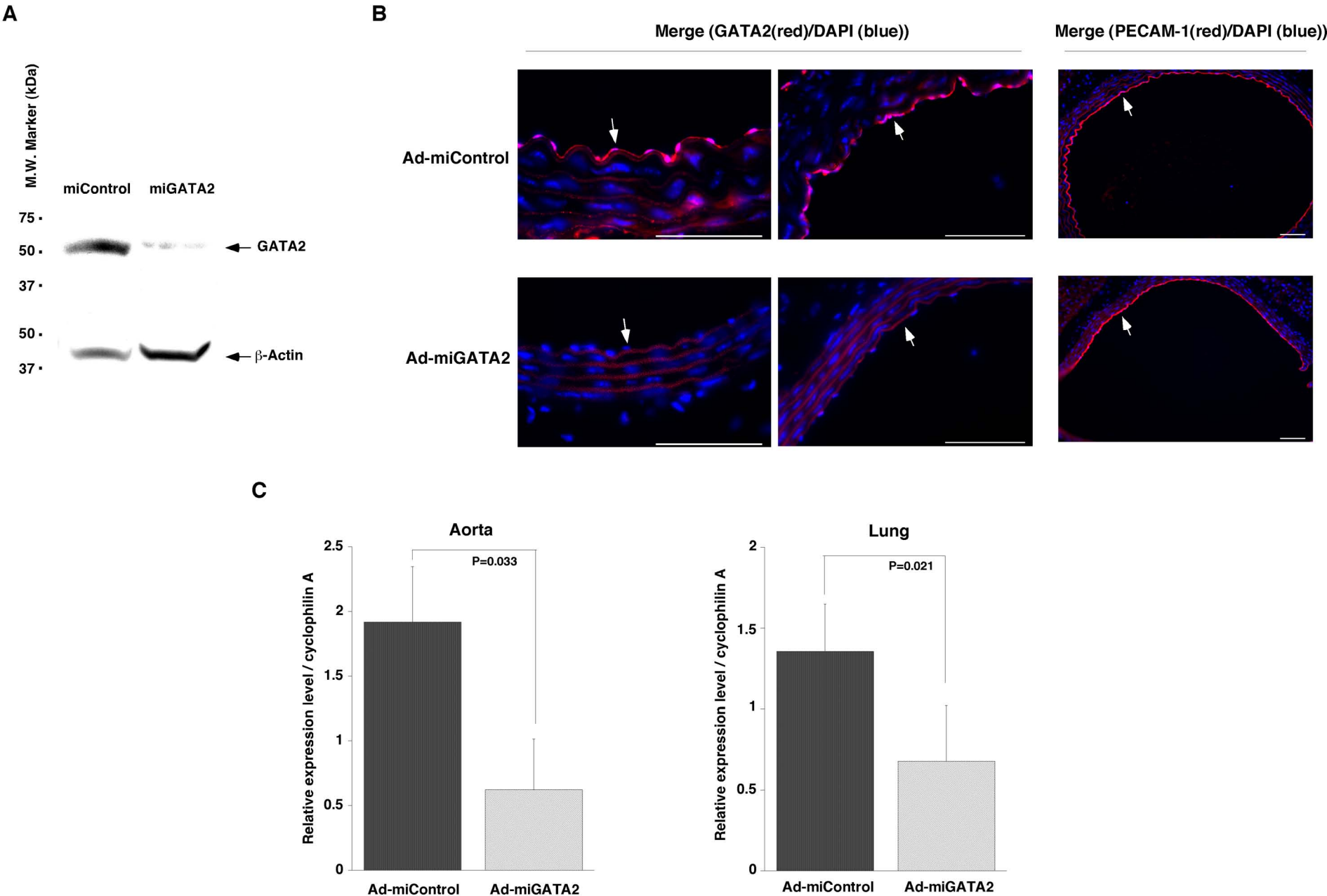


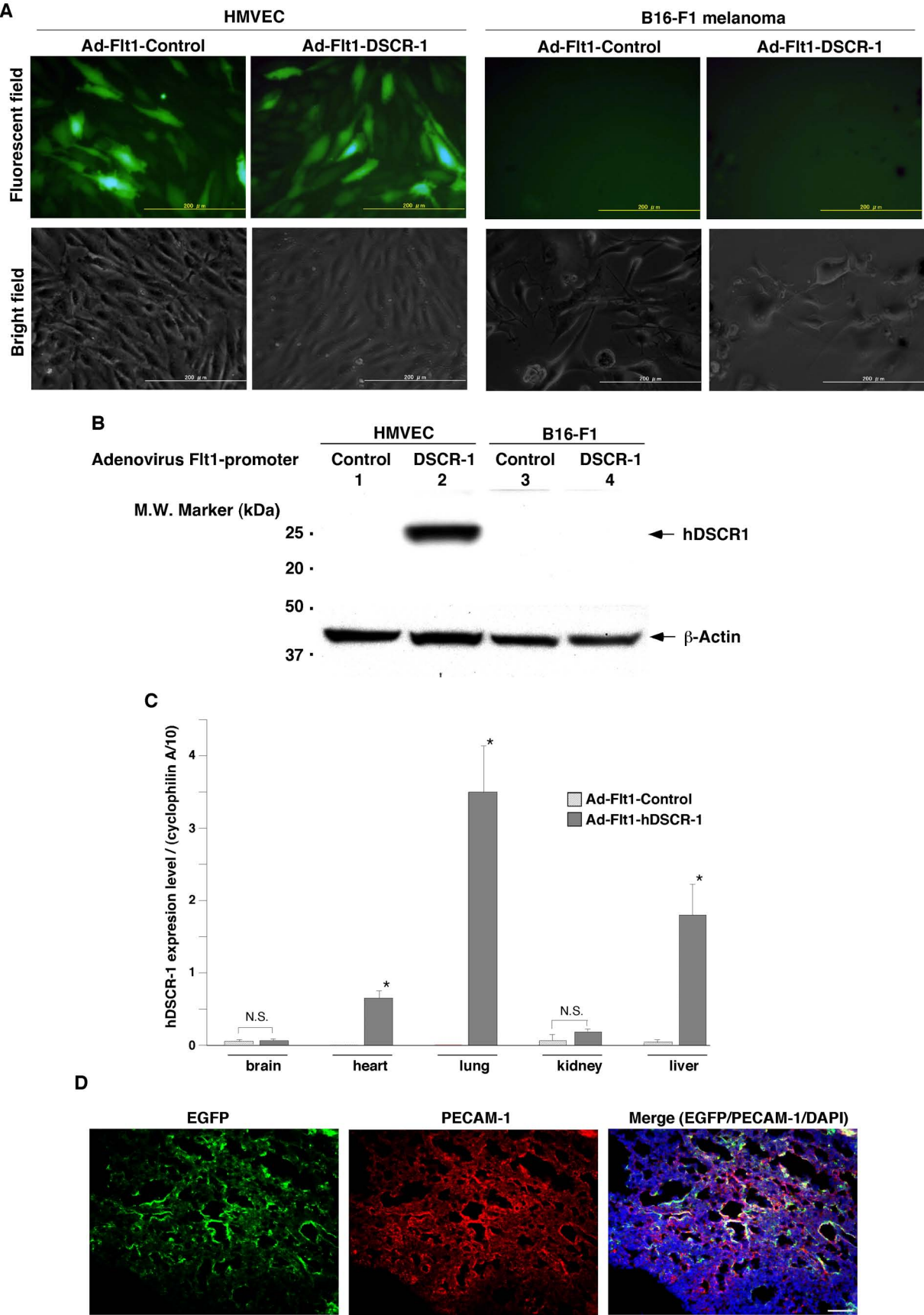
Supplemental_Fig. VI



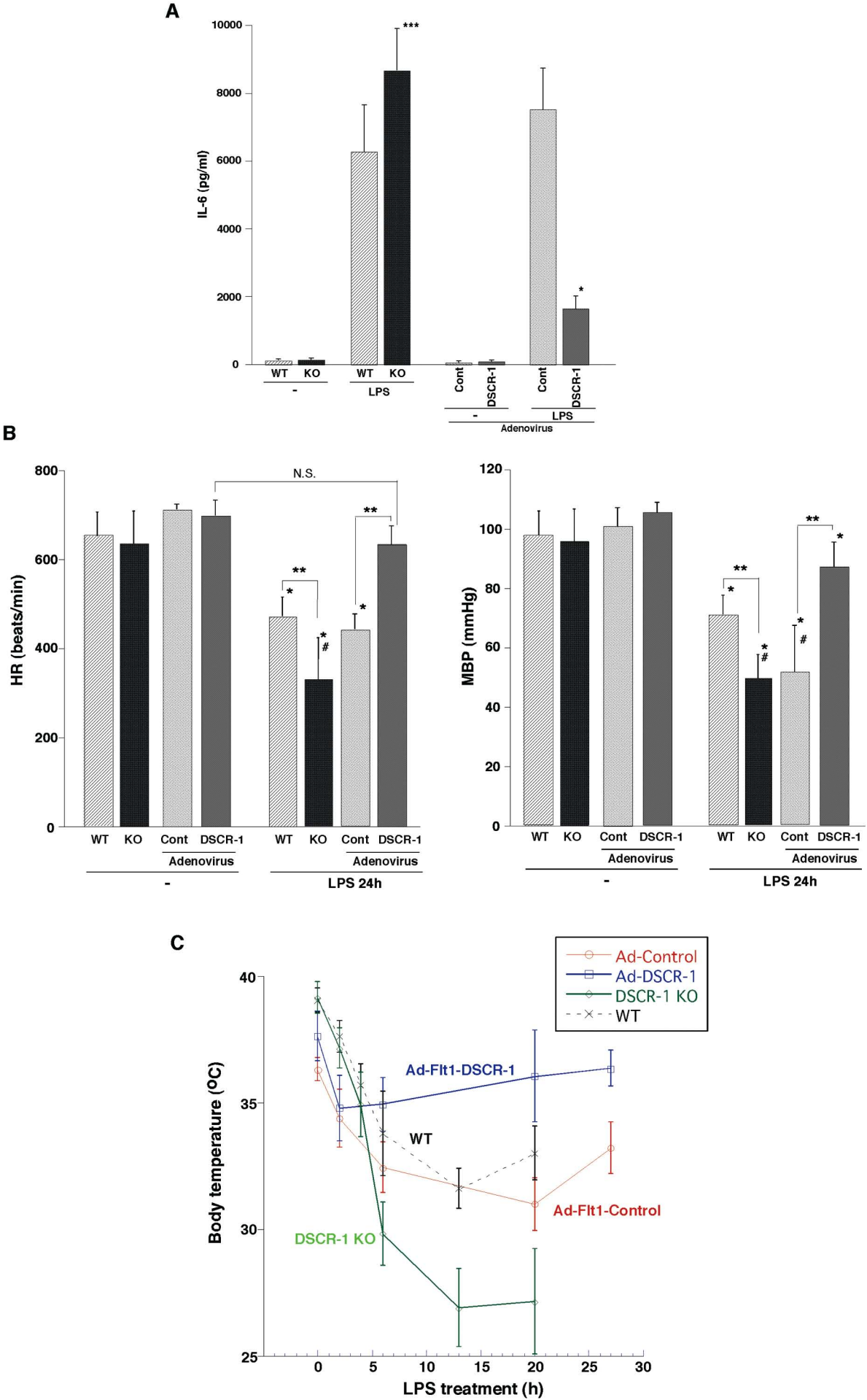
Supplemental_Fig. VII



Supplemental_Fig. VIII



Supplemental_Figure VIIII



Real-time primers

mDSCR-1 L

Forward GAG ATG GAG GAG GTG GAT CTG

Reverse TCA TAT GTT CTG AAG AGG GAT TCA

mDSCR-1s

Forward GCA GAA TGC ATT TTA GGG ACT TTA

Reverse TAA AAT ACT GGA AGG TGG TGT CCT

mGATA-2

Forward TAC CAC AAG ATG AAT GGA CAG AAC

Reverse ACA TTG TGC AGC TTG TAG TAG AGG

hGATA-2

used Hs_GATA2_1_SG QuantiTect Primer Assay

(QT00045381) (Qiagen)

hNFATc1

Forward GCA TGG CTA CTT GGA GAA TGA G

Reverse AGT TCA ATG TCG GAG TTT CTG AGT

hNFATc2

Forward TTT ACT GAG AAG ACC ACA GAT GGA

