Supporting Information

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SI Materials and Methods

Materials. Human prostate cancer 3 (PC-3), mouse breast cancer Met-1, Lewis lung carcinoma (LLC), and mouse melanoma B16F10 cells were from ATCC. Human umbilical vein endothelial cells (HUVECs, Clonetics) from Lonza were cultured in endothelial basal medium-2 with supplements according to the manufacturer's instructions. Assays with HUVECs were conducted with cells from passages 2–6.

Cell Proliferation Assay. HUVECs or cancer cells were seeded in 24-well or 96-well plates in complete medium and allowed to attach overnight. The cells were then treated with test compounds for 24 h. Cell proliferation was measured using BrdU (Millipore) or MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay (Sigma-Aldrich).

Tube Formation Assay. The 96-well plates were coated with 35 μL per well of growth-factor reduced Matrigel (BD Biosciences), solidified at 37 °C for 30 min; then $1.5–2 \times 10^4$ HUVECs in 100 μL basal medium were added to each well (1). After a 6-h treatment, the cells were stained with Calcein AM and fluorescence microscope images were recorded and analyzed by Wimasis Image Analysis (2).

Gelatin Zymography. HUVECs were seeded in six-well plates in complete endothelial medium and allowed to attach overnight; then the cells were treated with test compounds for 4–6 h. Matrix metalloproteinase (MMP) activity in the cell culture medium was analyzed by zymography using Novex 10% Zymogram (gelatin) gel (Invitrogen).

HUVEC Migration Assay. Cell culture inserts for 24-well plate containing membrane with 8-μm pores (BD Biosciences) were coated with 10 μg/mL fibronectin (BD Biosciences) or vitronectin (R&D Systems) at 37 °C for 1 h. HUVECs (5×10^4 cells per well) were seeded onto the upper chamber of cell culture inserts in 400 μL serum-free medium, the bottom chamber was filled with 500 μL basal medium containing 10 ng/mL human vascular endothelial growth factor (VEGF) 165 (R&D Systems) as chemoattractants. The test compounds were added into both top and bottom chambers. After an 18-h incubation, the inserts were washed by PBS, fixed by 5% glutaraldehyde for 30 min, and the unmigrated cells were removed by cotton swabs. The migrated cells were stained with crystal violet, and microscope images were recorded. Cell counting was carried out using ImageJ software (3).

RT-PCR Angiogenesis Array and RT-PCR. HUVECs were seeded in six-well plates in complete endothelial medium and allowed to attach overnight; then the cells were treated with 3 μM 19,20-epoxydocosapentaenoic acid (19,20-EDP) in basal medium for 6 h. Total RNA was isolated and was subjected to a commercial human Angiogenesis RT^2 Profiler PCR Array (SABiosciences. The target genes from the array were further verified by RT-PCR, including TIMP3 (primer catalog Hs00165949_m1; Applied Biosystems), ANGPTL4 (Hs01101127_m1), VEGF-A (Hs00900055_m1), and VEGF-C (Hs01099203_m1).

Immunoblotting. HUVECs were seeded in six-well plates in complete endothelial medium and allowed to grow to ∼90% confluence, followed by serum-starvation in basal endothelial medium for 24 h. The cells were treated with 1 μM 19,20-EDP or 14,15-epoxyeicosatrienoic acid (EET), and then immediately stimulated with 50 ng/mL human VEGF 165 (R&D Systems) for 10 min. The medium was decanted, washed with cold PBS buffer, and then the cells were lysed and the cell lysates were resolved using SDS/PAGE and transferred onto a nitrocellulose membrane. The membranes were blocked in 5% nonfat dry milk for 1 h at room temperature and probed with rabbit monoclonal phospho VEGFR2 (Tyr1175) antibody (Cell Signaling Technology) and mouse monoclonal anti–β-actin antibody (Sigma-Aldrich). The membranes were then probed with horseradish peroxidase (HRP)-tagged secondary antibodies. The secondary antibodies on the blot were detected by an ECL Plus Western blotting detection reagent (GE Healthcare).

Cancer Cell Invasion Assay. Cell culture inserts for 24-well plate containing membrane with 8-μm pores were coated with 20 μL of 1:6 diluted Matrigel (BD Biosciences) and the Matrigel was allowed to solidify at 37 °C for 30 min. PC-3 cells (5×10^4 cells per well) were seeded onto the upper chamber of cell culture inserts in 100 μL serum-free medium; the bottom chamber was filled with 300 μL complete medium containing 10% FBS as chemoattractants. The test compounds were added into both top and bottom chambers. After a 24-h incubation, the inserts were washed by PBS, fixed by 5% glutaraldehyde for 30 min, and the uninvaded cells were removed by cotton swabs. The whole membrane of the insert was cut out using a surgical blade and stained with ProLong Gold antifade reagent with DAPI (Invitrogen) overnight. The fluorescence image of the whole membrane was scanned by a Nikon Eclipse TE2000-E microscope and cell counting was carried out using Velocity software (PerkinElmer) (4).

