

# Targeted phospholipidomic analysis of synovial fluid as a tool for osteoarthritis deep phenotyping

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**Supplementary Figure 1. PLS-DA loadings and VIP scores of first discriminant function.** A) Loading values show the top ten phospholipid species selected by the PLS-DA for component 1 (non OA-control vs OA). B) VIP scores show the top ten phospholipid species selected by the PLS-DA for component 1 (non OA-control vs OA). Each phospholipid is ranked by the absolute values of their loadings.

**Supplementary Figure 2. PLS-DA displayed differences in phospholipid profiles between eOA and IOA patients.** A) PLS-DA revealed clear separation with minimum overlap between eOA and IOA. 95% confidence ellipses illustrate sample separation. B) PLS-DA shows a good prediction (with  $Q^2=0.46$ ,  $R^2=0.74$  and accuracy=0.87). C) VIP scores show the top twelve phospholipid species selected by the PLS-DA for component 1 (eOA vs IOA). Each phospholipid is ranked by the absolute values of their loadings.

**Supplementary Figure 3.** Heatmap showing highly positive correlations among PC concentrations in OA SF. Correlation coefficient was obtained by the Pearson's correlation method. Correlation cut-off: 0.7.

**Supplementary Table 1.** MRM/MS method in positive ion mode for the determination of PC species in synovial fluid (SF).

<b>ID</b>	<b>Q1 (m/z)</b>	<b>Q3 (m/z)</b>	<b>MODE</b>	<b>DP (V)</b>	<b>CE (V)</b>	<b>DWT (msec)</b>	<b>CXP (V)</b>
<b>D-<math>\alpha</math>-PC dipalmitoyl</b>	734,60	184,10 734,60	POS	40	47	25	9
<b>Ceramide</b>	551,94	264,40 551,94	POS	40	47	25	9
<b>LPC</b>	505,00	505,00 184,10	POS	40	47	25	9
<b>PC 22:0</b>	594,40	184,10	POS	40	47	25	9
<b>PC 22:1</b>	592,40	184,10	POS	40	47	25	9
<b>PC 24:0</b>	622,40	184,10	POS	40	47	25	9
<b>PC 24:1</b>	620,40	184,10	POS	40	47	25	9
<b>PC 26:0</b>	650,50	184,10	POS	40	47	25	9
<b>PC 26:1</b>	648,50	184,10	POS	40	47	25	9
<b>PC 28:0</b>	678,50	184,10	POS	40	47	25	9
<b>PC 28:1</b>	676,50	184,10	POS	40	47	25	9
<b>PC 28:2</b>	674,50	184,10	POS	40	47	25	9
<b>PC 30:0</b>	706,50	184,10	POS	40	47	25	9
<b>PC 30:1</b>	704,50	184,10	POS	40	47	25	9
<b>PC 30:2</b>	702,50	184,10	POS	40	47	25	9
<b>PC 32:0</b>	734,60	184,10	POS	40	47	25	9
<b>PC 32:1</b>	732,60	184,10	POS	40	47	25	9
<b>PC 32:2</b>	730,50	184,10	POS	40	47	25	9
<b>PC 34:1</b>	760,60	184,10	POS	40	47	25	9
<b>PC 34:2</b>	758,60	184,10	POS	40	47	25	9
<b>PC 36:0</b>	790,60	184,10	POS	40	47	25	9
<b>PC 36:1</b>	788,60	184,10	POS	40	47	25	9
<b>PC 36:2</b>	786,60	184,10	POS	40	47	25	9
<b>PCaa 24:0</b>	622,44	184,10	POS	40	47	25	9
<b>PCaa 40:4</b>	838,62	184,10	POS	40	47	25	9
<b>PCaa 42:5</b>	864,64	184,10	POS	40	47	25	9
<b>PCae 36:0</b>	776,64	184,10	POS	40	47	25	9
<b>PCae 38:0</b>	804,68	184,10	POS	40	47	25	9
<b>PCae 38:3</b>	798,63	184,10	POS	40	47	25	9
<b>Pcae 40:1</b>	830,69	184,10	POS	40	47	25	9
<b>PCae 40:5</b>	822,63	184,10	POS	40	47	25	9
<b>PCae 40:6</b>	820,61	184,10	POS	40	47	25	9
<b>PCae 42:0</b>	860,74	184,10	POS	40	47	25	9
<b>PCae 42:3</b>	854,69	184,10	POS	40	47	25	9
<b>PCae 42:5</b>	850,66	184,10	POS	40	47	25	9

