

Supplementary Materials

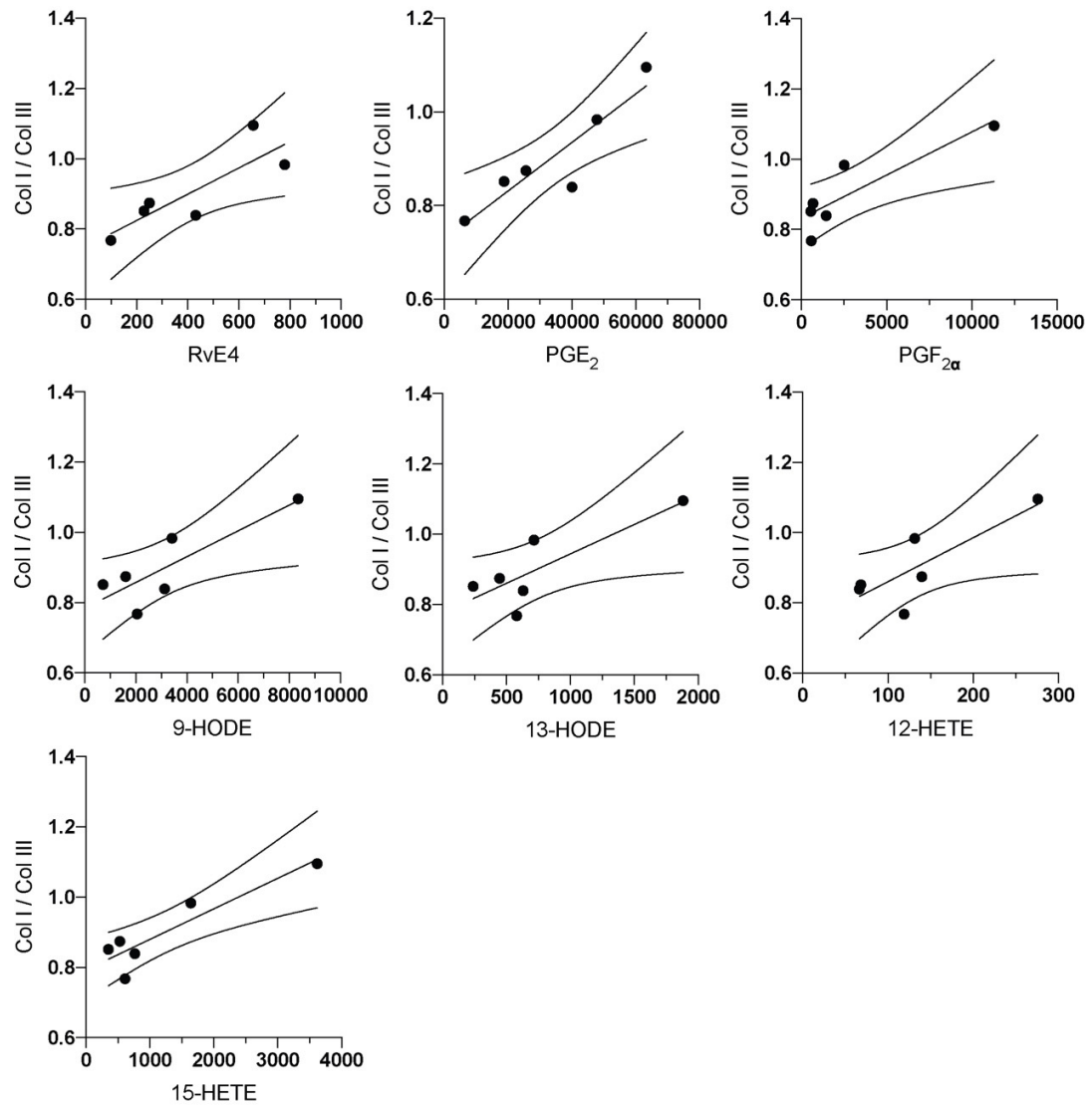


Figure S1. Linear regression analyses assessing the correlation of ECM proteins to specific lipid mediators. The correlation coefficient was determined according to Pearson's correlation coefficient (r), and the significance according to two-tailed test p -value (p).