Lipidomics. For plasma lipid mediator extraction, a Waters Oasis solid phase extraction (SPE) cartridge were prewashed, 250 μL plasma with surrogate solution was loaded onto the SPE column, and washed with 95:5 (vol/vol) water/methanol with 0.1% acetic acid. The analytes were eluted with methanol and ethyl acetate, dried, and then reconstituted in methanol for LC-MS/MS analysis. For tumor lipid mediator extraction, ∼100 mg of tumor tissues were mixed with the antioxidant solution (0.2 mg/mL butylated hydroxytoluene and 0.2 mg/mL triphenylphosphine in methanol), the surrogate solution, and 400 μL extract solution (0.1% acetic acid with 0.2 mg/mL butylated hydroxytoluene in a methanol solution), and then homogenized; the resulting homogenates were kept in −80 °C overnight. After centrifugation of the homogenates, the pellets were washed with methanol (0.1% butylated hydroxytoluene and 0.1% acetic acid) and then combined with the supernatant. The combined solutions were extracted using SPE columns similar to the description above for the plasma lipid mediator extraction. The LC-MS/MS analysis was carried out on an Agilent 1200SL liquid chromatographic system (Agilent) coupled to a 4000 QTRAP MS/MS (AB SCIEX) as we previously described (5).

Imaging. Contrast-enhanced ultrasound images were acquired using an Acuson Sequoia 512 system (Siemens Medical Solutions), with a 15L8 linear array transducer at 7 MHz with a mechanical index of 0.28. After injection of the Definity contrast agent through a 24-gauge tail vein catheter in the tail vein, the time required for each pixel of the tumor to reach 80% of the final amplitude was assessed and values were used to create a parametric map.

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2. Khoo CP, Micklem K, Watt SM (2011) A comparison of methods for quantifying angiogenesis in the Matrigel assay in vitro. *Tissue Eng Part C Methods* 17(9):895–906.
3. Panigrahy D, et al. (2012) Epoxyeicosanoids stimulate multiorgan metastasis and tumor dormancy escape in mice. *J Clin Invest* 122(1):178–191.
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5. Yang J, Schmelzer K, Georgi K, Hammock BD (2009) Quantitative profiling method for oxylipin metabolome by liquid chromatography electrospray ionization tandem mass spectrometry. *Anal Chem* 81(19):8085–8093.

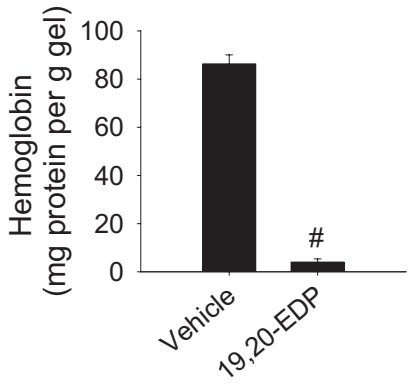

Fig. S1. Effect of 19,20-EDP on FGF-2–induced angiogenesis in a Matrigel plug assay in C57BL/6 mice (n = 4 mice per group). Assay condition: Matrigels containing 500 ng FGF-2, 20 units heparin, with or without 10 μg 19,20-EDP, were s.c. injected into mice. After 4 d of treatment, the gel plugs were dissected and hemoglobin in the gels were measured. All values represent means ± SD. $^{\#}P < 0.001$.