**Supplementary Table 2.** MRM/MS method in negative ion mode for the determination of PA, PE, PI, PG and PS species in SF.

ID	Q1 (m/z)	Q3 (m/z)	MODE	DP (V)	CE (V)	DWT (msec)	CXP (V)
PA 28:1	589,4	171,1 199,2 253,2 281,2	NEG	-180	-50	25	-13
PA 28:0	591,4	171,1 199,2 255,2 283,2	NEG	-180	-50	25	-13
PA 30:1	617,4	227,2 253,2	NEG	-180	-50	25	-13
PA 30:0	619,4	199,2 227,2 255,2 283,2	NEG	-180	-50	25	-13
PE 28:1	632,4	199,2 253,2	NEG	-180	-50	25	-13
PE 28:0	634,4	199,2 255,5	NEG	-180	-50	25	-13
PA 32:2	643,4	253,2	NEG	-180	-50	25	-13
PA 32:1	645,4	227,2 253,2 281,3	NEG	-180	-50	25	-13
PA 32:0	647,4	255,2	NEG	-180	-50	25	-13
PE 30:2	658,5	225,2 253,2	NEG	-180	-50	25	-13
PE 30:1	660,5	199,2 227,2 253,2 281,3	NEG	-180	-50	25	-13
PE 30:0	662,5	199,2 227,2 255,2 283,2	NEG	-180	-50	25	-13
PA 34:2	671,5	253,2 281,3	NEG	-180	-50	25	-13
PA 34:1	673,5	253,2 283,3 281,3 255,2	NEG	-180	-50	25	-13

PE 32:2	686,5	253,3	NEG	-180	-50	25	-13
PE 32:1	688,5	227,2 281,3 255,2 253,2	NEG	-180	-50	25	-13
PA 36:2	699,5	281,3	NEG	-180	-50	25	-13
PA 36:1	701,5	281,3 283,3	NEG	-180	-50	25	-13
PE 34:2	714,5	253,2 281,3	NEG	-180	-50	25	-13
PE 34:1	716,5	255,2 281,3	NEG	-180	-50	25	-13
PG 32:2	717,5	253,2	NEG	-180	-50	25	-13
PG 32:1	719,5	253,2 255,2	NEG	-180	-50	25	-13
PI 26:1	723,5	171,1 253,2	NEG	-180	-50	25	-13
PI 26:0	725,5	171,1 199,2 227,2 255,2	NEG	-180	-50	25	-13
PS 32:3	730,5	253,2	NEG	-180	-50	25	-13
PS 32:1	732,5	227,2 253,2 255,2 281,3	NEG	-180	-50	25	-13
PS 32:0	734,5	255,2	NEG	-180	-50	25	-13
PE 36:2	742,5	281,3	NEG	-180	-50	25	-13
PE 36:1	744,5	281,3 283,3	NEG	-180	-50	25	-13
PG 34:2	745,5	253,2 281,3	NEG	-180	-50	25	-13
PG 34:1	747,6	255,2 281,3	NEG	-180	-50	25	-13
PI 28:1	751,6	199,2 225,2 227,2 253,2	NEG	-180	-50	25	-13
PI 28:0	753,6	171,1 199,2 227,2 255,2 283,3	NEG	-180	-50	25	-13
PS 34:2	758,6	253,2 281,3	NEG	-180	-50	25	-13