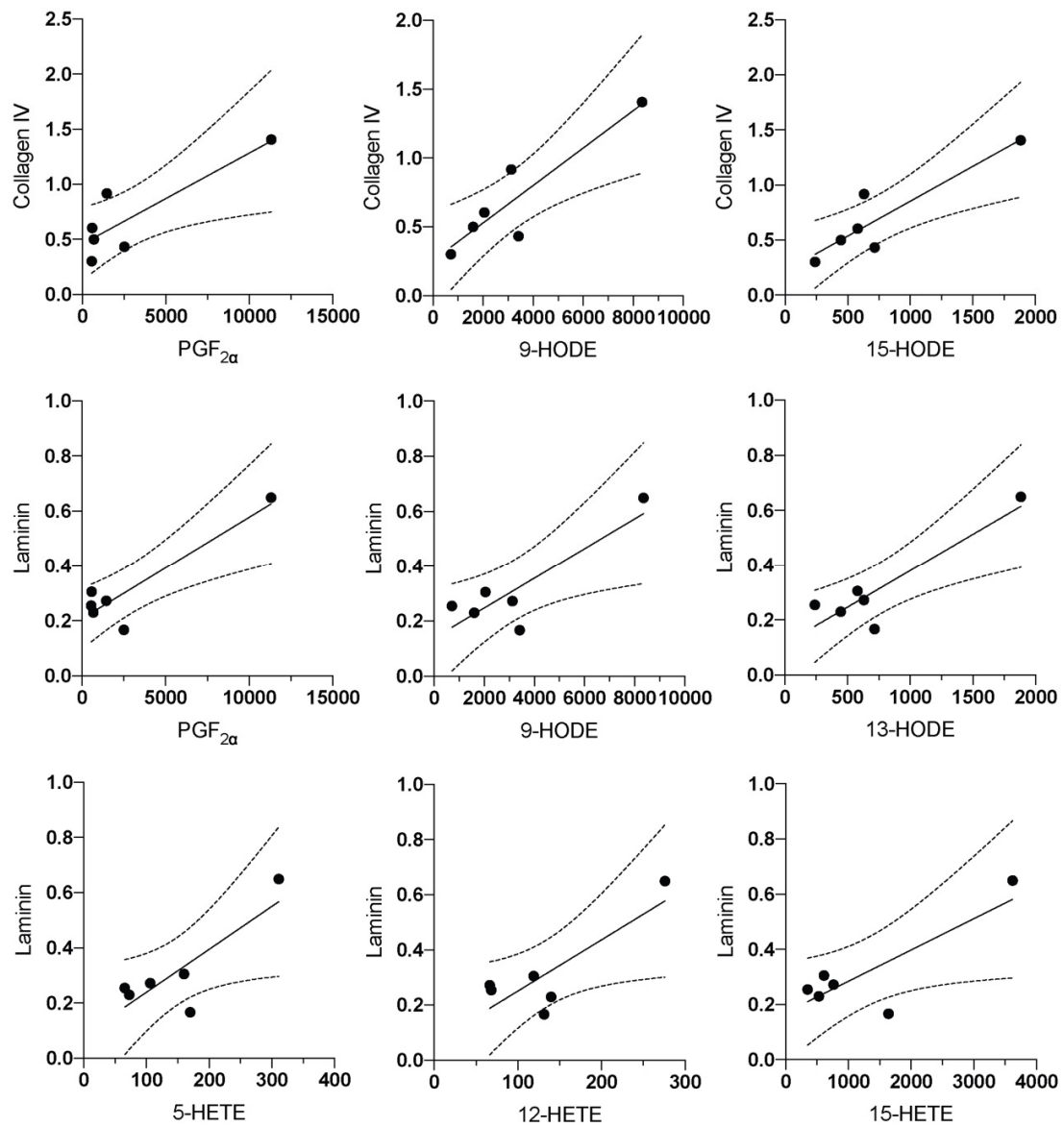


Figure S2. Linear regression analyses assessing the correlation of ECM proteins to specific lipid mediators. The correlation coefficient was determined according to Pearson's correlation coefficient (r), and the significance according to two-tailed test p -value (p).

Table S1. Antibodies used for immunofluorescence and dot blot analyses.

Antibody	Species	Manufacturer	Catalog number	Dilution IF	Dilution DB
Anti-Collagen I	Polyclonal rabbit	Cedarlane (Burlington, ON, Canada)	CL50111AP-1	1:100	1:2000
Anti-Collagen III	Polyclonal rabbit	Cedarlane (Burlington, ON, Canada)	CL50311AP-1	1:100	1:2000
Anti-Collagen IV	Polyclonal rabbit	Abcam (Cambridge, UK)	ab21295	1:100	1:1000
Anti-Fibronectin	Monoclonal mouse	ATCC (Manassas, VA, USA)	CRL-1606	1:100	1:500
Anti-Elastin	Polyclonal rabbit	Abcam (Cambridge, UK)	ab21610	1:30	1:1000
Anti-Laminin	Polyclonal rabbit	Abcam (Cambridge, UK)	ab11575	1:100	1:1000
Anti-GAPDH	Polyclonal mouse	BioLegend (San Diego, CA, USA)	649202	-	1:8000
Anti-rabbit Alexa 488	Polyclonal donkey	Life Technologies (Oakville, ON, Canada)	A21206	1:1600	-
Anti-rabbit Alexa 594	Polyclonal goat	Life Technologies (Oakville, ON, Canada)	A11012	1:1400	-
Anti-mouse Alexa 594	Polyclonal goat	Life Technologies (Oakville, ON, Canada)	A11005	1:1400	-
Anti-Rabbit Horseradish Peroxidase (HRP)	Polyclonal goat	Jackson ImmunoResearch (West Grove, PA, USA)	111-035-003	-	1:60000
Anti-Mouse Horseradish Peroxidase (HRP)	Polyclonal goat	Jackson ImmunoResearch (West Grove, PA, USA)	115-035-003	-	1:60000

Abbreviations: IF, immunofluorescence; DB, dot blot

Table S2. Specific mass transitions and retention times of the metabolites analyzed by LC-MS/MS.