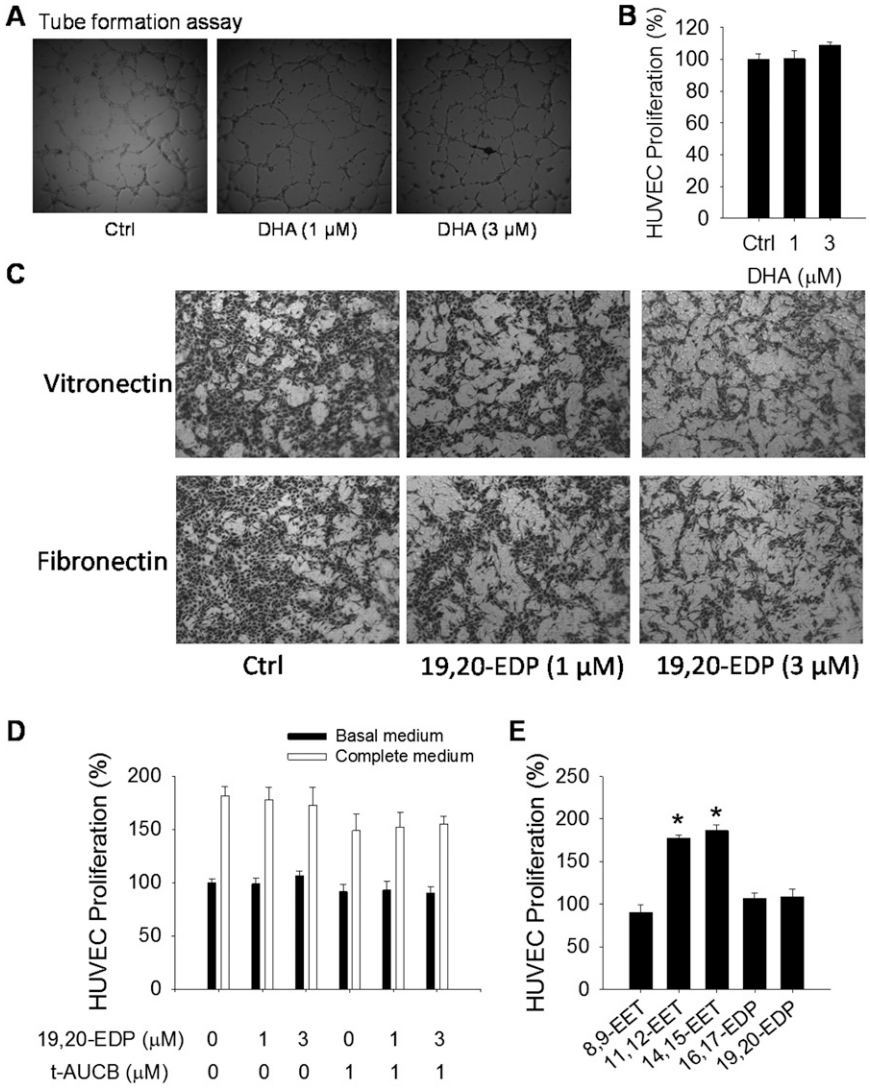

Fig. S2. (*A*) DHA (1–3 μM) has no effect on tube formation after 6-h treatment in HUVECs. Here shows representative HUVEC microscopy. In comparison, 19,20-EDP causes ~63% inhibition at 1 μM and ~91% inhibition at 3 μM as shown in Fig. 1*C*. (*B*) DHA has no effect on HUVEC proliferation after 24-h treatment. The 19,20-EDP (1–3 μM) also has no effect on HUVEC proliferation as shown in Fig. S2*D*. (*C*) The 19,20-EDP shows similar potency to inhibit VEGF-induced HUVEC migration on extracellular matrix proteins vitronectin and fibronectin. (*D*) Lack of effect of 19,20-EDP and *t*-AUCB on HUVEC proliferation after 24-h treatment in basal and complete medium. (*E*) Effects of 1 μM EET or EDP on HUVEC proliferation after 24-h treatment in basal medium. All values represent means ± SD. $^*P < 0.05$.

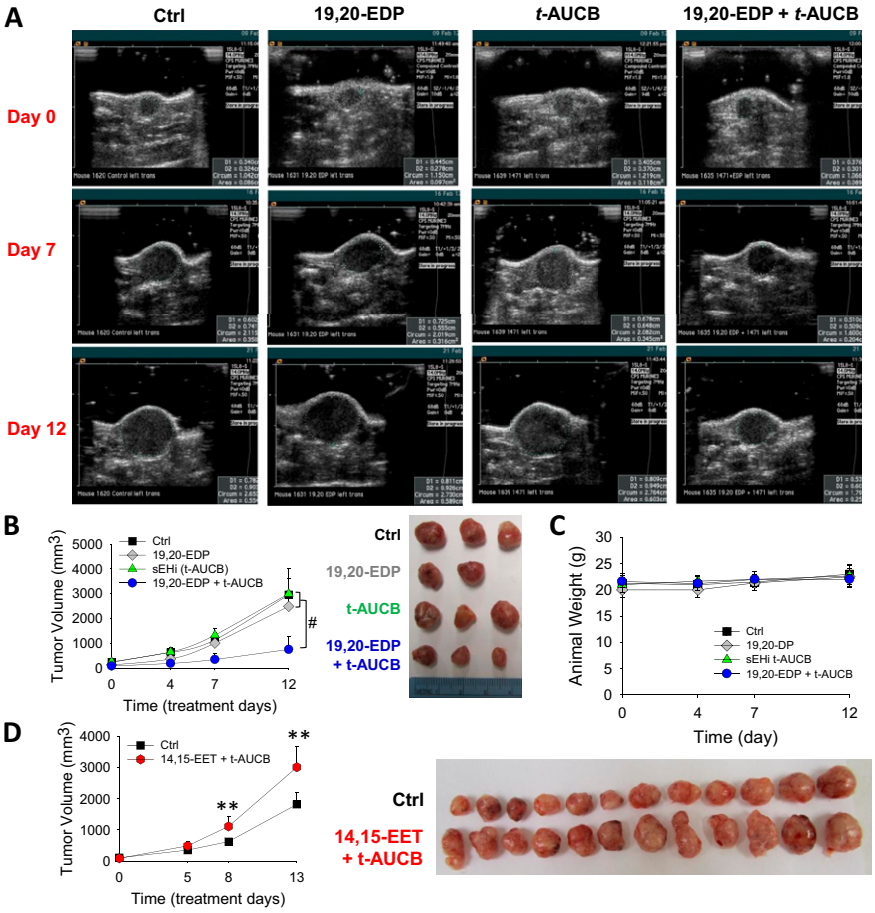

Fig. S3. (*A*) Images of representative ultrasound imaging of Met-1 tumors. Mice were continuously infused with (*i*) vehicle control, (*ii*) 0.05 mg·kg^{-1}·d^{-1} 19,20-EDP, (*iii*) 1 mg·kg^{-1}·d^{-1} *t*-AUCB, and (*iv*) 19,20-EDP + *t*-AUCB for 12 d. Only the combination of 19,20-EDP and *t*-AUCB significantly suppressed Met-1 tumor growth. (*B*) Representative images of Met-1 tumors of mice treated with 19,20-EDP (0.05 mg·kg^{-1}·d^{-1}) and/or *t*-AUCB (1 mg·kg^{-1}·d^{-1}). *Left* is from Fig. 2*A*. (*C*) Effect of 19,20-EDP and *t*-AUCB on animal weight in Met-1 experiment. (*D*) Representative images of Met-1 tumors of mice treated with 14,15-EET (0.05 mg·kg^{-1}·d^{-1}) and *t*-AUCB (1 mg·kg^{-1}·d^{-1}). *Left* is from Fig. 2*D*.

