

Supplementary materials

Table S1. Cell passage and donor features

Primary cell type	Cell passage	Gender	Age	Surgery
BMSC-1	VI	M	47	Total hip replacement
BMSC-2	VI	F	69	Total hip replacement
BMSC-3	VII	F	60	Total hip replacement
BMSC-4	VIII	F	73	Total hip replacement
BMSC-5	VI	M	74	Total hip replacement
ASC-1	IX	F	39	Total hip replacement
ASC-2	VII	F	35	Plastic surgery
ASC-3	VII	F	58	Plastic surgery
ASC-4	VIII	F	56	Total hip replacement
ASC-5	X	F	56	Total hip replacement
ASC-6	XI	F	26	Plastic surgery
ASC-7	V	F	46	Plastic surgery
ASC-8	VIII	F	34	Plastic surgery
DF-1	V	F	46	Abdominoplasty
DF-2	IV	F	46	Abdominoplasty
DF-3	V	F	26	Abdominoplasty

Table S2. Lipids quantitation in CM and EV samples from BMSC, ASC and DF

Compound	BMSC				ASC				DF			
	CM pg/ml x10 ⁶ cells		EV pg x10 ⁶ cells		CM pg/ml x10 ⁶ cells		EV pg x10 ⁶ cells		CM pg/ml x10 ⁶ cells		EV pg x10 ⁶ cells	
	Mean	CI95	Mean	CI95	Mean	CI95	Mean	CI95	Mean	CI95	Mean	CI95
AA	43.1	32.9	2.68	1.99	16.7	13.8	1.37	1.00	2.64	2.80	1.20	1.65
EPA	0.70	0.61	0.04	0.03	0.93	0.29	0.03	0.02	-	-	-	-
DHA	3.34	2.04	0.10	0.08	1.58	1.10	0.07	0.04	0.70	0.98	0.01	0.01
PGE2	163	145	-	-	38.1	14.5	-	-	28.8	12.5	-	-
2AG	287	159	118	59.2	53.2	28.3	18.7	14.9	16.2	3.69	10.9	4.94
OEA	55.4	39.3	14.5	6.41	3.14	0.77	2.46	1.03	4.96	3.24	2.53	1.66
SEA	549	577	59.7	38.9	81.2	36.6	12.0	10.1	31.3	20.5	9.27	11.02
DHEA	12.7	6.51	3.40	2.43	15.5	11.2	1.04	0.80	17.2	13.1	0.13	0.13
PEA	259	319	62.3	27.9	23.1	12.7	14.4	8.69	4.42	3.81	13.6	17.6

Fig S4. Lipids quantified in untreated and 2AG or PEA treated CH cell media (absence of TNF α) at day 3 analyzed by UHPLC-MS/MS analysis. Data (n=5 independent experiments) were expressed in ng/ml.

