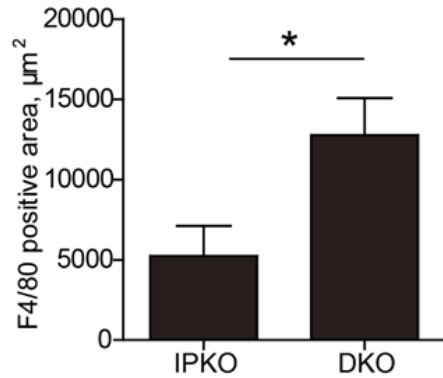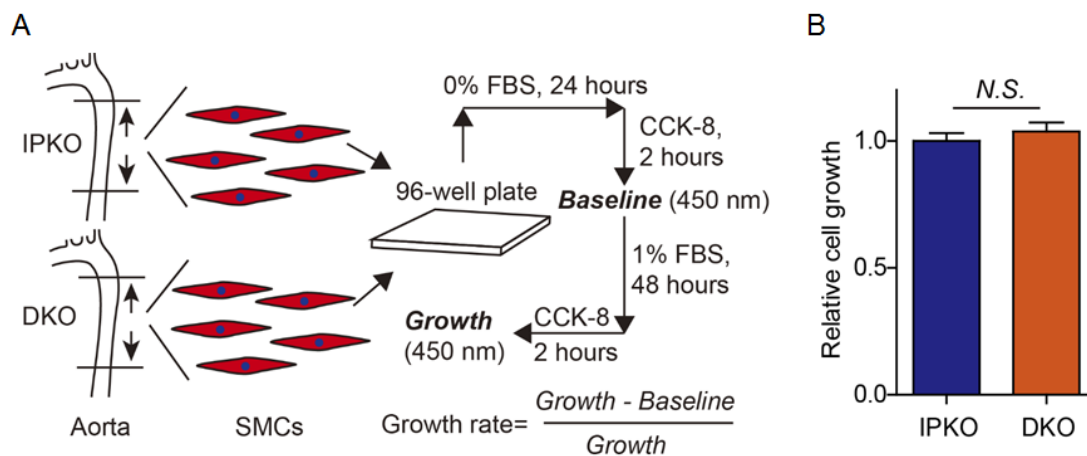**Supplemental Material**

Supplemental Figures and Figure Legends

Supplemental Figure Ⅰ. Quantification of F4/80 positive area in the vessels from IP KO and DKO mice 7 days after injury. n=4 IPKO, 5 DKO; *P<0.05; Student's unpaired t-test.


