

Supplementary Methods:

Materials. Dulbecco's Modified Eagle Medium (DMEM) with and without Phenol red and Insulin-Transferrin-Selenium (ITS) were purchased from ThermoFisher Scientific (Massachusetts, United States). Phospholipids 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphocholine (PAPC) and 1-palmitoyl-2-stearoyl-sn-glycero-3-phosphocholine (PSPC) were purchased from Avanti Polar Lipids (25mg in chloroform, Alabama, USA). PureLink RNA Mini kit was purchased from ThermoFisher Scientific for isolation of total RNA and iScript[™] Reverse Transcription Supermix kit purchased from Bio-Rad. Forward and reverse primers for qPCR were purchased from Integrated DNA Technologies (IDT, Iowa, United States) and suspended in TE buffer for storage at -20°C. SSoFast[™] EvaGreen Supermix from Bio-Rad (California, United States) was used to perform qPCR. A table of primer sequences and information can be found in table S1. COX2 antibody (#12282) and COX1 antibody (#4841) were purchased from Cell Signaling Technology (Massachusetts, United States). Protein kinase C (PKC) inhibitor GF-109203X (Cat. No. 0741) was purchased from Tocris (Bristol, United Kingdom). Cytokine analysis in cell supernatants were performed using bead-based Luminex technology (Eve Technologies, Calgary Canada) and Meso Scale Discovery (MSD, Maryland, USA) System custom U-Plex panel. Protein concentration in cell lysates was quantified using the Bio-Rad protein assay. For kinomics array, PRO-Q Phosphoprotein stain was purchased from ThermoFisher/Invitrogen.

DE3 Study design: Thirteen allergen-sensitized volunteers participated in the randomized, double-blinded, controlled human exposure crossover study taking place between April 2013 and April 2017 (Clinical Trials ID: NCT02017431). All participants gave written informed consent to the study protocol, which was approved by the University of British Columbia Research Ethics Board (H11-01831), Vancouver.

For inhaled allergen challenge, standardized allergenic extracts for HDM (*Dermatophagoides pteronyssinus*), Timothy grass, and Birch mix were purchased from Hollister-Stier Laboratories (Spokane, WA, USA). On two occasions separated by minimum 4-weeks washout period, participants inhaled either saline (0.9% NaCl) or diluted skin prick test allergen (HDM, grass or birch mix). 2 mL of diluted allergen or saline was delivered to participants using VixOne™ Nebulizer Mask Kit (Westmed, Tucson, AZ, USA) with flow rate of medical air set at 5 L/min for 2 minutes. The concentration of diluted allergen used for the inhalation challenge was allergen provocative concentration (PC)₂₀, the concentration causing a 20% forced expiratory volume in one second (FEV₁) fall. Allergen PC₂₀ was calculated by methacholine PC₂₀ and skin prick wheal size (1), and then was confirmed at one of the screening visits. Research participants, research coordinators, medical staff, and the study physician were blinded to allergen inhalation challenge.

2 days after allergen inhalation challenge, each participant underwent flexible bronchoscopy. Bronchoalveolar lavage (BAL) was collected by instilling and suctioning 20 mL of sterile saline (0.9% NaCl) twice and pooled them together to obtain bronchial wash (BW) and instilling and suctioning 50 mL of normal saline twice and pooled them together to obtain bronchoalveolar lavage (BAL). Both fractions were passed through a mesh filter (40 µm pore size) and centrifuged for 15 mins at 475 x g. Acellular supernatant of BW and BAL was separated, aliquoted and stored at -80 °C. For the purpose of this study, only BAL was assayed for O₂PCs.

DC Study Design: Ten subjects (aged 22-66 years) with positive skin test responses to relevant aeroallergens (>2 mm in diameter) were recruited. All subjects had mild, stable allergic asthma with FEV₁ values greater than or equal to 70%, and baseline methacholine PC₂₀ of less than or equal to 16 mg/ml.. All subjects were nonsmokers, not on inhaled steroid with or without long acting inhaled β₂ agonist therapy and infrequently used inhaled β₂ agonists.