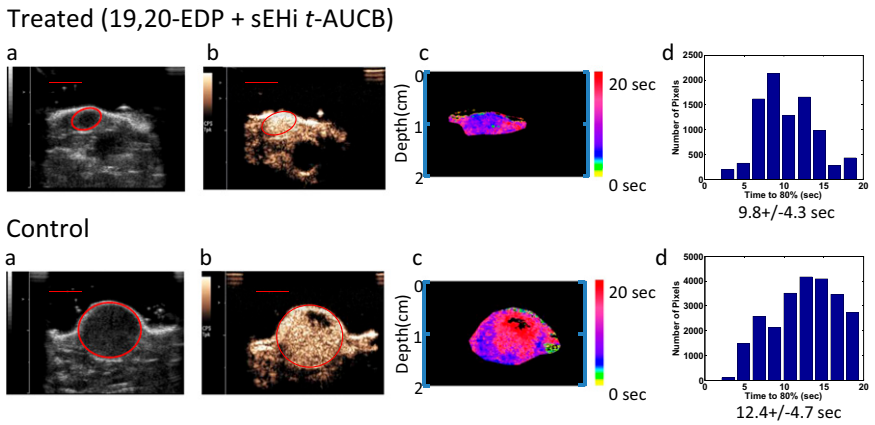

Fig. S4. Ultrasound imaging obtained after 12 d of coadministration of 19,20-EDP and sEHi *t*-AUCB (*Upper*), and sham-treated control (*Lower*). (*A*) Tumor (red circle) imaged in b-mode. (*B*) Contrast pulse sequence demonstrating microbubble concentration within the tumor. (*C*) Time to perfusion map. Color scale is in seconds, ranging up to 20 s. (*D*) Quantification of time required for contrast agent arrival. Color scale is normalized image intensity. Data show that tumor perfusion is maintained after treatment, whereas the larger, untreated tumors eventually become necrotic.

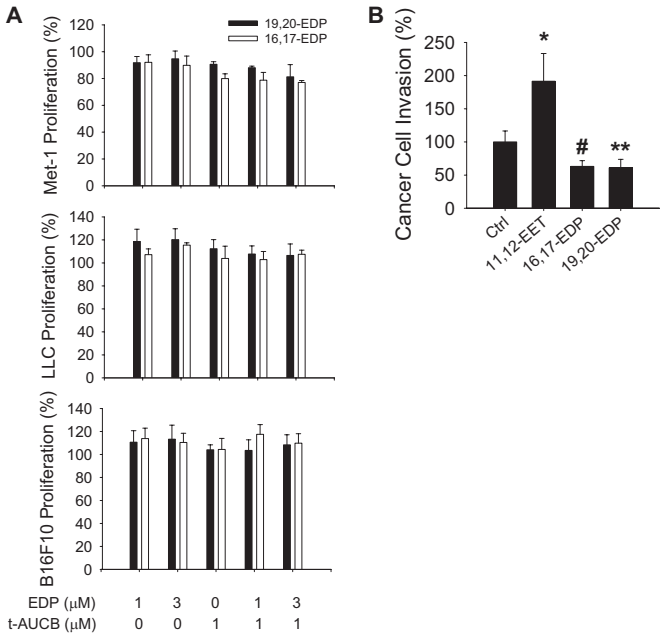

Fig. S5. (*A*) Lack of effects of EDPs and *t*-AUCB on cancer cell proliferation after 24-h treatment in basal medium. Three cancer cell lines were tested, including Met-1 mouse breast cancer, LLC mouse Lewis lung cancer, and B16F10 mouse melanoma. (*B*) Effects of EETs and EDPs on FBS-induced PC-3 cancer cell invasion. At 1 μM, 11,12-EET almost doubled PC-3 invasion, whereas 16,17- and 19,20-EDP inhibited ~40% of invasion. EETs and EDPs had no effect on PC-3 cancer cell proliferation (data not shown). All values represent means ± SD. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{\#}P < 0.001$.