Supplemental Figure Ⅱ. Determination of proliferation of the aortic smooth muscle cells isolated from IPKO and DKO mice.
Smooth muscle cells (SMCs) were isolated from the descending aortae of IPKO and DKO mice, and their cell proliferation was analyzed in vitro (A) and compared (B). n=8 wells from 2 independent experiments.
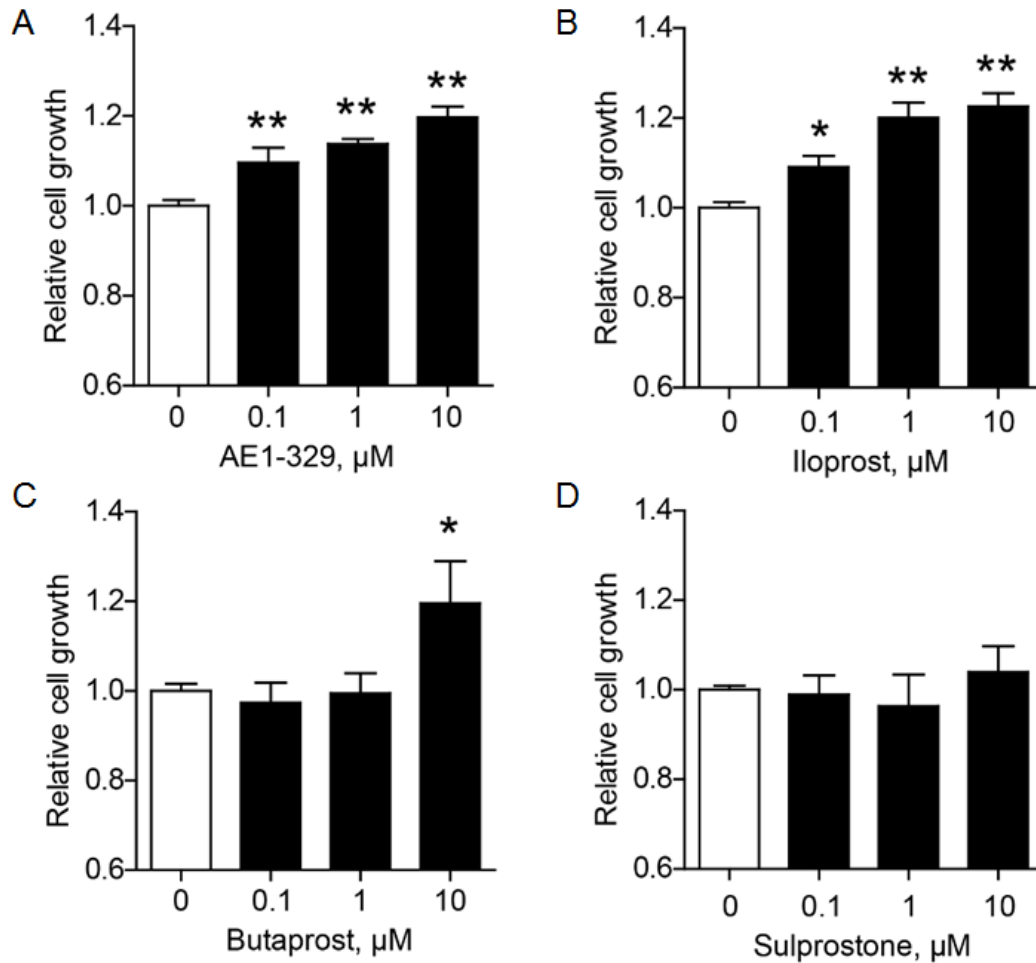
**Supplemental Figure Ⅲ. The concentration-response of AE1-329 (A), iloprost (B), butaprost (C) and sulprostone (D) on endothelial proliferation.** n=9 wells from three independent experiments; *$p<0.05$, **$p<0.01$, One-way ANOVA with Turkey's post tests.
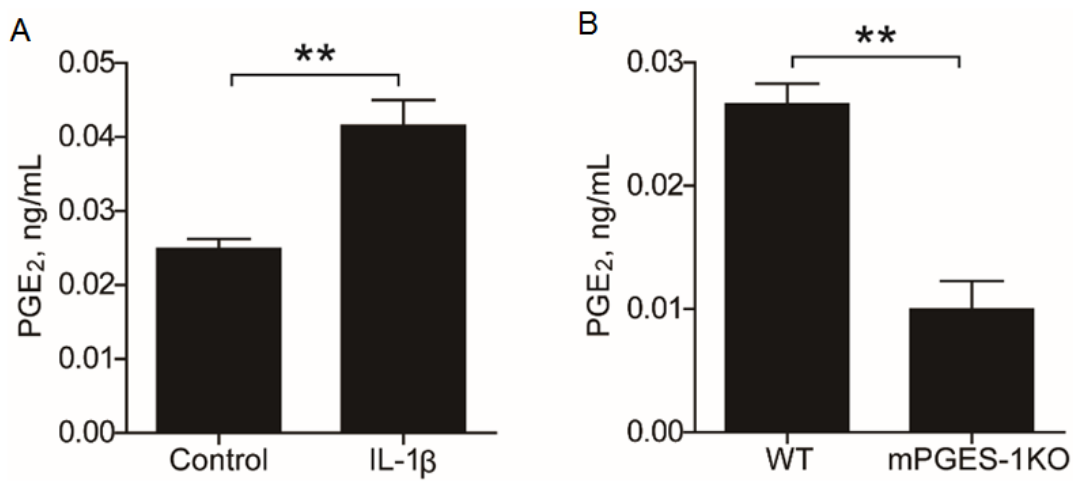

Supplemental Figure Ⅳ. Supernatant PGE_2 levels of cultured mouse aortic endothelial cells (MAECs) determined by HPLC-MS/MS method.