Reverse GTA GGT AAA GTG CTG AGG CTG ACT

hNFATc3

Forward AAG CCA AGA GAT AAT AAT TGC CAG

Reverse TAT ATC TGA ATT GCG GAG TTT CAA

hDSCR-1s

Forward ATC TCT TAT ATG CCA TCT CCA AGC

Reverse TGG ATA ATT TTT GGC TTA GGT CTC

hCyclophilin A

Forward TGG TTC CCA GTT TTT CAT CTG C

Reverse CCA TGG CCT CCA CAA TAT TCA

mCyclophilin A

Forward CAA AGA CAC CAA TGG CTC ACA G

Reverse CCA CAT CCA TGC CCT CTA GAA

mEgr1

Forward GCC TCG TGA GCA TGA CCA AT

Reverse GCA GAG GAA GAC GAT GAA GCA

mVCAM-1

Forward GAA CCC AAA CAG AGG CAG AGT G

Reverse GGA CTG CCC TCC TCT AGT ATA GGA

mE-selectin

Forward TTG AGT GCA CAT CTC AGG GAA A

Reverse GAC GTC AAG GCT TGG ACA TTG

mICAM-1

Forward GGT GAC TGA GGA GTT CGA CAG AA

Reverse TCT GCG TCT CCA GGA TCT GG

lacZ

Forward ACG CGC GAA TTG AAT TAT GG

Reverse GTT GAC TGT AGC GGC TGA TGT T

for knock down oligomers

SiRNA target sequences

hGATA2 Forward UUC UUG GAC UUG UUG GAC AUC UUC C

Reverse GGA AGA UGU CCA ACA AGU CCA AGA A

hNFATc1 Forward UUC CGG CAC AGU CAA UGA CGG CUC G

Reverse CGA GCC GUC AUU GAC UGU GCC GGA A

hNFATc2 Forward UUU CUC UUC CCA UUG AUG ACG UAG A

Reverse UCU ACG UCA UCA AUG GGA AGA GAA A

hNFATc3 Forward GCU GCC UCU AGU CAA GAA UUU GAU U

Reverse AAU CAA AUU CUU GAC UAG AGG CAG C

miRNA target sequence

mGATA2 Forward TGC TGA AGA GAT GGG AGC CCG AGT GGG TTT TGG CCA
CTG ACT GAC CCA CTC GGT CCC ATC TCT T

Reverse CCT GAA GAG ATG GGA CCG AGT GGG TCA GTC AGT GGC
CAA AAC CCA CTC GGG CTC CCA TCT CTT C