		255,2					
PS 34:1	706,6	255,2 281,3	NEG	-180	-50	25	-13
PI 30:2	777,6	253,2 225,2	NEG	-180	-50	25	-13
PI 30:1	779,6	199,2 225,2 227,2 253,2	NEG	-180	-50	25	-13
PI 30:0	781,6	199,2 227,2 255,2 283,3	NEG	-180	-50	25	-13
PS 32:2	786,6	281,3	NEG	-180	-50	25	-13
PS 36:0	790,6	283,3	NEG	-180	-50	25	-13
PI 32:2	805,6	253,2	NEG	-180	-50	25	-13
PI 32:1	807,6	227,2 225,2 283,3 253,2	NEG	-180	-50	25	-13
PI 32:0	809,6	255,2	NEG	-180	-50	25	-13
PI 34:2	833,6	253,2 281,3	NEG	-180	-50	25	-13
PI 34:1	835,6	253,2 255,2 281,3 283,3	NEG	-180	-50	25	-13
PI 34:0	837,7	255,2 283,3	NEG	-180	-50	25	-13
PI 36:2	861,7	281,3	NEG	-180	-50	25	-13
PI 36:1	863,7	281,3	NEG	-180	-50	25	-13
PI 36:0	865,7	283,3	NEG	-180	-50	25	-13

**Supplementary Table 3.** Phospholipid species quantified in SF using MRM/MS lipidomic analysis and modulated between non-OA control vs eOA.

N	Lipid species	m/z	MS mode	Control (n=4)	eOA (n=7)	p-value
1	PC 30:1	704.50	POS	4992.00 ± 2559.00	6789.00 ± 2060.00	0.360
2	PC 36:1	788.60	POS	113.00 ± 71.34	290.40 ± 199.70	0.291
3	PC 36:2	786.60	POS	2294.00 ± 2652.00	2682.00 ± 1084.00	0.405
4	PCaa 24:0	622.44	POS	9675.00 ± 3690.00	16992.00 ± 4246.00	0.068
5	D- $\alpha$ -PC dipalmitoyl	734.60	POS	3793.00 ± 2196.00	4420.00 ± 1451.00	0.613
6	PC 28:1	676.50	POS	378.70 ± 140.40	829.40 ± 389.50	0.069
7	PC 30:0	706.50	POS	807.00 ± 538.20	1034.00 ± 385.50	0.317
8	PC 30:2	702.50	POS	869.30 ± 568.10	1413.00 ± 539.10	0.351
9	PC 32:1	732.60	POS	3524.00 ± 2149.00	4342.00 ± 1465.00	0.437
10	PC 32:2	730.50	POS	1537.00 ± 1336.00	2490.00 ± 683.00	0.112
11	PC 34:1	760.60	POS	215.20 ± 51.09	667.30 ± 285.40*	0.001
12	PC 34:2	758.60	POS	12985.00 ± 5144.00	16386.00 ± 3784.00	0.379