MAECs were treated with vehicle (Control) or IL-1β (10 ng/mL) for 12 hours, PGE_2 levels were shown (**A**). Supernatant levels of PGE_2 were significantly depressed in mPGES-1 deficient (mPGES-1KO) MAECs, compared with that in wildtype (WT) cells (**B**). n=4, **P<0.01; Student's unpaired t-test.


Vehicle + - + -
Forskolin - + - +
H 89 2HCl - - + +
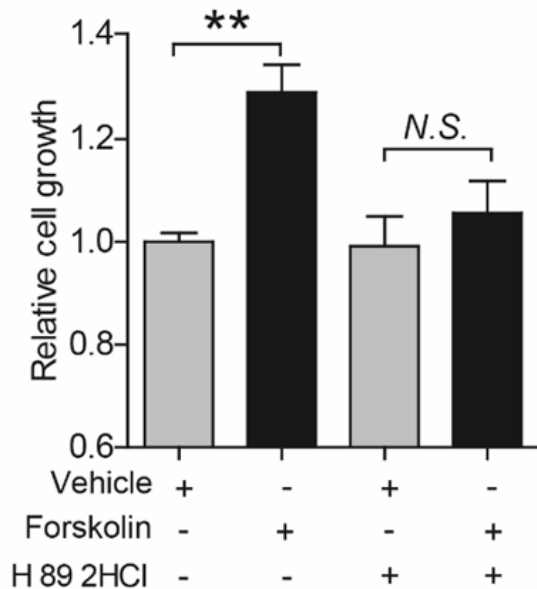
Supplemental Figure Ⅴ. Forskolin (an adenylate cyclase activator, 3 µmol/L) promoted endothelial proliferation, which were blunted by H89 2HCl (a PKA inhibitor). n=7; **P<0.01; One-way ANOVA with Bonferroni's post-test.
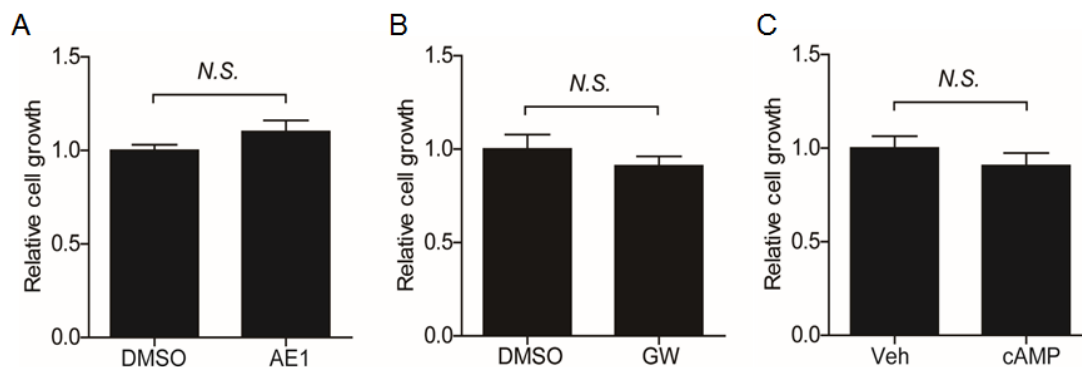
Supplemental Figure Ⅵ. AE1-329, GW627368X and db-cAMP did not affect EC proliferation under condition of PKA inhibition.
When MAECs were treated with PKI (a PKA inhibitor, 10 µmol/L), EP4 agonist (AE1-329, abbreviated as AE1, 1 µmol/L), EP4 antagonist (GW627368X, abbreviated as GW, 1 µmol/L), or db-cAMP (a cell permeable cAMP analogue, 30 µmol/L) failed to affect cell proliferation. Each result was from three independent data sets.