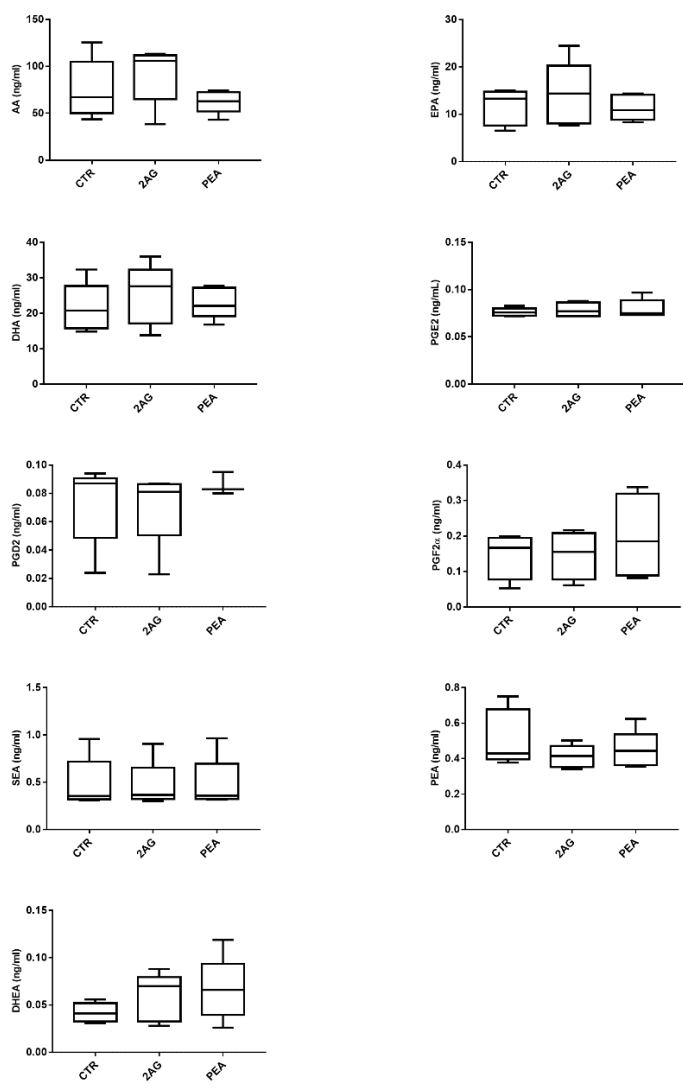


Fig S5. Lipids quantified in TNF α -stimulated CH cell media at day 3 analyzed by UHPLC-MS/MS analysis. Data (n=8 independent experiments) were expressed in ng/ml

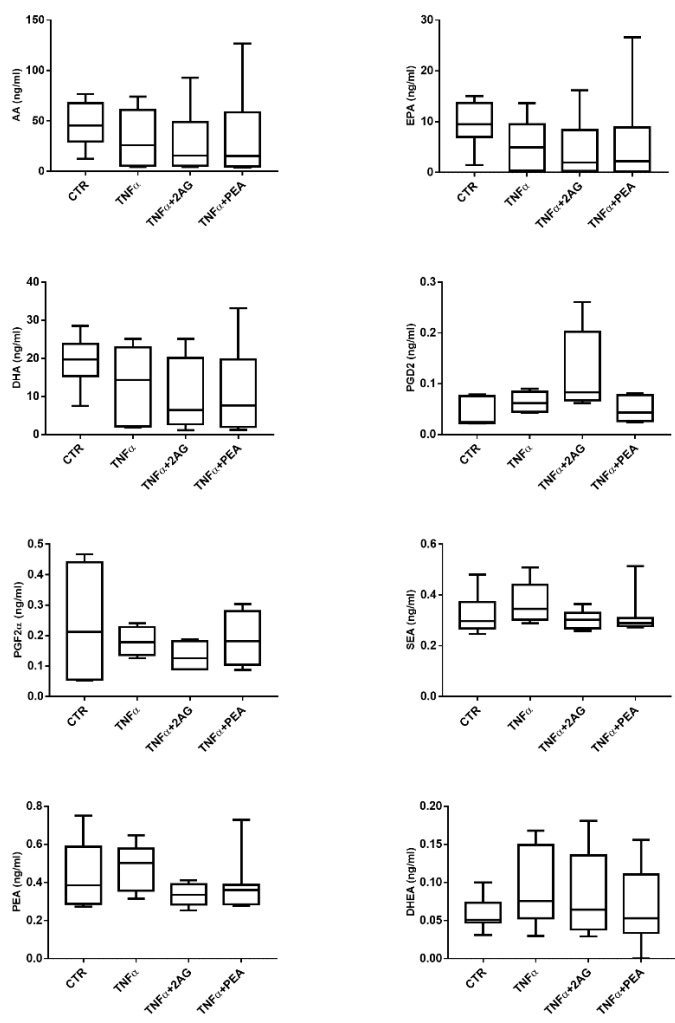


Table S6. Quantification data of lipids in EV (ng per 10⁶ cells) and CM (ng/mL per 10⁶) cells from BMSC, ASC and DF