13	PC 36:0	790.60	POS	9586.00 ± 4083.00	18282.00 ± 5341.00	0.058
14	PA 28:0	591.40	NEG	1267.00 ± 48.71	1135.00 ± 170.00	0.087
15	PA 30:0	619.40	NEG	290.90 ± 40.75	213.50 ± 26.3*	0.014
16	PA 34:1	673.50	NEG	650.40 ± 14.43	575.90 ± 68.93*	0.035
17	PA 36:1	701.50	NEG	146.50 ± 83.51	83.38 ± 16.88	0.202
18	PE 30:0	622.50	NEG	111.10 ± 4.02	144.20 ± 15.05*	0.000
19	PE 32:1	688.50	NEG	90.38 ± 9.46	67.82 ± 21.97	0.058
20	PE 34:1	716.50	NEG	257.70 ± 96.12	210.90 ± 20.66	0.609
21	PE 36:2	742.50	NEG	325.50 ± 65.38	162.60 ± 30.85*	0.003
22	PE 36:1	744.50	NEG	905.04 ± 533.40	1672.00 ± 328.70	0.116
23	PG 32:1	719.50	NEG	147.40 ± 12.89	128.70 ± 36.59	0.193
24	PG 34:1	747.60	NEG	270.60 ± 60.55	185.20 ± 46.83*	0.046
25	PG 34:2	745.50	NEG	218.10 ± 86.04	74.76 ± 16.90*	0.008
26	PS 32:1	732.50	NEG	98.56 ± 6.82	197.00 ± 59.97*	0.004
27	PS 32:0	734.50	NEG	497.20 ± 111.00	1070.00 ± 174.00*	0.003
28	PS 36:0	790.60	NEG	222.90 ± 111.30	184.80 ± 63.30	0.593
29	PI 26:0	725.50	NEG	344.20 ± 26.65	455.60 ± 13.88*	0.003
30	PI 28:1	751.60	NEG	118.90 ± 55.48	120.60 ± 12.72	0.724
31	PI 28:0	753.60	NEG	1079.00 ± 36.03	925.00 ± 144.70*	0.033
32	PI 30:2	777.60	NEG	176.70 ± 110.10	76.93 ± 20.83	0.178
33	PI 30:1	779.60	NEG	114.10 ± 2.86	113.10 ± 24.20	0.752
34	PI 30:0	781.60	NEG	797.00 ± 39.04	649.40 ± 48.82*	0.001
35	PI 32:1	807.60	NEG	596.10 ± 45.55	900.50 ± 102.60*	<0.000
36	PI 32:0	809.60	NEG	362.80 ± 112.10	265.70 ± 47.31	0.167
37	PI 34:1	835.60	NEG	1366.00 ± 73.98	1711.00 ± 115.50*	0.000
38	PI 36:2	861.70	NEG	362.60 ± 63.57	648.20 ± 74.20*	0.003
39	PI 36:1	863.70	NEG	452.70 ± 148.80	669.10 ± 79.20	0.072
40	PI 36:0	865.70	NEG	186.50 ± 37.84	319.80 ± 56.48*	0.004