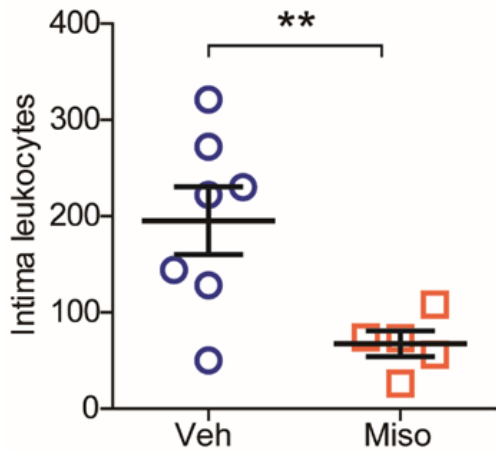
Supplemental Figure Ⅶ. Misoprostol administration (100 µg/Kg, i.p., three times a day) decreased the number of leukocytes infiltrated to intima, as examined at 7 days after the vascular injury. **P<0.01; Student's unpaired t-test.
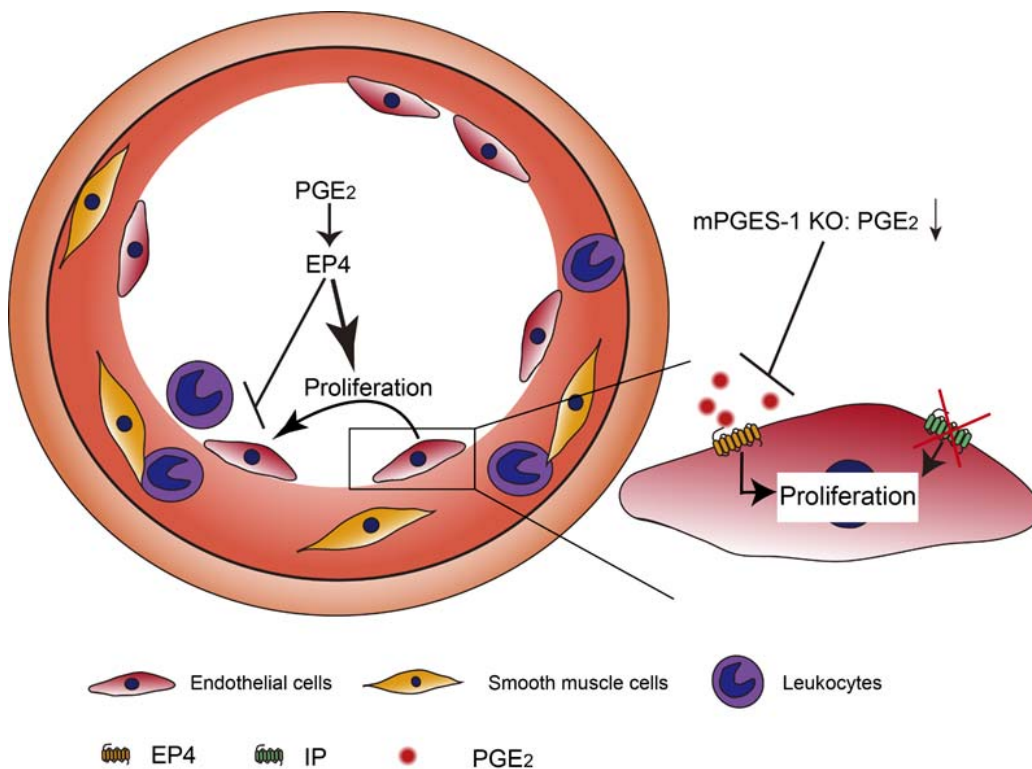
Supplemental Figure Ⅷ. Schematic illustration of the mechanism of mPGES-1 derived PGE$_2$ in the vascular response to injury.
Knockout of mPGES-1 decreases PGE$_2$, and increases PGI$_2$. In IP deficient mice, a protective role of mPGES-1 derived PGE$_2$ was discovered. PGE$_2$, via EP4 receptor on endothelial cells, stimulates endothelial proliferation, suppresses leukocytes adhering to endothelial cells, and protected the injured vessels against development of neointimal hyperplasia. Arrow indicates stimulating effect, while line with a blunt end indicates inhibitory effect.