Table S1. Angiogenesis RT-PCR array of 19,20-EDP in HUVEC cells

Gene	Description	Fold change	*P* value
AKT1	V-akt murine thymoma viral oncogene homolog 1	1.0639	0.434999
ANG	Angiogenin, ribonuclease, RNase A family, 5	1.0517	0.389077
ANGPT1	Angiopoietin 1	0.7593	0.012155
ANGPT2	Angiopoietin 2	1.0837	0.183883
ANGPTL4	Angiopoietin-like 4	3.5129	0.000086
ANPEP	Alanyl (membrane) aminopeptidase	0.9812	0.775906
BAI1	Brain-specific angiogenesis inhibitor 1	0.5381	0.227189
CCL11	Chemokine (C-C motif) ligand 11	0.9858	0.819806
CCL2	Chemokine (C-C motif) ligand 2	0.8289	0.364874
CDH5	Cadherin 5, type 2 (vascular endothelium)	0.9283	0.389882
COL18A1	Collagen, type XVIII, alpha 1	0.9566	0.335365
COL4A3	Collagen, type IV, alpha 3 (Goodpasture antigen)	1.0468	0.892614
CTGF	Connective tissue growth factor	0.8425	0.032492
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	0.72	0.18266
CXCL10	Chemokine (C-X-C motif) ligand 10	0.4895	0.157361
CXCL5	Chemokine (C-X-C motif) ligand 5	0.7915	0.132829
CXCL6	Chemokine (C-X-C motif) ligand 6 (granulocyte chemotactic protein 2)	0.8582	0.260726
CXCL9	Chemokine (C-X-C motif) ligand 9	2.0411	0.377672
EDN1	Endothelin 1	0.8444	0.026741
EFNA1	Ephrin-A1	0.9633	0.635974
EFNB2	Ephrin-B2	1.2947	0.048037
EGF	Epidermal growth factor	1.242	0.429438
ENG	Endoglin	1.0276	0.803019
EPHB4	EPH receptor B4	1.0762	0.539671
ERBB2	V-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)	0.95	0.494111
F3	Coagulation factor III (thromboplastin, tissue factor)	1.3654	0.284544
FGF1	Fibroblast growth factor 1 (acidic)	1.0614	0.702239
FGF2	Fibroblast growth factor 2 (basic)	0.9903	0.863181
FGFR3	Fibroblast growth factor receptor 3	0.7842	0.436079
FIGF	C-fos induced growth factor (vascular endothelial growth factor D)	1.0963	0.418671
FLT1	Fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	1.0182	0.833684
FN1	Fibronectin 1	1.0963	0.253789
HGF	Hepatocyte growth factor (hepapoietin A; scatter factor)	0.827	0.254285
HIF1A	Hypoxia inducible factor 1, alpha subunit (basic helix–loop–helix transcription factor)	1.042	0.8182
HPSE	Heparanase	0.9677	0.135877
ID1	Inhibitor of DNA binding 1, dominant negative helix–loop–helix protein	0.95	0.636255
IFNA1	IFN, alpha 1	2.1033	0.139338
IFNG	IFN, gamma	0.9858	0.819806
IGF1	Insulin-like growth factor 1 (somatomedin C)	1.9899	0.340659
IL1B	Interleukin 1, beta	1.3007	0.605766
IL6	Interleukin 6 (IFN, beta 2)	0.7879	0.002859
IL8	Interleukin 8	1.042	0.454881
ITGAV	Integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	1.2249	0.044954
ITGB3	Integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	0.8661	0.359791
JAG1	Jagged 1	1.1014	0.680348
KDR	Kinase insert domain receptor (a type III receptor tyrosine kinase)	1.1219	0.514564
LECT1	Leukocyte cell derived chemotaxin 1	1.8956	0.051173
LEP	Leptin	0.9113	0.97042
MDK	Midkine (neurite growth-promoting factor 2)	1.0444	0.526297
MMP14	Matrix metalloproteinase 14 (membrane inserted)	0.8582	0.134235
MMP2	Matrix metalloproteinase 2 (gelatinase A, 72 kDa gelatinase, 72 kDa type IV collagenase)	1.0276	0.60313
MMP9	Matrix metalloproteinase 9 (gelatinase B, 92 kDa gelatinase, 92 kDa type IV collagenase)	1.8566	0.070132
NOS3	Nitric oxide synthase 3 (endothelial cell)	0.9972	0.987876
NOTCH4	Notch 4	0.9881	0.962319
NRP1	Neuropilin 1	0.9903	0.849161
NRP2 2	Neuropilin	1.1219	0.062026
PDGFA	Platelet-derived growth factor alpha polypeptide	1.0253	0.691344

Table S1. Cont.

Gene	Description	Fold change	*P* value
PECAM1	Platelet/endothelial cell adhesion molecule	0.8988	0.132547
PF4	Platelet factor 4	0.8156	0.104725
PGF	Placental growth factor	1.0812	0.675377
PLAU	Plasminogen activator, urokinase	1.0158	0.846356
PLG	Plasminogen	1.1723	0.198452
PROK2	Prokineticin 2	0.9858	0.819806
PTGS1	Prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	0.9903	0.89772
S1PR1	Sphingosine-1-phosphate receptor 1	0.9478	0.298686
SERPINE1	Serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	1.0639	0.298782
SERPINF1	Serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1	0.697	0.096001
SPHK1	Sphingosine kinase 1	0.9522	0.710641
TEK	TEK tyrosine kinase, endothelial	1.0324	0.783316
TGFA	Transforming growth factor, alpha	0.9903	0.890406
TGFB1	Transforming growth factor, beta 1	0.9456	0.571621
TGFB2	Transforming growth factor, beta 2	0.8063	0.181045
TGFBR1	Transforming growth factor, beta receptor 1	1.0253	0.77697
THBS1	Thrombospondin 1	1.1376	0.070326
THBS2	Thrombospondin 2	0.3903	0.162237
TIE1	Tyrosine kinase with Ig-like and EGF-like domains 1	0.9722	0.377212
TIMP1	TIMP metalloproteinase inhibitor 1	1.0862	0.382847
TIMP2	TIMP metalloproteinase inhibitor 2	1.0042	0.902882
TIMP3	TIMP metalloproteinase inhibitor 3	1.5576	0.005168
TNF	Tumor necrosis factor	0.9858	0.819806
TYMP	Thymidine phosphorylase	0.661	0.486351
VEGFA	Vascular endothelial growth factor A	1.831	0.196409
VEGFB	Vascular endothelial growth factor B	1.0913	0.132982
VEGFC	Vascular endothelial growth factor C	**0.2851**	**0.222407**

Bold font indicates the most down-regulated gene.