Data are presented as mean $\pm$ SD, unless indicated. ANOVA F-test (FDR corrected <0.05) was used.

eOA: early-stage osteoarthritis; POS: positive ion mode; NEG: negative ion mode; PC: phosphatidylcholine; PA: phosphatidic acid; PE: phosphatidylethanolamine; PG: phosphatidylglycerol; PS: phosphatidylserine; PI: phosphatidylinositol

\*significant difference from control SF



**Supplementary Table 4.** Phospholipid species quantified in SF using MRM/MS lipidomic analysis and modulated between non-OA control vs IOA.

N	Lipid species	m/z	MS mode	Control (n=4)	IOA (n=8)	p-value
1	PC 30:1	704.50	POS	4992.00 ± 2559.00	4169.00 ± 1777.00	0.902
2	PC 36:1	788.60	POS	113.00 ± 71.34	253.10 ± 96.20	0.346
3	PC 36:2	786.60	POS	2294.00 ± 2652.00	1354.00 ± 621.90	0.848
4	PCaa 24:0	622.44	POS	9675.00 ± 3690.00	11444.00 ± 3658.00	0.498
5	D-α-PC dipalmitoyl	734.60	POS	3793.00 ± 2196.00	2033.00 ± 743.80	0.397
6	PC 28:1	676.50	POS	378.70 ± 140.40	322.10 ± 126.70	0.566
7	PC 30:0	706.50	POS	807.00 ± 538.20	454.40 ± 147.40	0.941
8	PC 30:2	702.50	POS	869.30 ± 568.10	684.10 ± 317.10	0.871
9	PC 32:1	732.60	POS	3524.00 ± 2149.00	2057.00 ± 741.40	0.342
10	PC 32:2	730.50	POS	1537.00 ± 1336.00	1098.00 ± 333.00	0.547
11	PC 34:1	760.60	POS	215.20 ± 51.09	311.80 ± 80.76	0.088
12	PC 34:2	758.60	POS	12985.00 ± 5144.00	9784.00 ± 3116.00	0.638
13	PC 36:0	790.60	POS	9586.00 ± 4083.00	12515.00 ± 3860.00	0.316
14	PA 28:0	591.40	NEG	1267.00 ± 48.71	1092.00 ± 179.60*	0.027
15	PA 30:0	619.40	NEG	290.90 ± 40.75	228.40 ± 32.35*	0.034
16	PA 34:1	673.50	NEG	650.40 ± 14.43	564.90 ± 81.16*	0.023
17	PA 36:1	701.50	NEG	146.50 ± 83.51	90.04 ± 24.28	0.259
18	PE 30:0	622.50	NEG	111.10 ± 4.02	139.30 ± 26.06*	0.015
19	PE 32:1	688.50	NEG	90.38 ± 9.46	54.93 ± 19.57*	0.004
20	PE 34:1	716.50	NEG	257.70 ± 96.12	235.10 ± 50.66	0.874
21	PE 36:2	742.50	NEG	325.50 ± 65.38	179.10 ± 11.08*	0.004
22	PE 36:1	744.50	NEG	905.04 ± 533.40	1634.00 ± 311.60	0.124
23	PG 32:1	719.50	NEG	147.40 ± 12.89	131.30 ± 28.90	0.177
24	PG 34:1	747.60	NEG	270.60 ± 60.55	204.70 ± 46.58	0.110
25	PG 34:2	745.50	NEG	218.10 ± 86.04	87.17 ± 24.50*	0.012
26	PS 32:0	732.50	NEG	497.20 ± 111.00	1079.00 ± 156.00*	0.004
27	PS 32:1	734.50	NEG	98.56 ± 6.82	163.00 ± 37.54*	0.000
28	PS 36:0	790.60	NEG	222.90 ± 111.30	200.10 ± 72.45	0.772
29	PI 26:0	725.50	NEG	344.20 ± 26.65	455.90 ± 12.41*	0.004
30	PI 28:1	751.60	NEG	118.90 ± 55.48	116.90 ± 7.78	0.801
31	PI 28:0	753.60	NEG	1079.00 ± 36.03	937.80 ± 131.80*	0.017
32	PI 30:2	777.60	NEG	176.70 ± 110.10	100.40 ± 22.78	0.378
33	PI 30:1	779.60	NEG	114.10 ± 2.86	115.50 ± 22.71	0.956
34	PI 30:0	781.60	NEG	797.00 ± 39.04	686.30 ± 63.13	0.005
35	PI 32:1	807.60	NEG	362.80 ± 112.10	343.20 ± 88.49	0.802
36	PI 32:0	809.60	NEG	596.10 ± 45.55	923.60 ± 178.30*	<0.000
37	PI 34:1	835.60	NEG	1366.00 ± 73.98	1725.00 ± 96.94*	0.000
38	PI 36:2	861.70	NEG	362.60 ± 63.57	708.00 ± 52.91*	0.003
39	PI 36:1	863.70	NEG	452.70 ± 148.80	675.20 ± 95.91	0.069
40	PI 36:0	865.70	NEG	186.50 ± 37.84	326.30 ± 63.73*	0.004

Data are presented as mean±SD, unless indicated. ANOVA F-test (FDR corrected <0.05) was used.

IOA: late-stage osteoarthritis; POS: positive ion mode; NEG: negative ion mode; PC: phosphatidylcholine; PA: phosphatidic acid; PE: phosphatidylethanolamine; PG: phosphatidylglycerol; PS: phosphatidylserine; PI: phosphatidylinositol

\*significant difference from control SF

**Supplementary Table 5.** Pearson's coefficients showed highly positive correlations among PC concentrations in OA synovial fluid.

