Supplementary Methods

S-phase Entry

S-phase entry was evaluated by BrdU incorporation and indirect immunofluorescence. Cells were grown on coverslips, serum-deprived, and treated with stimuli for 24 h. BrdU was added at a concentration of 10 μM for the last 30 min. BrdU-positive cells were revealed with Texas Red-conjugated secondary Abs (Jackson ImmunoResearch Laboratories, West Grove, PA). Cell nuclei were identified by Hoechst staining. Fluorescence was visualized with a Zeiss 140 epifluorescent microscope.

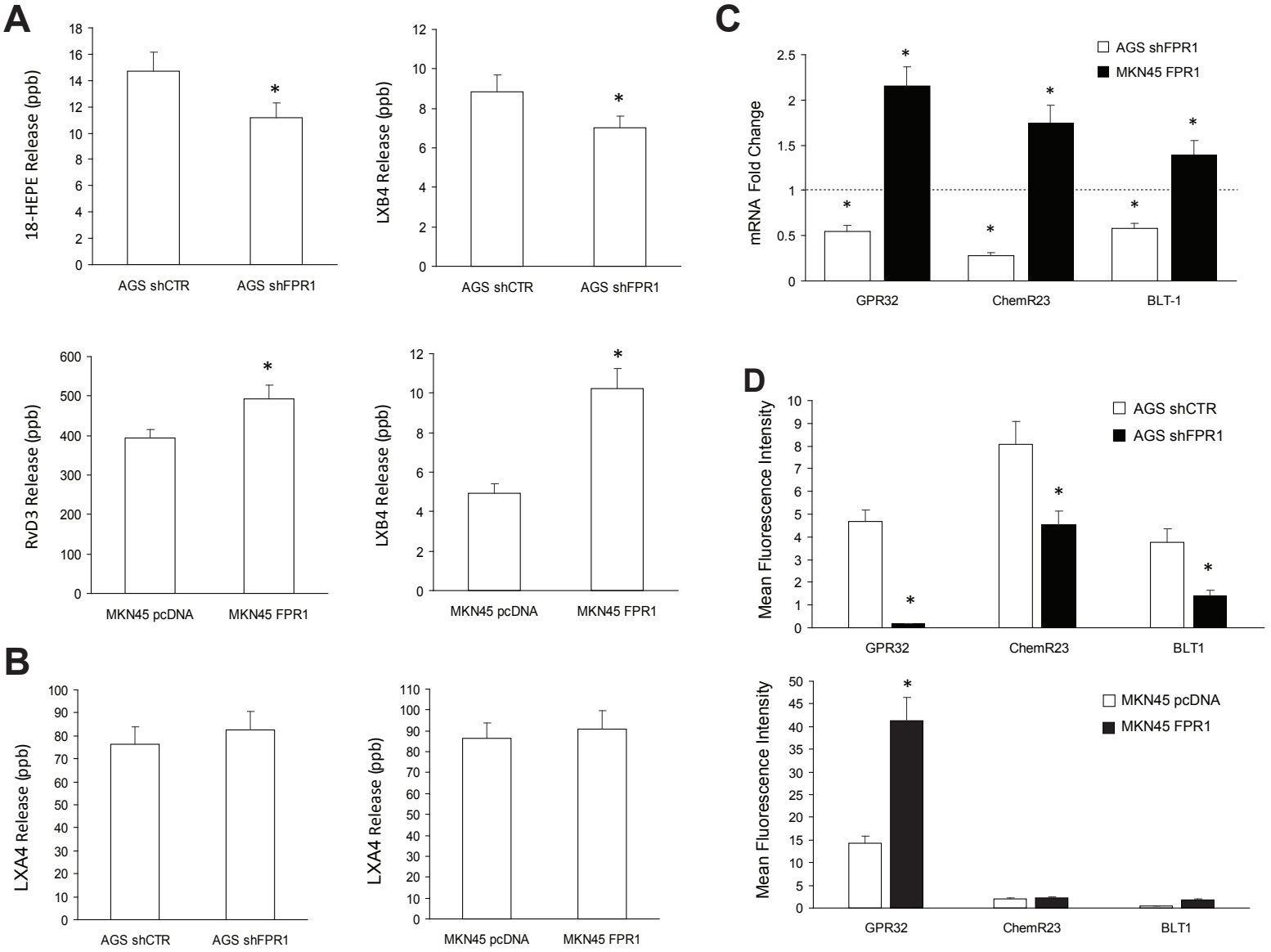
Supplementary Table 1. List of primers

GPR32 F	ACTATATTGTCTCCAGGCAGTG
GPR32 R	ACAGTGCGGTGGTTCAGG
ChemR23 F	CTGTCCACACCTGGGTCTTC
ChemR23 R	CCCCACAGGGTCCATTTGG
BLT-1 F	GCCCTGGAAAACGAACATGA
BLT-1 R	TTAGATGGAAGGCCCGGTG
VEGF-A F	GTGAATGCAGACCAAAGAAAG