The study was a randomized, diluent-controlled, crossover design approved by the Hamilton Integrated Research Ethics Committee (Project 14-122). On day 1 subjects provided consent, completed a skin prick test, a medical history and methacholine PC20 was measured. On day 2 subjects were randomized to inhale diluent or allergen and spirometry was measured until 7h post-challenge. On day 3, 24 hours after the inhalation challenge, bronchoscopy was performed to obtain BAL fluid. This triad was repeated after a 4-week recovery period.

Airway challenges: Methacholine inhalation challenges were performed using Wright nebulizer and the tidal breathing method, as previously described (2). PC20 was calculated as the provocative concentration of methacholine inducing a 20% decrease in FEV1.

Allergen inhalation challenge was performed as previously described (3). Briefly, doubling doses of allergen extract was delivered by a Wright nebulizer and the tidal breathing method. Subjects inhaled doubling concentrations of allergen extract for 2 minutes using a nebulizer with a mouthpiece on a one-way Hans-Rudolph valve, until a greater than 20% fall in FEV1 at 10 minutes post allergen was reached. The FEV1 was then measured at 10, 20, 30, 45, 60, 90, and 120 minutes after inhalation challenge, and each hour until 7 hours after challenge. The early bronchoconstrictor response (EAR) is taken to be the largest fall in FEV1 within 2 hours after allergen inhalation, and the late response (LAR) is taken to be the largest fall in FEV1 between 3 hours and 7 hours after allergen inhalation. LAR was defined as at least 15% fall in FEV₁ between 3 and 7 hours after allergen challenge. Diluent challenge consisted of 3 inhalations of normal saline (0.9% NaCl) followed by spirometry for 7 hours.

Bronchoscopy: Fiberoptic bronchoscopy was performed as previously described (4) using a Pentax fiberoptic bronchoscope passed through the vocal cords and introduced into the airways and wedged into a segmental or subsegmental bronchus. BAL was collected from the right middle lobe using 3X60ml aliquots of normal saline (0.9% NaCl) introduced via the

bronchoscope and then aspirated through the bronchoscope using a closed, sterile collecting system.

Primary cell culture. Primary HASM cells were isolated from lung tissue obtained through lung resection surgery following approval from the Human Research Ethics Board (University of Manitoba). Subjects had no previous history of chronic lung disease (asthma/COPD) and were never smokers or had quit 30 years prior to lung resection surgery. Detailed demographics along with information about which experiments utilized which subjects are presented in the online supplement (Table S1). HASM were grown to confluence on 6-well plates in DMEM media supplemented with 5% fetal bovine serum (FBS) and 1% penicillin-streptomycin. To induced phenotype differentiation, cells were serum-deprivation in DMEM supplemented with ITS for 7 days. Cells were used between passage 4-6 for all experiments.

Lipid Peroxidation. 25mg of PAPC and PSPC, were oxidized in room air for 4 days and then re-suspended at a concentration of 1mg/mL in chloroform:methanol (2:1). A small sample of oxidized PAPC (OxPAPC) was tested for degree of oxidation using HPLC/electrospray ionization tandem mass spectrometry system as previously described (29684044). PSPC, which lacks fatty acid double bonds, does not undergo oxidation and therefore acts as the control lipid in these experiments. OxPAPC and PSPC were maintained in chloroform methanol at a stock concentrations of 1 mg/mL and stored under nitrogen gas at -20 °C. For exposure in cell culture, desired volumes of OxPAPC- and PSPC-containing chloroform:methanol were transferred to a falcon tube and, under nitrogen gas, the evaporated, leaving behind OxPAPC and PSPC in the tubes. Media was added to tubes containing OxPAPC and PSPC and sonicated to form liposomes prior to the addition to cells.