Supplemental Tables

Supplemental Table Ⅰ. Data analysis with gender information in the IPKOs and DKOs.

Gender	Male		Female		Gender mixed	
Genotype	IPKO	DKO	IPKO	DKO	IPKO	DKO
Intima area (28 days)	24.1±2.7 (n=10)	44.6±6.4 (n=10)	20.3±5.9 (n=4)	38.5±3.3 (n=6)	23±2.5 (n=14)	42.3±4.2 (n=16)
Ratio of I to M (28 days)	1.85±0.2 (n=10)	2.39±0.2 (n=10)	1.15±2.7 (n=4)	2.68±0.3 (n=6)	1.69±0.2 (n=14)	2.5±0.17 (n=16)
Intima area (7 days)	16.3±2.5 (n=11)	22.4±3.2 (n=12)	12.5±0.5 (n=3)	21.4±0.9 (n=4)	15.5±2.0 (n=14)	22.1±2.4 (n=16)
Ratio of I to M (7 days)	1.05±0.2 (n=11)	1.68±0.3 (n=12)	1.14±0.1 (n=3)	1.84±0.2 (n=4)	1.12±0.1 (n=14)	1.72±0.2 (n=16)
Intima leukocytes	140±17 (n=5)	193±26 (n=5)	161±23 (n=3)	246±21 (n=5)	148±13 (n=8)	219±18 (n=10)
Reendothelialization (%)	49.0±3.0 (n=6)	38.0±2.7 (n=5)	47.7 (n=1)	41.9±6.6 (n=2)	48.8±2.5 (n=7)	39.2±2.5 (n=7)

Note: Area ($\times 10^3$ μm^2).

Supplemental Table Ⅱ. Data analysis with gender information in the EP4 Ctls and EP4 cKOs.

Gender	Male		Female		Gender mixed	
Genotype	EP4 Ctl	EP4 cKO	EP4 Ctl	EP4 cKO	EP4 Ctl	EP4 cKO
Intima area (28 days)	19.3±4.1 (n=6)	30.5±6.7 (n=4)	17.1±2.6 (n=8)	23.4±3.0 (n=6)	18±2.2 (n=14)	26.2±3.2 (n=10)
Ratio of I to M (28 days)	1.20±0.3 (n=6)	2.14±0.3 (n=4)	1.26±0.2 (n=8)	1.76±0.4 (n=6)	1.24±0.1 (n=14)	1.91±0.3 (n=10)
Intima area (7 days)	11.6±1.7 (n=5)	20.6±4.0 (n=5)	8.1±2.4 (n=2)	11.7±0.7 (n=2)	10.7±1.4 (n=7)	18.3±3.2 (n=7)
Ratio of I to M (7 days)	0.66±0.2 (n=5)	1.37±0.2 (n=5)	0.61±0.2 (n=2)	1.15±0.1 (n=2)	0.65±0.1 (n=7)	1.31±0.1 (n=7)
Intima leukocytes	57±15 (n=6)	105±17 (n=6)	33±8 (n=2)	41±13 (n=2)	51±12 (n=8)	89±16 (n=8)
Reendothelialization (%)	62.3±5.7 (n=6)	42.1±7.0 (n=5)	59.6 (n=1)	39.6±5.2 (n=2)	61.9±4.8 (n=7)	41.3±4.6 (n=7)

Note: Area ($\times 10^3$ μm^2).