Table S2. Profile of lipid mediators in the plasma of treated mice in Met-1 tumor experiment

Lipid mediator	Ctrl, nM	19,20- EDP, nM	*t*-AUCB, nM	19,20-EDP + *t*-AUCB, nM
6-keto PGF1a	5.65 ± 2.29	10.58 ± 7.34	12.45 ± 10.15	1.68 ± 0.59
TXB2	6.67 ± 3.39	6.61 ± 6.07	101.54 ± 136.24	2.66 ± 1.11
9,12,13-TriHOME	11.76 ± 4.34	7.67 ± 0.69	13.14 ± 6.79	8.56 ± 1.73
9,10,13-TriHOME	2.46 ± 0.79	1.50 ± 0.15	2.74 ± 1.33	1.82 ± 0.32
PGE2	0.74 ± 0.26	0.47 ± 0.19	1.36 ± 1.05	0.38 ± 0.18
PGD2	0.73 ± 0.30	0.50 ± 0.06	1.45 ± 1.22	0.53 ± 0.33
15,16-DiHODE	3.43 ± 0.60	3.62 ± 0.57	5.11 ± 2.21	3.18 ± 0.74
9,10-DiHODE	2.04 ± 0.65	1.74 ± 0.03	2.60 ± 1.02	1.80 ± 0.83
12,13-DiHODE	4.22 ± 1.05	4.90 ± 0.60	5.07 ± 1.75	4.44 ± 1.38
14,15-DiHETE	0.07 ± 0.05	0.10 ± 0.04	0.16 ± 0.05	0.10 ± 0.03
11,12-DiHETE	0.05 ± 0.02	0.04 ± 0.02	0.12 ± 0.03	0.05 ± 0.01
12,13-DiHOME	81.13 ± 20.10	89.83 ± 5.69	114.63 ± 39.19	85.60 ± 23.32
8,9-DiHETE	0.09 ± 0.06	0.20 ± 0.11	0.17 ± 0.10	0.18 ± 0.08
9,10-DiHOME	16.49 ± 4.25	13.28 ± 1.22	24.13 ± 7.63	14.60 ± 4.34
19,20-DiHDPA	4.16 ± 0.57	4.12 ± 1.53	4.20 ± 0.47	4.04 ± 0.69
14,15-DiHETrE	0.98 ± 0.23	1.13 ± 0.48	1.40 ± 0.17	0.80 ± 0.07
16,17-DiHDPA	0.44 ± 0.09	0.51 ± 0.16	0.71 ± 0.11	0.42 ± 0.03
11,12-DiHETrE	0.58 ± 0.15	0.58 ± 0.24	0.76 ± 0.05	0.44 ± 0.01
13,14-DiHDPA	0.20 ± 0.05	0.23 ± 0.08	0.28 ± 0.07	0.18 ± 0.02
10,11-DiHDPA	0.14 ± 0.08	0.20 ± 0.04	0.21 ± 0.04	0.19 ± 0.03
8,9-DiHETrE	0.47 ± 0.09	0.41 ± 0.13	0.49 ± 0.02	0.39 ± 0.07
EKODE	2.77 ± 1.57	1.91 ± 0.81	2.86 ± 1.53	1.45 ± 0.40
5,6-DiHETrE	2.05 ± 1.35	1.58 ± 0.30	1.79 ± 0.41	2.14 ± 0.36
13-HODE	106.88 ± 31.22	91.90 ± 19.61	177.95 ± 72.01	96.74 ± 33.58
9-HODE	35.38 ± 10.31	28.50 ± 5.54	49.10 ± 16.59	29.34 ± 9.13
15(16)-EpODE	81.00 ± 41.81	89.17 ± 21.65	114.38 ± 22.37	140.60 ± 77.21
15-HETE	4.42 ± 2.17	5.16 ± 2.73	33.86 ± 32.94	2.38 ± 0.39
9(10)-EpODE	13.28 ± 16.78	16.79 ± 3.82	19.41 ± 9.84	30.27 ± 20.94
17(18)-EpETE	1.89 ± 1.38	1.40 ± 0.28	1.93 ± 0.70	2.58 ± 0.80
11-HETE	3.40 ± 1.72	4.17 ± 2.39	28.49 ± 32.49	1.75 ± 0.43
12(13)-EpODE	11.45 ± 9.58	12.85 ± 2.65	16.26 ± 5.34	26.16 ± 19.28
13-oxo ODE	4.44 ± 1.87	5.40 ± 1.76	7.37 ± 2.78	10.30 ± 6.99
15-oxo ETE	0.84 ± 0.30	0.64 ± 0.31	1.14 ± 0.52	0.49 ± 0.07
9-oxo ODE	6.73 ± 2.73	4.77 ± 1.76	8.16 ± 1.96	4.71 ± 0.98
14(15)-EpETE	0.67 ± 0.91	0.73 ± 0.12	0.95 ± 0.50	1.44 ± 0.57
8-HETE	3.36 ± 1.07	3.56 ± 1.46	9.71 ± 10.08	3.05 ± 0.90
12-HETE	239.63 ± 133.33	332.83 ± 214.62	325.75 ± 184.20	223.20 ± 91.01
11(12)-EpETE	1.01 ± 0.94	0.81 ± 0.13	0.93 ± 0.32	1.55 ± 0.65
9-HETE	1.16 ± 0.68	0.62 ± 0.32	1.12 ± 0.41	0.52 ± 0.09
15 (s)-HETrE	0.83 ± 0.28	1.29 ± 0.63	2.75 ± 2.08	0.71 ± 0.10
5-HETE	3.48 ± 0.95	3.09 ± 0.82	4.11 ± 0.77	2.74 ± 0.49
19,20-EDP	10.12 ± 4.38	10.53 ± 2.4	9.3 ± 2.63	24.67 ± 8.52
12(13)-EpOME	121.08 ± 137.48	135.00 ± 27.73	177.65 ± 76.28	255.88 ± 200.06
14(15)-EpETrE	17.22 ± 23.12	11.72 ± 2.97	16.60 ± 9.84	21.76 ± 15.40
9(10)-EpOME	92.43 ± 122.81	98.23 ± 11.14	117.60 ± 70.59	187.26 ± 163.24
16,17-EDP	2.42 ± 2.46	2.71 ± 0.78	2.9 ± 1.55	6.32 ± 3.54
13,14-EDP	1.99 ± 1.67	2.54 ± 1.05	2.5 ± 1.38	4.97 ± 2.01
10,11-EDP	2.85 ± 1.95	3.63 ± 1.48	3.8 ± 2.07	8.14 ± 2.52
11(12)-EpETrE	12.48 ± 10.27	12.11 ± 2.77	18.24 ± 8.38	21.84 ± 7.22
8(9)-EpETrE	7.26 ± 7.41	5.83 ± 0.42	8.26 ± 3.46	11.41 ± 4.80
5(6)-EpETrE	7.93 ± 8.24	8.60 ± 1.23	12.95 ± 7.81	16.64 ± 9.50
9-HOTrE	1.26 ± 0.38	1.05 ± 0.22	1.53 ± 0.48	1.01 ± 0.31
13-HOTrE	2.38 ± 0.75	2.05 ± 0.37	3.22 ± 1.24	2.03 ± 0.70
15-HEPE	0.34 ± 0.23	0.17 ± 0.21	0.19 ± 0.06	0.05 ± 0.06
8-HEPE	0.34 ± 0.29	0.14 ± 0.09	0.11 ± 0.03	0.11 ± 0.07
12-HEPE	11.89 ± 6.77	18.96 ± 10.18	36.56 ± 26.46	15.17 ± 10.39
5-HEPE	0.34 ± 0.09	0.32 ± 0.10	0.39 ± 0.05	0.25 ± 0.06