VEGF-A R	AAACCCTGAGGGAGGCTC
VEGF-B F	TGTCCCTGGAAGAACACAGCC
VEGF-B R	GCCATGTGTCACCTTCGCA
VEGF-C F	ATGTTTTCCTCGGATGCTGGA
VEGF-C R	CATTGGCTGGGGAAGAGTTT
VEGF-D F	GTATGGACTCTCGCTCAGCAT
VEGF-D R	AGGCTCTCTTCATTGCAACAG
ANG1 F	CCTCGCTGCCATTCTGACTC
ANG1 R	ACTCTCACGACAGTTGCCATC
CXCL1 F	CACCATGGCCCGCGCTGCTCTC
CXCL1 R	GTTGGATTTGTCACTGTT
ALOX15A F	GACTTTGAGGTTTCGCTGGC
ALOX15A R	GACCACACCAGAAAATCCGG
ALOX15B F	GAGGGTACAGCCAAGGTGTC
ALOX15B R	AAAGCAGAGCCAGCCTGTAG
ALOX5 F	AGTCCTCAGGCTTCCCCAAGT
ALOX5R	CATGCCCAGGAACAGCTCGTT
β-ACT F	TGCGTGACATTAAGGAGAAG
β-ACT R	GCTCGTAGCTCTTCTCCA

Supplementary Table 2. LC-MS/MS ion products

For LC-MS/MS Multiple Reaction Monitoring (MRM) was performed by the detection of a unique product ion arising from collision-induced fragmentation of the reported protonated parent compound