Cytokine analysis. Quantification of inflammatory mediators secreted by OxPAPC-stimulated HASM was performed on cell supernatants. Cytokines tested were GM-CSF, IFN- γ , IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12(p70), IL-13, MCP-1, and TNF- α (Eve Technologies). MSD custom panel with IL-6, IL-8, and GM-CSF was used to test impact of inhibitors on cytokine secretion.

qPCR. Isolation of total RNA from HASM for qPCR was done according to kit instructions. A total of 1ug of extracted total RNA was reverse transcribed to cDNA using manufacturer's instructions. qPCR was performed according to the SsoFastTM EvaGreen Supermix protocol on the CFX96 thermocycler (Bio-Rad) which included a melting curve.

Western Blotting. 10 μ g of total protein was run on a 10% SDS-PAGE gel and blotted onto nitrocellulose. Primary antibody exposure was done at 4 °C overnight at a concentration of 1:500 (COX1) and 1:750 (COX2) according to vendor specifications. Secondary anti-rabbit HRP antibody was used at a concentration of 1:3000 for both COX1 and COX2.

Oxidized Phospholipid and Oxylipin Quantification. Cells used for assessment of the levels of oxylipins were grown as mentioned above with the exception of phenol-free DMEM media used for supernatant collection. Analysis of oxylipin profile was conducted using high-performance liquid chromatography/tandem mass spectrometry (HPLC-MS/MS) as previously described (5). Oxidized phospholipids were measured in lipid extracts as previously described (6, 7).

Briefly, lipid extracts were reconstituted in RP eluent consisting of 60:40 acetonitrile:water, 10 mM ammonium formate and 0.1% formic acid immediately prior to injection. Thirty microlitres of the sample were injected onto an Ascentis Express C18 HPLC column (15 cm \times 2.1 mm, 2.7 μ m; Supelco Analytical, Bellefonte, Pennsylvania, USA) with separation by a Prominence

UFLC system from Shimadzu Corporation (Canby, OR, USA). Elution was performed using a linear gradient of solvent A (acetonitrile/water, 60:40 v/v) and solvent B (isopropanol/acetonitrile, 90:10, v/v) with both solvents containing 10 mM ammonium formate and 0.1% formic acid. The mobile phase composition that was used is as follows: initial solvent B at 32% until 4.00 min; switched to 45% B; 5.00 min 52% B; 8.00 min 58% B; 11.00 min 66% B; 14.00 min 70% B; 18.00 min 75% B; 21.00 min 97% B; 25.00 min 97% B; and 25.10 min 32% B. A flow rate of 260 μ L/min was used for analysis, and the sample tray and column oven were held at 4°C and 45°C, respectively.

Detection of OxPL was carried out by mass spectrometry in positive polarity mode. MRM scans were performed on 6 transitions using a product ion of 184.3 m/z, corresponding to the cleaved phosphocholine moiety. Ten nanograms of internal standard 9:0-9:0 PC was added to all samples during extraction. A 4000 QTRAP® triple quadrupole mass spectrometer system with a Turbo V electrospray ion source from AB Sciex (Framingham, MA, USA) was coupled to the liquid chromatography system.

Kinomics Array. Following exposure of HASM to 80 μ g/mL of OxPAPC for 1, 3, or 6 hours, cell lysates were collected in a Phosphoarray lysis buffer and run on a peptide array as previously described (8). In brief, 100 μ g of protein from the cell lysates were loaded onto a peptide array in the presence of activation mixture containing 50 μ M ATP and incubated at 37°C for 2 hours.

Results were visualized using PRO-Q Diamond Phosphoprotein stain and subsequently scanned on a PowerScanner (Tecan, Morrisville, NC, USA) microarray scanner with a filter at 580 nm to detect fluorescence. Signal intensity values were collected with Array-Pro Analyzer version 6.3 software (Media Cybernetics, Rockville, MD, USA).

Statistics. qPCR results were analyzed using the delta-delta CT method correcting for PCR efficiency and normalized to the geometric mean of the housekeeping genes (YWHAZ, UBC,

and GAPDH). Relative abundance of cytokines and COX2 mRNA were calculated for comparison of PKC inhibitor effects. Differential phosphorylation results were calculated using the Platform for Integrated, Intelligent Kinome Analysis 2 (PIIKA2) software (9). Significantly upregulated phospho-signals at 1,3, and 6 hours were analyzed using Kinase Enrichment Analysis (KEA, (10)) to identify underlying activated kinases in the kinome data. Data was analyzed using a One-way ANOVA with a Dunnet's post-hoc comparison. Significant threshold set at $p < 0.05$. All results were completed in at least triplicate (3 different primary human cells). Data analysis was done in R (version 3.5.1) and graphs made using ggplot2 package (version 3.1.1).