Table S3. Profile of lipid mediators in the tumor tissues of treated mice in Met-1 tumor experiment

Lipid mediator	Ctrl, pmol/g	19,20 EDP, pmol/g	*t*-AUCB, pmol/g	19,20 EDP + *t*-AUCB, pmol/g
6 keto PGF1a	733.35 ± 148.22	1,318.13 ± 786.45	724.98 ± 142.53	1,065.15 ± 255.22
TXB2	1,170.39 ± 1,319.91	889.23 ± 761.51	958.25 ± 573.85	1,947.67 ± 1,498.07
9,12,13-TriHOME	89.22 ± 66.15	124.26 ± 91.08	103.38 ± 29.38	193.29 ± 134.37
9,10,13-TriHOME	25.57 ± 14.66	36.40 ± 26.40	37.46 ± 13.55	56.44 ± 39.32
PGF2a	323.08 ± 105.53	330.51 ± 116.61	388.04 ± 144.26	487.56 ± 111.72
PGE2	553.45 ± 241.17	632.11 ± 358.57	619.70 ± 271.78	935.47 ± 349.41
PGD2	1,104.70 ± 843.12	941.28 ± 556.63	818.76 ± 344.51	1,672.63 ± 759.82
11,12,15-TriHETrE	356.16 ± 304.37	468.72 ± 502.61	292.31 ± 107.03	591.53 ± 509.12
PGJ2	42.16 ± 17.35	39.42 ± 14.19	35.78 ± 12.44	51.67 ± 15.98
15,16-DiHODE	3.10 ± 1.60	3.23 ± 1.45	4.40 ± 1.44	6.41 ± 2.84
9,10-DiHODE	0.88 ± 0.98	1.68 ± 2.06	1.00 ± 0.26	2.84 ± 2.79
12,13-DiHODE	1.83 ± 0.40	1.76 ± 0.63	2.96 ± 0.61	4.02 ± 1.46
6 *trans* LTB4	23.53 ± 27.15	23.80 ± 19.89	18.05 ± 5.54	35.47 ± 29.04
5,15-DiHETE	4.21 ± 4.13	4.73 ± 3.88	3.12 ± 0.62	7.26 ± 2.95
17,18-DiHETE	3.58 ± 2.67	4.31 ± 3.42	3.95 ± 1.16	5.57 ± 2.38
LTB4	17.26 ± 5.54	14.16 ± 2.03	9.77 ± 1.66	20.10 ± 5.59
14,15-DiHETE	0.25 ± 0.27	0.54 ± 0.50	0.21 ± 0.07	0.63 ± 0.59
11,12-DiHETE	0.33 ± 0.38	0.44 ± 0.44	0.21 ± 0.09	0.54 ± 0.44
12,13-DiHOME	48.69 ± 27.77	53.19 ± 30.89	82.17 ± 24.43	100.13 ± 46.82
8,9-DiHETE	0.41 ± 0.36	0.59 ± 0.75	0.60 ± 0.25	1.96 ± 1.89
9,10-DiHOME	23.63 ± 27.61	38.42 ± 44.50	21.79 ± 4.28	53.32 ± 53.27
19,20-DiHDPA	36.51 ± 21.48	43.23 ± 35.10	33.10 ± 6.39	49.53 ± 26.08
14,15-DiHETrE	23.01 ± 30.00	45.97 ± 60.00	11.69 ± 4.81	55.87 ± 52.01
16,17-DiHDPA	3.08 ± 3.10	4.62 ± 5.07	2.22 ± 0.32	5.98 ± 4.64
11,12-DiHETrE	8.28 ± 11.41	14.82 ± 19.65	4.16 ± 1.12	15.62 ± 16.00
13,14-DiHDPA	1.56 ± 1.96	3.01 ± 3.82	0.73 ± 0.23	3.19 ± 3.51
10,11-DiHDPA	2.13 ± 2.95	3.73 ± 4.84	0.98 ± 0.35	4.20 ± 4.89
8,9-DiHETrE	8.07 ± 11.34	13.83 ± 18.02	4.57 ± 0.69	14.57 ± 15.07
EKODE	3.54 ± 2.33	4.11 ± 2.80	5.96 ± 4.01	13.51 ± 9.41
5,6-DiHETE	3.70 ± 3.44	3.57 ± 2.16	3.32 ± 1.74	4.95 ± 1.36
15-deoxy PGJ2	19.62 ± 17.71	19.62 ± 14.61	13.87 ± 6.10	25.22 ± 9.94
5,6-DiHETrE	125.41 ± 158.74	194.41 ± 259.89	90.48 ± 73.01	222.70 ± 265.99
13-HODE	429.51 ± 257.38	524.15 ± 302.74	451.12 ± 122.99	872.48 ± 474.06
9-HODE	300.96 ± 142.03	357.87 ± 192.88	325.08 ± 143.77	585.73 ± 296.41