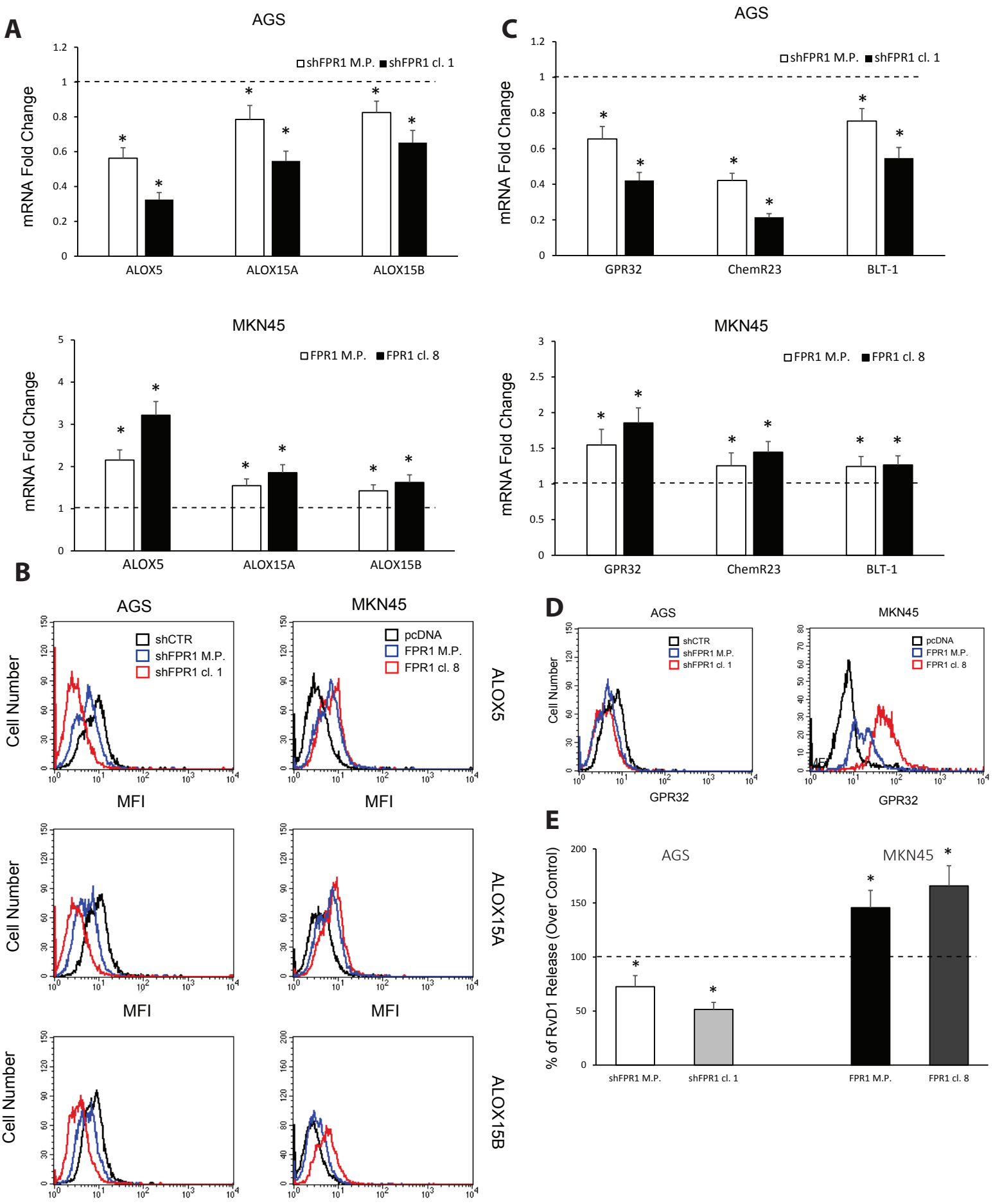
Precursor ion	Product ion	Name	CE (V)	Dwell(sec)	DP (V)
301.300	257.100	EPA	-41	25	-60
303.300	259.100	AA	-41	25	-60
317.200	115.100	5-HEPE	-22	25	-60
317.200	179.100	12-HEPE	-21	25	-60
317.200	219.100	15-HEPE	-19	25	-60
317.200	259.100	18-HEPE	-18	25	-60
319.200	115.100	5-HETE	-21	25	-60
319.200	179.100	12-HETE	-21	25	-60
319.200	219.100	15-HETE	-19	25	-60
325.000	281.000	20-HETE -d6	-20	25	-60
327.300	283.100	DHA	-41	25	-60
333.200	235.200	5,15DIHEPE	-22	25	-60
333.300	253.200	Resolvin E2	-22	25	-60
333.300	201.100	Resolvin E3	-22	25	-60
335.200	115.200	5,15DIHETE	-30	25	-60
335.300	195.200	LTB4	-22	25	-60
343.200	101.100	4-HDHA	-18	25	-60
343.200	141.100	7-HDHA	-18	25	-60
343.200	205.100	15- HDHA	-21	25	-60
343.200	245.100	17-HDHA	-20	25	-60
349.200	215.100	LXA5	-22	25	-60
349.200	221.200	LXB5	-30	25	-60
349.200	195.100	Resolvin E1	-24	25	-60
351.200	235.100	LXA4	-22	25	-60
351.200	221.100	LXB4	-30	25	-60
351.300	233.200	PGD2	-30	25	-60
351.300	175.100	PGE2	-30	25	-60
353.300	193.100	PGF2a	-30	25	-60
355.000	275.000	PGE2_D4	-27	25	-60
355.000	255.000	PGE2_D4	-27	25	-60
359.200	199.100	Resolvin D5	-23	25	-60
359.200	159.100	Resolvin D6	-22	25	-60
359.200	250.100	Maresin 1	-22	25	-60
359.200	221.100	4,14DHDHA	-22	25	-60
359.200	153.100	PGD1	-22	25	-60
369.300	169.100	TXB2	-30	25	-60
375.200	215.200	Resolvin D1	-22	25	-60
375.200	141.200	Resolvin D2	-24	25	-60
375.200	147.100	Resolvin D3	-28	25	-60