Table S1: qPCR Primer Information.

Gene	NCBI Accession Number	Forward Primer	Reverse Primer
COX2 (PTGS2)	NM_000963.4	CAAATTGCTGGCAGGGTT G	GGTCAATGGAAGCCTGTG ATA
UBC	NM_021009.7	TGGCACAGCTAGTTCCGT C	CACGAAGATCTGCATTGTC AAGTG

GAPDH	NM_00125679 9.2	CTGACTTCAACAGCGACAC C	CGTTGTCATACCAGGAAAT GAG
YWHAZ	NM_00113569 9.1	CTTCACAAGCAGAGAGCA AAG	CGACAATCCCTTTCTTGTC ATC

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166 Supplementary Results:

167 Table S2: Oxylipin abundance in OxPC treated ASM cell supernatant. CYP - Cytochrome P450,

168 LOX - Lipoxygenase, COX- Cyclooxygenase. Data presented as mean \pm SD (ng/mL). * $p < 0.05$

169 vs. PSPC 160

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<u>Oxylipin</u>	<u>Enzyme</u>	<u>NT</u>	<u>PSPC 160</u>	<u>Ox 20</u>	<u>Ox 40</u>	<u>Ox 80</u>	<u>Ox 160</u>
11,12 DiHETrE	CYP	0.040 \pm 0.017	0.025 \pm 0.006	0.089 \pm 0.030 *	0.103 \pm 0.031 *	0.143 \pm 0.022 *	0.290 \pm 0.015 *
14,15 DiHETrE	CYP	0.043 \pm 0.012	0.039 \pm 0.003	0.133 \pm 0.022	0.186 \pm 0.054 *	0.228 \pm 0.068 *	0.258 \pm 0.028*
16-HETE	CYP	0.056 \pm 0.037	0.034 \pm 0.031	0.052 \pm 0.027	0.128 \pm 0.035	0.068 \pm 0.018	0.254 \pm 0.079 *
17-HETE	CYP	2.393 \pm 4.145	0.000 \pm 0.000	0.000 \pm 0.000	0.000 \pm 0.000	0.000 \pm 0.000	4.274 \pm 7.402
18-HETE	CYP	0.053 \pm 0.010	0.000 \pm 0.000	0.010 \pm 0.018	0.044 \pm 0.042	0.034 \pm 0.047	0.145 \pm 0.173
19-HETE	CYP	5.472 \pm 1.641	8.505 \pm 1.407	6.263 \pm 0.971	8.222 \pm 0.684	7.713 \pm 0.994	8.450 \pm 1.750
20-COOH AA	CYP	0.000 \pm 0.000	0.078 \pm 0.135	0.000 \pm 0.000	0.000 \pm 0.000	0.000 \pm 0.000	0.321 \pm 0.556
5,6 DiHETrE	CYP	0.008 \pm 0.014	0.000 \pm 0.000	0.000 \pm 0.000	0.014 \pm 0.013	0.000 \pm 0.000	0.037 \pm 0.039
8,9 DiHETrE	CYP	0.004 \pm 0.007 *	0.083 \pm 0.052	0.017 \pm 0.001 *	0.041 \pm 0.021	0.022 \pm 0.007	0.065 \pm 0.007