Bioactive lipids	ISTD	Q1 → Q3	Retention time (min)	Detection limit (fmol)
9-HODE	13-HODE-d ₄	295.30 → 171.35	9.48	5
13-HODE	13-HODE-d ₄	295.50 → 195.30	9.48	5
PGE ₂	PGE ₂ -d ₄	351.20 → 271.15	5.07	5
PGF _{2a}	PGE ₂ -d ₄	353.40 → 309.30	4.83	5
5-HETE	15-HETE-d ₈	319.30 → 115.05	10.19	25
12-HETE	15-HETE-d ₈	319.10 → 179.25	10.11	50
15-HETE	15-HETE-d ₈	319.40 → 219.30	9.76	50
PGE ₃	PGE ₂ -d ₄	349.30 → 269.35	4.3	5
PGF _{3a}	PGE ₂ -d ₄	351.30 → 193.30	4.08	5
12-HEPE	15-HETE-d ₈	317.30 → 179.35	9.13	25
15-HEPE	15-HETE-d ₈	317.40 → 219.25	9.04	50
18-HEPE	15-HETE-d ₈	317.30 → 259.40	8.7	25
RvE4	RvD2-d ₅	349.30 → 195.20	3.91	50
LTB ₅	LTB ₄ -d ₄	333.40 → 195.25	6.61	50
14-HDHA	15-HETE-d ₈	343.50 → 281.30	10.59	50
17-HDHA	15-HETE-d ₈	343.50 → 281.30	10.43	50
RvD5	RvD2-d ₅	359.40 → 199.25	7.51	50
MaR2	RvD2-d ₅	359.40 → 221.05	8.2	50

Table S3 Levels of bioactive lipids in skin substitutes after ALA supplementation.

Bioactive lipid mediators	Mean \pm SD (pmol/g of tissue)			P-value	
	HS ⁻	PS ⁻	PS ^{ALA+}	PS ⁻ vs PS ^{ALA+}	PS ⁻ vs HS ⁻
LA derivatives					
9-HODE	1000.9 \pm 723.9	4968.4 \pm 2936.2	1456.4 \pm 678.7	0.0341	0.0324
13-HODE	2205.1 \pm 1089.5	1076.6 \pm 698.9	421.9 \pm 171.6	NS	NS
AA derivatives					
PGE ₂	4137.4 \pm 1984.2	50412.4 \pm 11836.0	16988.0 \pm 9699.4	0.0001	0.0001
PGF _{2α}	956.9 \pm 965.3	5090.0 \pm 5407.7	604.9 \pm 64.4	NS	NS
5-HETE	138.3 \pm 91.6	195.6 \pm 104.8	99.3 \pm 52.5	NS	NS
12-HETE	177.3 \pm 88.4	157.9 \pm 107.3	109.1 \pm 36.9	NS	NS
15-HETE	448.5 \pm 500.4	2009.1 \pm 1462.8	497.9 \pm 132.7	0.0120	0.0198
AEA	0.9 \pm 1.5	102.4 \pm 18.1	89.9 \pm 30.0	NS	0.0021
ALA derivatives					
13-HOTrE	ND	ND	115.5 \pm 82.9	NS	NS
EPA derivatives					
PGE ₃	82.8 \pm 25.7	1001.0 \pm 399.5	9395.1 \pm 6651.4	0.0069	NS
PGF _{3α}	119.6 \pm 37.1	ND	137.9 \pm 143.2	NS	NS
12-HEPE	2.5 \pm 2.7	ND	61.8 \pm 30.2	NS	NS
15-HEPE	24.0 \pm 18.0	39.3 \pm 43.4	240.7 \pm 80.9	0.0001	NS
18-HEPE	13.9 \pm 11.7	ND	251.7 \pm 60.8	0.0001	NS
RvE4	ND	622.6 \pm 176.8	192.7 \pm 81.6	0.0081	0.0012
EPEA	2.2 \pm 2.0	0.5 \pm 0.3	7.1 \pm 4.7	NS	NS
DHA derivatives					
14-HDHA	100.9 \pm 77.0	55.1 \pm 51.0	403.5 \pm 166.9	NS	NS
17-HDHA	364.2 \pm 282.1	1365.6 \pm 1736.1	186.7 \pm 99.3	NS	NS
MaR2	333.4 \pm 112.9	40.3 \pm 3.5	26.8 \pm 4.9	NS	0.0031
DHEA	37.7 \pm 40.4	4.4 \pm 2.4	14.5 \pm 10.0	NS	NS

Abbreviations: AA, arachidonic acid; ALA, α -linolenic acid; DGLA, dihomo-gamma-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; HEPE, hydroxyeicosapentaenoic acid; HETE, hydroperoxyeicosatetraenoic acid; HETrE, hydroxyeicosatrienoic acid; HDHA, hydroxydocosahexaenoic acid; HODE, hydroxyoctadecadienoic acid; LA, linoleic acid; LT, Leukotriene; ND, not detected; NS, not significant; PG, prostaglandin; Rv, Resolvin; SD, standard deviation.