15(16)-EpODE	41.99 ± 10.65	58.27 ± 53.02	72.58 ± 37.97	160.67 ± 154.83
15-HETE	530.27 ± 369.30	561.41 ± 289.02	467.12 ± 128.14	830.23 ± 712.96
9(10)-EpODE	14.64 ± 7.40	26.67 ± 32.51	24.28 ± 15.63	58.63 ± 70.88
17(18)-EpETE	15.01 ± 2.57	18.29 ± 14.34	17.64 ± 12.61	25.73 ± 22.93
17-HDoHE	52.52 ± 53.47	56.20 ± 42.74	43.30 ± 9.63	94.58 ± 55.83
11-HETE	479.43 ± 233.23	520.98 ± 232.56	441.54 ± 166.07	743.38 ± 544.91
12(13)-EpODE	9.43 ± 5.16	15.49 ± 17.75	14.66 ± 9.19	36.27 ± 41.57
13-oxo ODE	5.35 ± 3.55	7.94 ± 8.43	8.44 ± 3.93	16.13 ± 15.88
15-oxo ETE	28.35 ± 11.36	26.28 ± 6.28	36.84 ± 17.58	49.23 ± 37.41
9-oxo ODE	19.83 ± 8.09	19.05 ± 10.21	38.79 ± 25.37	58.68 ± 42.81
14(15)-EpETE	8.10 ± 1.49	9.11 ± 8.75	9.00 ± 6.40	15.86 ± 14.14
8-HETE	59.14 ± 42.31	57.76 ± 25.66	53.96 ± 25.02	99.69 ± 82.55
12-HETE	3,623.41 ± 1,393.06	4,041.11 ± 1,373.67	3,516.29 ± 1,039.37	5,499.60 ± 2,641.56
11(12)-EpETE	8.72 ± 1.82	11.56 ± 9.33	11.14 ± 6.90	19.15 ± 15.95
9-HETE	33.02 ± 19.78	31.18 ± 3.44	30.21 ± 10.84	48.75 ± 41.37
15 (s)-HETrE	66.98 ± 29.94	63.66 ± 34.26	56.41 ± 16.78	104.82 ± 82.51
12-oxo ETE	92.32 ± 86.22	60.61 ± 36.88	126.61 ± 113.44	141.26 ± 130.63
5-HETE	275.06 ± 127.94	398.68 ± 183.15	319.10 ± 127.92	436.65 ± 133.64
19,20-EDP	120.36 ± 12.91	121.37 ± 20.55	141.71 ± 14.74	353.40 ± 109.26
12(13)-EpOME	357.34 ± 161.64	312.48 ± 278.77	286.16 ± 179.65	1,045.58 ± 1,105.50
14(15)-EpETrE	816.49 ± 267.57	631.05 ± 514.45	582.48 ± 363.19	1,731.52 ± 1,494.55
9(10)-EpOME	308.57 ± 190.41	283.10 ± 269.86	253.98 ± 151.28	815.65 ± 919.41
16,17-EDP	68.23 ± 20.80	60.10 ± 49.89	59.65 ± 41.92	97.45 ± 82.72
13,14-EDP	56.56 ± 26.37	52.94 ± 44.60	52.00 ± 37.51	78.55 ± 74.00
10,11-EDP	79.19 ± 39.09	78.13 ± 78.07	78.91 ± 53.33	186.22 ± 126.44
11(12)-EpETrE	651.10 ± 395.40	500.53 ± 408.36	614.46 ± 394.47	883.27 ± 826.33
8(9)-EpETrE	229.53 ± 168.09	182.33 ± 159.70	220.90 ± 142.52	324.66 ± 328.30
5(6)-EpETrE	192.27 ± 130.29	59.74 ± 27.56	382.23 ± 246.78	112.96 ± 83.87
9-HOTrE	1.23 ± 0.83	1.61 ± 0.57	1.65 ± 0.35	2.71 ± 1.85

Table S3. Cont.

Lipid mediator	Ctrl, pmol/g	19,20 EDP, pmol/g	*t*-AUCB, pmol/g	19,20 EDP + *t*-AUCB, pmol/g
13-HOTrE	16.38 ± 18.13	17.19 ± 10.93	14.96 ± 4.13	43.94 ± 37.21
15-HEPE	14.98 ± 14.73	14.18 ± 9.87	11.53 ± 1.92	26.43 ± 21.31
8-HEPE	0.61 ± 0.15	0.77 ± 0.64	0.56 ± 0.42	0.21 ± 0.07
12-HEPE	87.35 ± 16.53	104.88 ± 10.20	92.62 ± 13.35	105.84 ± 28.82
5-HEPE	3.63 ± 1.48	3.54 ± 0.65	3.65 ± 1.30	5.12 ± 1.51