Supplementary Figure 1

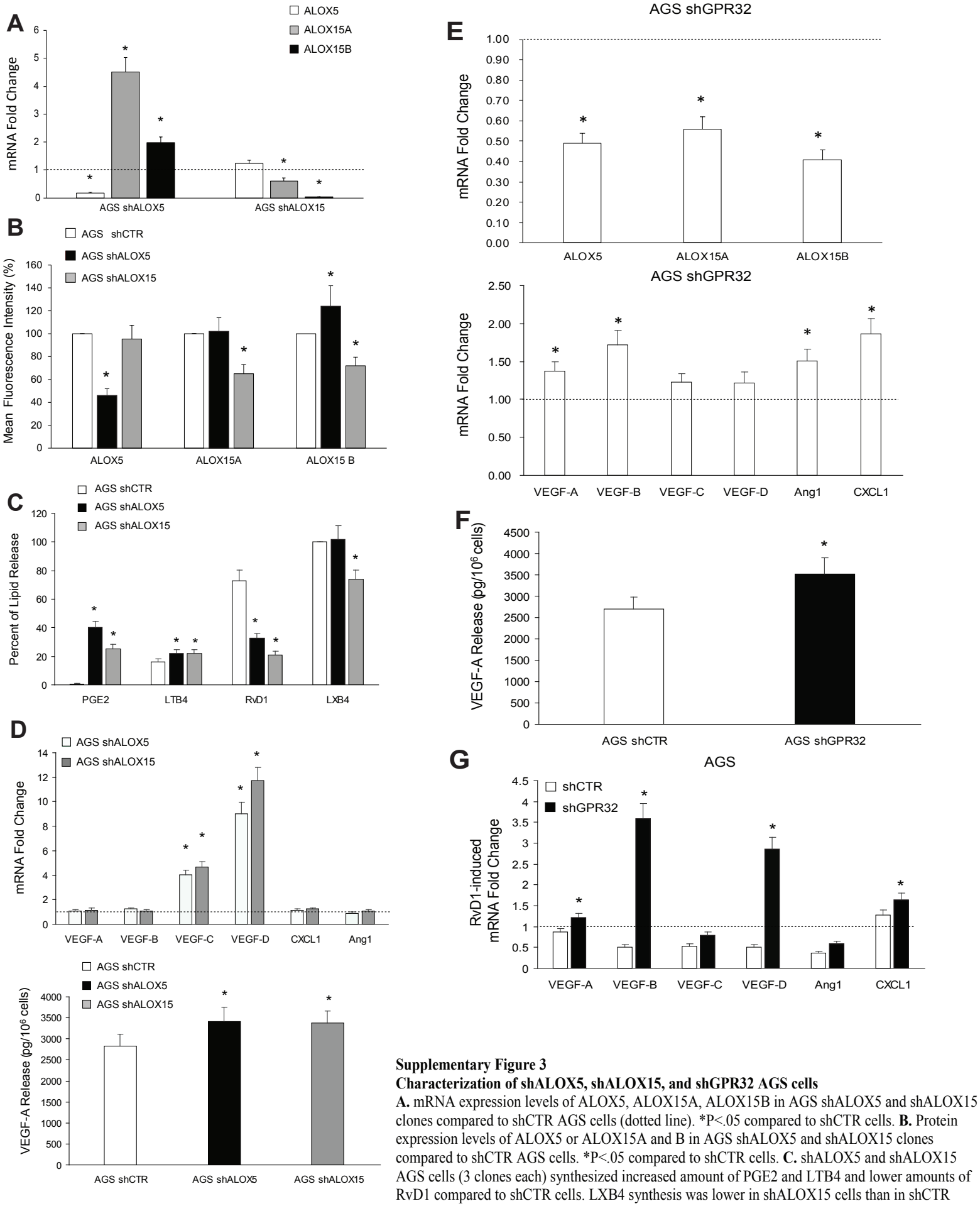
Lipidomic prolife of gastric cancer cells expressing different levels of FPR1

A. Release of 18-HEPE and LXB4 from shCTR and shFPR1 AGS cells, and of RvD3 and LXB4 from MKN45 pcDNA and FPR1 cells assessed by LC-MS/MS. *P<.05 compared to the relative control. **B.** Release of LXA4 from shCTR and shFPR1 AGS cells, and from MKN45 pcDNA and FPR1 cells assessed by LC-MS/MS. **C.** AGS shFPR1 expressed significantly lower levels and MKN45 FPR1 expressed significantly higher levels of GPR32, ChemR23 and BLT1 mRNAs compared to relative controls (dotted line). *P<.05 compared to the relative control. **D.** GPR32, ChemR23 and BLT1 expression levels were lower in AGS shFPR1 versus shCTR cells. MKN45 FPR1 expressed significantly higher levels of GPR32 compared to empty vector transfected cells, as evaluated by cytofluorimetric analysis. *P<.05 compared to the relative control.