12-Epi LTB4	LOX	0.000 ± 0.000	0.000 ± 0.000	0.038 ± 0.007	0.094 ± 0.025	0.305 ± 0.062 *	0.863 ± 0.192 *
12-HETE	LOX	0.000 ± 0.000	0.000 ± 0.000	0.026 ± 0.026	0.091 ± 0.036 *	0.121 ± 0.027 *	0.414 ± 0.029 *
14,15-LTC4 (EXC4)	LOX	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.061 ± 0.055	0.357 ± 0.397	0.288 ± 0.131
15-HETE	LOX	0.000 ± 0.000	0.000 ± 0.000	0.162 ± 0.060	0.340 ± 0.013 *	0.711 ± 0.058 *	2.370 ± 0.153 *
15-oxoETE	LOX	2.212 ± 1.917	6.584 ± 9.975	3.075 ± 2.613	2.293 ± 2.123	2.132 ± 0.811	5.486 ± 6.068
6R-LXA4	LOX	0.000 ± 0.000	0.000 ± 0.000	1.456 ± 0.255	4.175 ± 0.366	7.399 ± 2.081	26.454 ± 9.451*
6S-LXA4	LOX	0.000 ± 0.000	0.000 ± 0.000	0.553 ± 0.062	1.673 ± 0.175	2.851 ± 0.675	10.648 ± 3.610 *
6-trans LTB4	LOX	0.000 ± 0.000	0.000 ± 0.000	0.095 ± 0.026	0.364 ± 0.034	0.860 ± 0.240 *	2.445 ± 0.271 *
6-trans, 12(S) LTB4	LOX	0.000 ± 0.000	0.000 ± 0.000	0.058 ± 0.051	0.207 ± 0.033	0.598 ± 0.120 *	1.724 ± 0.304 *
8,15 diHETE	LOX	0.074 ± 0.128	0.000 ± 0.000	0.000 ± 0.000	0.112 ± 0.194	0.060 ± 0.104	0.000 ± 0.000
8-HETE	LOX	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.213 ± 0.186 *
5,15 diHETE	LOX	0.000 ± 0.000	0.000 ± 0.000	0.043 ± 0.005	0.148 ± 0.005 *	0.325 ± 0.021 *	0.932 ± 0.053 *

5-HETE	LOX	0.037 ± 0.034	0.010 ± 0.017	0.119 ± 0.031	0.355 ± 0.036	1.231 ± 0.200 *	8.224 ± 0.570 *
HXA3	LOX	0.030 ± 0.034 *	0.546 ± 0.221	0.201 ± 0.059	0.537 ± 0.323	0.267 ± 0.172	0.466 ± 0.096
HXB3	LOX	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.036 ± 0.062	0.024 ± 0.042
LTB4	LOX	0.000 ± 0.000	0.000 ± 0.000	0.069 ± 0.119	0.000 ± 0.000	0.287 ± 0.285	0.568 ± 0.530
LXB4	LOX	0.093 ± 0.042	0.101 ± 0.030	1.251 ± 0.319	1.947 ± 0.453	1.825 ± 0.802	6.102 ± 1.549 *
Tetranor 12-HETE	LOX	0.055 ± 0.060	0.017 ± 0.029	0.412 ± 0.256	0.779 ± 0.237	1.232 ± 0.506	0.746 ± 0.376
11-HETE	Non-enz/ LOX/COX	0.004 ± 0.006	0.000 ± 0.000	0.050 ± 0.002	0.150 ± 0.032	0.241 ± 0.036 *	1.408 ± 0.178 *
9-HETE	Non-enz/ LOX/COX	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.582 ± 0.630
2,3-dinor-8- iso PGF2 alpha	Non-enz	0.040 ± 0.069	0.110 ± 0.123	0.133 ± 0.231	0.220 ± 0.381	0.339 ± 0.294	0.329 ± 0.323
5-iso PGF2 alpha VI	Non-enz	0.038 ± 0.036	0.040 ± 0.070	3.630 ± 0.826 *	7.291 ± 0.680 *	13.893 ± 1.151 *	20.738 ± 1.402 *
8-iso 15- keto PGF2 beta	Non-enz	0.000 ± 0.000	0.000 ± 0.000	0.070 ± 0.067	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000