Compound	BMSC-CM 1	BMSC-CM 2	BMSC-CM 3	BMSC-CM 4	BMSC-CM 5	ASC-CM 1	ASC-CM 2	ASC-CM 3	ASC-CM 4	ASC-CM 5	ASC-CM 6	ASC-CM 7	ASC-CM 8	DF-CM 1	DF-CM 2	DF-CM 3
								ng/mL x 10 ⁶ cells								
2AG	0.220	0.508	0.187	0.079	0.446	0.073	0.133	0.064	0.028	0.050	0.062	0.008	0.008	0.015	0.014	0.020
PEA	0.057	0.856	0.110	0.015	<LOQ	0.014	0.020	0.013	0.017	0.056	0.048	0.009	0.009	0.007	0.001	0.001
OGA	0.001	0.102	<LOQ	<LOQ	0.009	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
SEA	0.180	1.594	0.350	0.072	<LOQ	<LOQ	<LOQ	<LOQ	0.057	0.143	0.095	0.031	0.080	0.001	0.001	0.031
DHEA	<LOQ	<LOQ	0.015	0.009	0.014	0.051	0.018	0.008	<LOQ	0.015	0.011	<LOQ	<LOQ	0.011	0.023	0.001
AA	37.486	98.520	59.840	5.812	14.006	5.078	5.785	1.734	17.029	43.820	52.160	2.270	6.022	5.475	0.906	1.562
EPA	0.723	<LOQ	1.320	<LOQ	1.477	1.069	1.441	<LOQ	0.355	1.110	0.671	<LOQ	<LOQ	0.654	0.001	0.001
DHA	2.158	6.558	3.538	0.300	4.161	2.875	0.441	0.302	0.845	3.832	3.678	0.210	0.487	1.675	0.326	0.069
PGE2	0.065	0.448	0.127	0.029	0.151	0.046	0.075	0.024	0.017	0.056	0.038	0.012	0.037	0.034	0.036	0.016
Compound	BMSC-EV 1	BMSC-EV 2	BMSC-EV 3	BMSC-EV 4	BMSC-EV 5	ASC-EV 1	ASC-EV 2	ASC-EV 3	ASC-EV 4	ASC-EV 5	ASC-EV 6	ASC-EV 7	ASC-EV 8	DF-EV 1	DF-EV 2	DF-EV 3
								ng x 10 ⁶ cells								
2AG	0.052	0.188	0.108	0.056	0.189	0.012	0.034	0.002	0.016	0.017	0.065	0.002	0.002	0.014	0.006	0.013
PEA	0.018	0.062	0.102	0.049	0.080	0.013	0.019	0.004	0.009	0.039	0.024	0.004	0.004	0.031	0.002	0.008
OGA	0.010	0.015	0.019	<LOQ	0.014	0.003	0.002	0.003	<LOQ	0.001	0.004	<LOQ	<LOQ	0.003	<LOQ	<LOQ
SEA	0.056	0.121	0.077	0.044	<LOQ	<LOQ	<LOQ	<LOQ	0.015	0.042	0.022	0.008	0.009	0.019	0.001	0.008
DHEA	0.002	0.003	0.007	0.001	<LOQ	0.001	0.001	<LOQ	<LOQ	0.002	0.003	<LOQ	<LOQ	0.001	0.001	0.001
AA	2.030	6.167	3.623	0.908	0.695	1.289	1.020	0.213	1.619	1.997	4.509	0.150	0.188	0.055	0.702	2.845
EPA	0.000	0.049	0.060	0.002	0.068	0.000	0.000	<LOQ	0.017	<LOQ	0.068	<LOQ	<LOQ	0.001	0.001	0.022
DHA	0.095	0.231	0.123	0.025	0.018	0.090	0.079	0.017	0.061	0.093	0.179	0.006	0.006	0.007	0.001	0.024

Table S7. Quantification data of lipids in untreated and 2AG or PEA treated CH cell media (absence of TNF α) at day 3 analyzed by UHPLC-MS/MS analysis. Data (n=5 independent experiments) were expressed in ng/ml.