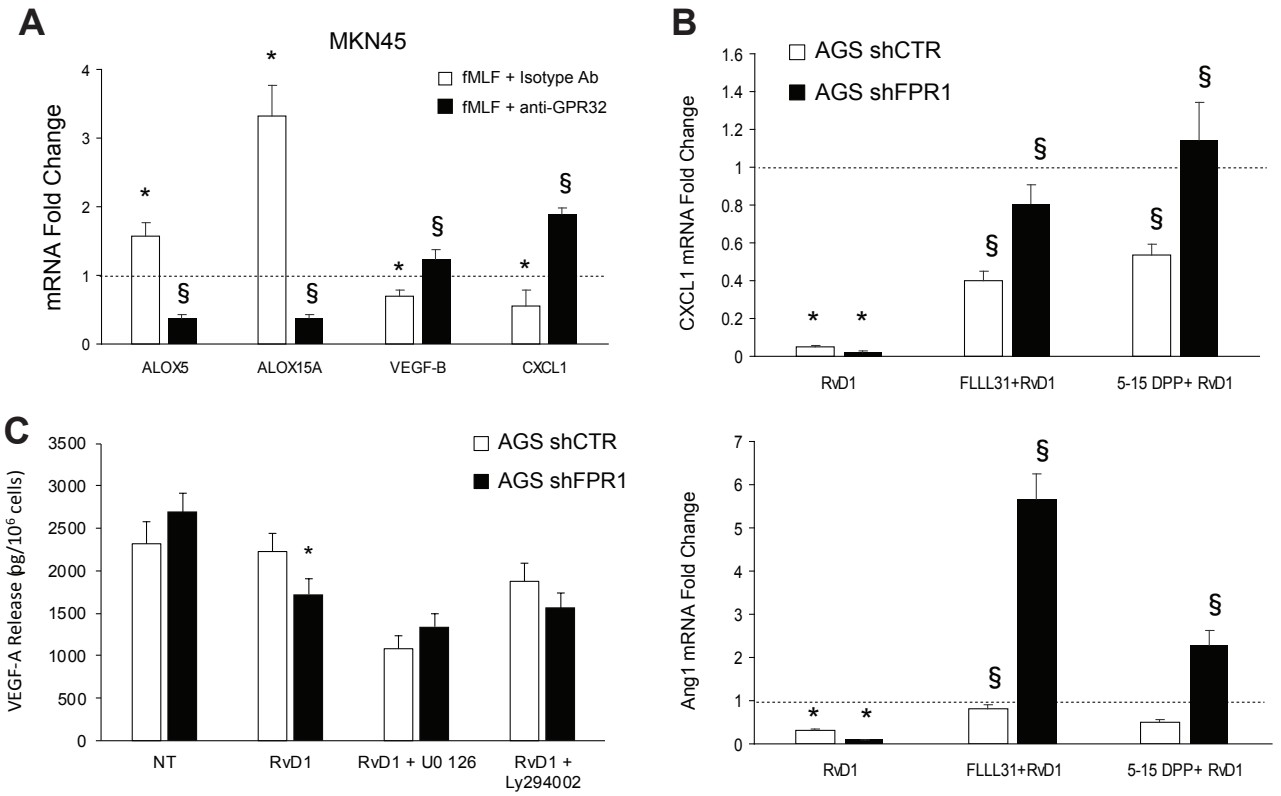


Supplementary Figure 2. Relation between FPR1 expression and SPM biosynthesis machinery in AGS shFPR1 cl. 1 and M.P. and MKN45 FPR1 cl. 8 and M.P.

A. AGS shFPR1 cl. 1 and M.P. expressed significantly lower levels and MKN45 FPR1 cl 8 and M.P. significantly higher levels of ALOX5, ALOX15A and ALOX15B mRNAs compared to relative controls (dotted line), as assessed by real time PCR. **B**. ALOX5, ALOX15A and ALOX15B protein levels were lower in AGS shFPR1 (cl. 1 red line and M.P. blue line) versus AGS shCTR (black line), and in MKN45 pcDNA versus MKN45 FPR1 cells (cl. 8 red line and M.P. blue line), as evaluated by cytofluorimetric analysis. **C**. AGS shFPR1 cl 1 and M.P. expressed significantly lower levels and MKN45 FPR1 cl 8 and M.P. significantly higher levels of GPR32, ChemR23 and BLT-1 mRNAs compared to relative controls (dotted line), as assessed by real time PCR. **D**. GPR32 protein levels were lower in AGS shFPR1 (cl. 1 red line and M.P. blue line) versus AGS shCTR (black line), and in MKN45 pcDNA versus MKN45 FPR1 cells (cl. 8 red line and M.P. blue line), as evaluated by cytofluorimetric analysis. **E**. AGS shFPR1 cl. 1 and M.P. cells produced significantly lower and MKN45 FPR1 cl 8 and M.P. significantly higher amounts of RvD1 compared to relative controls (dotted line), as evaluated by EIA assays.