11-beta Dihydroxy- PGF2 alpha	COX	0.311 ± 0.054	0.321 ± 0.022	0.722 ± 0.166	1.172 ± 0.500 *	1.417 ± 0.081 *	1.417 ± 0.211 *
11-beta PGE2	COX	0.181 ± 0.032	0.063 ± 0.110	4.469 ± 1.888	4.557 ± 2.619	9.595 ± 3.231 *	16.978 ± 3.457 *
11-delta TXB2	COX	0.149 ± 0.259	0.000 ± 0.000	0.553 ± 0.480	0.725 ± 0.678	0.597 ± 1.034	0.000 ± 0.000
12-HHTrE	COX	0.191 ± 0.096	0.000 ± 0.000	0.554 ± 0.480	0.725 ± 0.678	0.597 ± 1.034	0.000 ± 0.000
15-deoxy PGA2	COX	1.464 ± 0.185	0.814 ± 0.967	1.581 ± 0.852	3.696 ± 0.907	6.090 ± 3.966	6.764 1.055 *
12-deoxy PGD2	COX	0.000 ± 0.000	0.000 ± 0.000	0.037 ± 0.036	0.053 ± 0.011	0.104 ± 0.036	0.223 ± 0.129 *
15-deoxy PGJ2	COX	0.042 ± 0.010	0.055 ± 0.041	0.086 ± 0.032	0.199 ± 0.003	0.152 ± 0.056	0.225 ± 0.123 *
12-keto PGF2 alpha	COX	0.000 ± 0.000	0.000 ± 0.000	0.817 ± 0.419	1.103 ± 0.065	2.080 ± 0.231 *	2.724 ± 1.214 *
15-keto PGE2	COX	0.160 ± 0.042	0.133 ± 0.029	0.278 ± 0.187	0.207 ± 0.140	0.236 ± 0.104	0.797 ± 0.307 *
19oh PGE2	COX	0.505 ± 0.151	0.665 ± 0.139	0.555 ± 0.054	0.900 ± 0.165	0.850 ± 0.214	1.155 ± 0.637
2,3-dinor 11-beta PGF2 alpha	COX	0.002 ± 0.004	0.003 ± 0.005	0.028 ± 0.004	5.166 ± 8.864	0.083 ± 0.023	0.180 ± 0.114

2,3-dinor TXB2	COX	0.008 ± 0.013	0.000 ± 0.000	0.008 ± 0.013	0.010 ± 0.017	0.020 ± 0.019	0.038 ± 0.038
2,3-dinor-6 keto PGF1 alpha	COX	0.004 ± 0.008	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.003 ± 0.006
6-keto PGF1 alpha	COX	0.314 ± 0.122	0.326 ± 0.037	0.442 ± 0.176	0.272 ± 0.119	0.494 ± 0.156	0.564 ± 0.020
20oh PGE2	COX	0.116 ± 0.022	0.142 ± 0.032	0.129 ± 0.027	0.217 ± 0.026	0.181 ± 0.080	0.253 ± 0.141
Bicyclo PGE2	COX	0.000 ± 0.000	0.034 ± 0.069	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
Dihydroxy PGF2 alpha	COX	223.139 ± 51.046	209.954 ± 80.004	225.266 ± 54.268	257.601 ± 83.962	262.032 ± 53.537	234.956 ± 36.726
Dihydroxy- PGD2	COX	0.000 ± 0.000	0.000 ± 0.000	1.250 ± 0.548	1.644 ± 0.511	2.010 ± 0.634	2.619 ± 0.469
Dihydroxy- PGE2	VOC	0.000 ± 0.000	0.000 ± 0.000	2.403 ± 0.711	3.704 ± 1.611	5.176 ± 1.226	6.505 ± 0.939
PGA2	COX	0.000 ± 0.000	0.000 ± 0.000	2.008 ± 0.751	3.673 ± 1.351	9.176 ± 1.819	26.413 ± 11.077 *
PGB2	COX	0.500 ± 0.866	0.269 ± 0.466	29.719 ± 9.917	53.479 ± 19.729	141.215 ± 22.135	426.067 ± 161.622 *
PGD2	COX	0.040 ± 0.037	0.020 ± 0.018	2.949 ± 2.037	4.027 ± 2.464	3.754 ± 3.809	7.132 ± 3.582 *
PGE2	COX	0.028 ±	0.028 ±	1.342 ±	2.043 ±	2.867 ±	4.982 ±