Compound	CTR	2AG	PEA
	ng/mL		
AA	67,200	113,300	60,900
	125,400	105,700	70,100
	56,600	91,400	62,700
	43,624	38,618	43,094
	84,200	109,900	74,700
EPA	15,027	24,497	14,391
	13,250	8,438	10,816
	6,482	14,369	8,349
	8,697	7,671	9,333
	14,474	16,095	13,844
DHA	20,792	35,983	26,705
	32,304	20,404	27,676
	16,826	27,647	21,506
	14,820	13,801	16,843
	23,088	28,560	22,116
PGE2	0,077	0,088	0,097
	0,076	0,072	0,075
	0,073	0,077	0,073
	0,072	0,072	0,080
	0,083	0,085	0,073
PGD2	0,024	0,023	<LOQ
	0,087	0,081	<LOQ
	0,087	0,078	0,095
	0,073	0,086	0,080
	0,094	0,087	0,083
PGF2	<LOQ	0,061	0,082
	0,182	0,216	0,338
	0,199	0,201	0,261
	0,053	0,095	0,109
	0,152	0,155	<LOQ
SEA	0,956	0,905	0,966
	0,356	0,300	0,428
	0,326	0,349	0,335
	0,481	0,399	0,313
	0,312	0,365	0,358
PEA	0,604	0,502	0,372
	0,429	0,340	0,625
	0,378	0,364	0,450
	0,751	0,442	0,354

	0,415	0,415	0,444
DHEA	0,048	0,088	0,119
	0,041	0,037	0,068
	0,034	0,070	0,053
	0,031	0,028	0,026
	0,056	0,071	0,066

Table S8. Quantification data of lipids in TNF α -stimulated CH cell media at day 3 analyzed by UHPLC-MS/MS analysis. Data (n=8 independent experiments) were expressed in ng/ml

Compound	CTR	TNF α	TNF α +2AG	TNF α +PEA
	ng/mL			
AA	39,879	27,456	37,171	28,850
	25,891	4,977	5,240	8,395
	12,329	24,146	6,131	3,899
	67,192	4,128	7,801	4,229
	76,547	74,117	52,876	68,238
	46,888	35,396	23,419	22,116
	67,740	69,271	92,688	126,431
	43,624	6,758	4,159	6,060
EPA	10,232	5,818	8,018	6,166
	6,503	0,419	0,233	0,757
	1,472	3,958	0,715	0,408
	15,027	0,318	0,513	0,085
	11,074	10,698	8,494	9,716
	8,544	5,824	3,158	3,610
	14,572	13,602	16,190	26,582
	8,697	0,345	0,171	0,176
DHA	28,546	14,953	20,578	16,087
	17,097	2,625	2,476	4,745
	7,513	17,854	3,304	2,503
	20,792	1,900	3,382	1,799
	24,019	24,547	18,684	20,953
	18,703	13,654	9,469	10,539
	23,204	25,083	25,100	33,138
	14,820	1,830	1,093	1,233
PGD2	0,023	0,046	0,062	0,024
	0,022	0,043	0,144	0,029
	0,079	0,078	0,261	0,043
	0,024	0,062	0,073	0,074
	0,073	0,090	0,083	0,081
PGF2	0,467	0,240	0,090	0,304

	0,363	0,192	0,162	0,207
	0,062	0,166	0,188	0,156
	0,053	0,126	0,089	0,087
SEA	0,295	0,312	0,281	0,276
	0,290	0,509	0,283	0,283
	0,315	0,329	0,265	0,273
	0,391	0,409	0,365	0,513
	0,300	0,451	0,258	0,296
	0,247	0,289	0,322	0,284
	0,261	0,300	0,326	0,300
	0,481	0,363	0,331	0,311
PEA	0,366	0,348	0,282	0,372
	0,282	0,498	0,392	0,296
	0,406	0,316	0,288	0,282
	0,604	0,508	0,382	0,728
	0,305	0,648	0,253	0,277
	0,273	0,591	0,343	0,350
	0,538	0,386	0,326	0,391
DHEA	0,100	0,168	0,181	0,104
	0,069	0,090	0,060	0,113
	0,053	0,165	0,125	0,053
	0,048	0,102	0,139	0,156
	0,048	0,056	0,060	0,053
	0,047	0,061	0,069	0,000
	0,075	0,052	0,031	0,047
	0,031	0,030	0,029	0,029