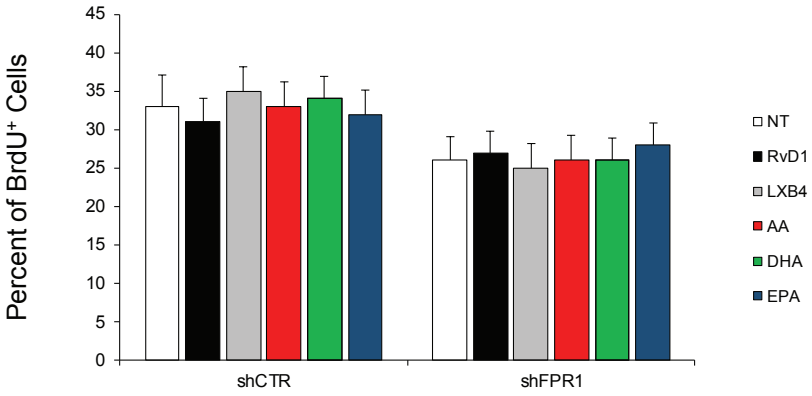


Supplementary Figure 3
Characterization of shALOX5, shALOX15, and shGPR32 AGS cells
A. mRNA expression levels of ALOX5, ALOX15A, ALOX15B in AGS shALOX5 and shALOX15 clones compared to shCTR AGS cells (dotted line). *P<.05 compared to shCTR cells. **B.** Protein expression levels of ALOX5 or ALOX15A and B in AGS shALOX5 and shALOX15 clones compared to shCTR AGS cells. *P<.05 compared to shCTR cells. **C.** shALOX5 and shALOX15 AGS cells (3 clones each) synthesized increased amount of PGE2 and LTB4 and lower amounts of RvD1 compared to shCTR cells. LXB4 synthesis was lower in shALOX15 cells than in shCTR cells, as evaluated by EIA. *P<.05 compared to shCTR cells. **D.** Increased mRNA levels for VEGF-C and VEGF-D and release of VEGF-A in shALOX5 and shALOX15 AGS cells versus shCTR cells (dotted line). *P<.05 versus shCTR cells. **E.** shGPR32 AGS cells (3 clones each) expressed lower levels of ALOX5, ALOX15A, and ALOX15B mRNA compared to shCTR cells. *P<.05 compared to shCTR cells (dotted line). shGPR32 AGS cells synthesized increased mRNA levels for pro-angiogenic mediators compared to shCTR cells (dotted line). *P<.05 compared to shCTR cells. **F.** shGPR32 AGS cells released higher amount of VEGF-A compared to shCTR cells. *P<.05 compared to shCTR cells. **G.** RvD1 (1nM) significantly inhibited pro-angiogenic molecule mRNAs synthesis in shCTR but not in shGPR32 AGS cells. *P<.05 compared to shCTR cells.



Supplementary Figure 4. fMLF activates pro-resolving pathways in AGS through a GPR32-STAT3 dependent pathway.

A. In MKN45 cells, fMLF induced ALOX5 and ALOX15A mRNA overexpression and concomitant VEGF-B and CXCL1 mRNA down-regulation. These effects were reverted by a neutralizing GPR32 antibody. An isotype-matched antibody was used as a control. *P<.05 compared to untreated cells (dotted line). §P<.05 compared to isotype-matched control. **B.** Two STAT3 inhibitors (5-15 DPP and FLLL31) reverted the anti-angiogenic effects of RvD1 in AGS shFPR1 cells assessed as reduction of CXCL1 and Ang1 mRNA synthesis. *P<.05 compared to untreated cells (NT). §P<.05 compared to RvD1 treated cells. **C.** MAPK [U0 126 (25 μM)] or Akt inhibitors [LY294002 (15 μM)] did not modify the anti-angiogenic effects of RvD1 in AGS shFPR1 cells. *P<.05 compared to untreated cells (NT). §P<.05 compared to RvD1 treated cells.



Supplementary Figure 5. Effects of ω-3, ω-6, and SPMs on gastric cancer cell proliferation
Proliferation index of AGS shCTR and shFPR1 AGS cells left untreated or treated with RvD1 (1 nM), LXB4 (1 nM), AA (20 μM), DHA (20 μM), or EPA (20 μM), assessed by BrdU incorporation.