		0.024	0.026	0.470	0.138 *	0.617 *	1.128 *
PGF2 alpha	COX	0.400 ± 0.071	0.448 ± 0.067	0.950 ± 0.204	1.513 ± 0.550 *	2.515 ± 0.142 *	3.455 ± 0.174 *
PGJ2	COX	0.054 ± 0.051	0.017 ± 0.029	2.783 ± 0.600	5.220 ± 1.618	13.085 ± 3.006	37.341 ± 14.232 *
PGK2	COX	0.000 ± 0.000	0.000 ± 0.000	0.007 ± 0.012	0.036 ± 0.033	0.124 ± 0.136	0.124 ± 0.076
Tetranor- PGEM	COX	1.469 ± 0.419	1.164 ± 0.225	0.936 ± 0.079	4.110 ± 4.514	1.568 ± 0.308	3.828 ± 2.058
Tetranor- PGFM	COX	1.096 ± 0.722	0.751 ± 0.421	0.403 ± 0.071	1.799 ± 2.273	0.517 ± 0.064	0.833 ± 0.388
TXB2	COX	0.000 ± 0.000	0.016 ± 0.028	0.015 ± 0.025	0.038 ± 0.066	0.000 ± 0.000	0.000 ± 0.000
12,13 diHOME	CYP	0.101 ± 0.027	0.088 ± 0.018	0.090 ± 0.010	0.098 ± 0.012	0.509 ± 0.699	0.112 ± 0.055
12,13 EpOME	CYP	0.037 ± 0.032	0.037 ± 0.064	0.014 ± 0.024	0.017 ± 0.029	0.045 ± 0.047	0.000 ± 0.000
13-HODE	LOX	0.338 ± 0.150	0.364 ± 0.118	0.480 ± 0.161	0.732 ± 0.312	0.985 ± 0.813	0.733 ± 0.243
13-oxoODE	LOX	1.002 ± 1.068	1.302 ± 1.362	0.863 ± 0.229	1.481 ± 0.566	17.041 ± 27.178	1.815 ± 0.793
15-oxoEDE	LOX	0.176 ± 0.305	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.744 ± 1.289	0.000 ± 0.000
8-HEPE	LOX	0.000 ±	0.000 ±	0.045 ±	0.000 ±	0.000 ±	0.056 ±

		0.000	0.000	0.039	0.000	0.000	0.097
LXA5	LOX	0.539 ± 0.259	0.373 ± 0.124	0.829 ± 0.626	1.534 ± 1.452	2.363 ± 1.434	4.436 ± 2.381 *
8-iso PGF3 alpha	Non-enz	2.901 ± 0.979	3.514 ± 0.918	3.212 ± 3.010	4.261 ± 3.354	2.253 ± 1.019	4.472 ± 1.703
D17 6-keto PGF-1 alpha	COX	0.000 ± 0.000	0.000 ± 0.000	0.004 ± 0.008	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
PGD3	COX	0.000 ± 0.000	0.037 ± 0.065	0.157 ± 0.183	0.224 ± 0.205	0.757 ± 1.312	0.627 ± 1.086
TXB3	COX	3.786 ± 1.270	6.929 ± 2.280	3.336 ± 1.222	3.433 ± 0.322 *	3.768 ± 0.214 *	3.404 ± 0.056 *
13-oxoOTrE	LOX	0.000 ± 0.000	0.904 ± 1.566	0.000 ± 0.000	0.000 ± 0.000	28.138 ± 44.669	2.664 ± 4.614
13-HOTrE	LOX	2.646 ± 4.582	5.291 ± 9.164	9.259 ± 1.212	0.000 ± 0.000	12.698 ± 11.252	26.984 ± 17.514
9-HOTrE	LOX	0.000 ± 0.000	0.013 ± 0.023	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
17-keto DHA	LOX	0.000 ± 0.000	0.000 ± 0.000	0.052 ± 0.090	0.102 ± 0.176	0.000 ± 0.000	0.000 ± 0.000
10S,17S- DiHDoHE (PDX)	LOX	0.010 ± 0.009	0.003 ± 0.006	0.013 ± 0.013	0.010 ± 0.017	0.018 ± 0.019	0.000 ± 0.000
RvD2	LOX	1.000 ±	0.914 ±	0.694 ±	1.075 ±	0.669 ±	0.722 ±

		0.399	0.389	0.116	0.356	0.177	0.235
19,20 DiHDoPE	CYP	0.053 ± 0.009	0.079 ± 0.069	0.042 ± 0.009	0.048 ± 0.048	0.032 ± 0.032	0.079 ± 0.088
20HDoHE	Non- enz/CYP	0.108 ± 0.188	0.000 ± 0.000	0.192 ± 0.332	0.000 ± 0.000	0.295 ± 0.511	0.000 ± 0.000
9-HODE	LOX	0.326 ± 0.132	0.310 ± 0.134	0.287 ± 0.057	0.525 ± 0.228	0.614 ± 0.485	0.423 ± 0.159
9-oxoODE	LOX	1.571 ± 1.235	1.175 ± 0.546	1.405 ± 0.352	1.646 ± 0.585	24.136 ± 39.195	1.790 ± 1.332
9,10,13 triHOME	LOX/CYP	0.133 ± 0.118	0.183 ± 0.169	0.114 ± 0.016	0.182 ± 0.051	1.112 ± 1.643	0.303 ± 0.192
9,12,13 triHOME	LOX/CYP	0.120 ± 0.127	0.209 ± 0.253	0.101 ± 0.087	0.130 ± 0.123	1.295 ± 1.866	0.286 ± 0.270
9,10 diHODE	CYP	0.008 ± 0.007	0.010 ± 0.009	0.010 ± 0.009	0.002 ± 0.004	0.018 ± 0.005	0.009 ± 0.008
9,10 diHOME	CYP	0.063 ± 0.011	0.055 ± 0.006	0.045 ± 0.018	0.055 ± 0.006	0.231 ± 0.298	0.067 ± 0.024
9,10 EpODE	CYP	0.009 ± 0.008	0.004 ± 0.008	0.007 ± 0.006	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
9,10 EpOME	CYP	0.138 ± 0.078	0.066 ± 0.115	0.066 ± 0.114	0.000 ± 0.000	0.068 ± 0.119	0.000 ± 0.000
15-HETrE	LOX	0.023 ± 0.010	0.034 ± 0.023	0.071 ± 0.026	0.134 ± 0.036	0.225 ± 0.058 *	0.352 ± 0.062 *
8-HETrE	LOX	0.000 ±	0.000 ±	0.011 ±	0.000 ±	0.000 ±	0.000 ±

		0.000	0.000	0.020	0.000	0.000	0.000
PGF1 alpha	COX	0.507 ± 0.018	0.523 ± 0.118	0.558 ± 0.022	0.601 ± 0.067	0.686 ± 0.074	0.563 ± 0.094
TXB1	COX	0.287 ± 0.025	0.267 ± 0.34	0.349 ± 0.102	0.532 ± 0.211	0.609 ± 0.073	0.638 ± 0.117
15-keto PGF1 alpha	COX	0.207 ± 0.190	0.219 ± 0.094	0.281 ± 0.052	0.190 ± 0.178	0.251 ± 0.217	0.193 ± 0.229
Arachidonic Acid	NA	0.001 ± 0.001	0.002 ± 0.003	0.000 ± 0.000	0.001 ± 0.001	0.001 ± 0.001	0.003 ± 0.001
DHA	NA	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.088 ± 0.152	0.000 ± 0.000	0.000 ± 0.000
EPA	NA	0.085 ± 0.022	0.107 ± 0.095	0.042 ± 0.014	0.041 ± 0.009	0.040 ± 0.014	0.030 ± 0.013
17-keto DPA	LOX	0.003 ± 0.006	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000

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