	<b>PC 30:1</b>	<b>PC 30:2</b>	<b>PC 36:0</b>	<b>PC 28:1</b>	<b>PC 34:2</b>	<b>PC 36:2</b>	<b>D-<math>\alpha</math>-PC dipalmitoyl</b>	<b>PC 32:1</b>	<b>PC 30:0</b>
<b>PC 30:1</b>	1	0.956**	0.701**	0.919**	0.805**	0	0	0	0
<b>PC 30:2</b>	0.956**	1	0.767**	0.963**	0.880**	0.756**	0	0	0
<b>PC 36:0</b>	0.701**	0.767**	1	0.785**	0.815**	0.952**	0	0	0
<b>PC 28:1</b>	0.919**	0.963**	0.785**	1	0.814**	0.790**	0	0	0
<b>PC 34:2</b>	0.805**	0.880**	0.815**	0.814**	1	0.856**	0	0	0
<b>PC 36:2</b>	0	0.756**	0.952**	0.790**	0.856**	1	0	0	0
<b>PCaa 24:0</b>	0	0	0.932**	0.725**	0.818**	0.963**	0	0	0
<b>D-<math>\alpha</math>-PC dipalmitoyl</b>	0	0	0	0	0	0	1	1	0.942**
<b>PC 30:0</b>	0	0	0	0	0	0	0.942**	0.937**	1
<b>PC 32:2</b>	0	0	0	0	0	0	0.958**	0.952**	0.982**

Correlation coefficients were obtained by the Pearson correlation method.

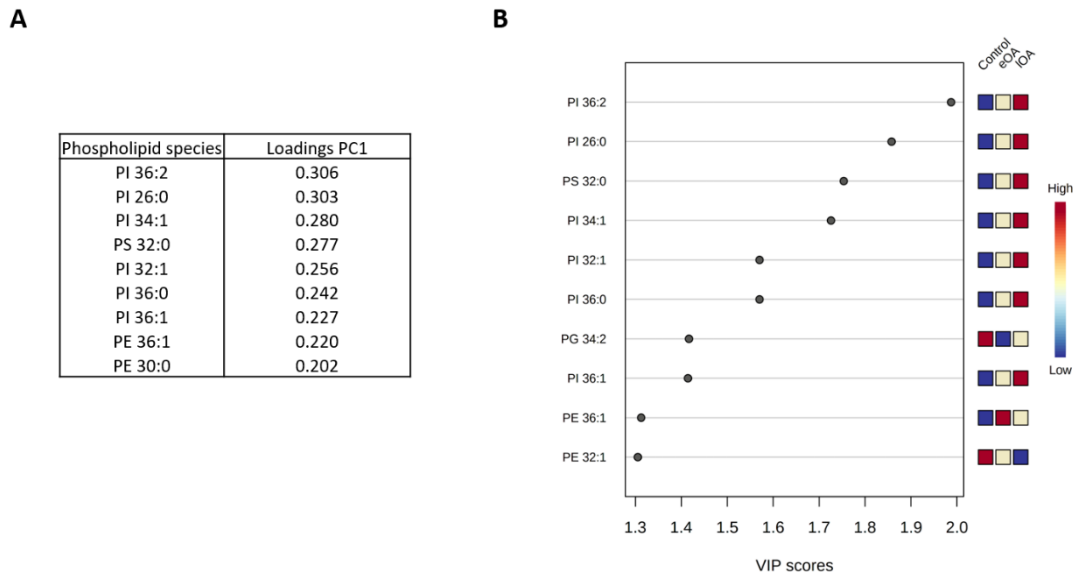
Correlation cut-off: 0.7.

\*\*  $p$ -value <0.01

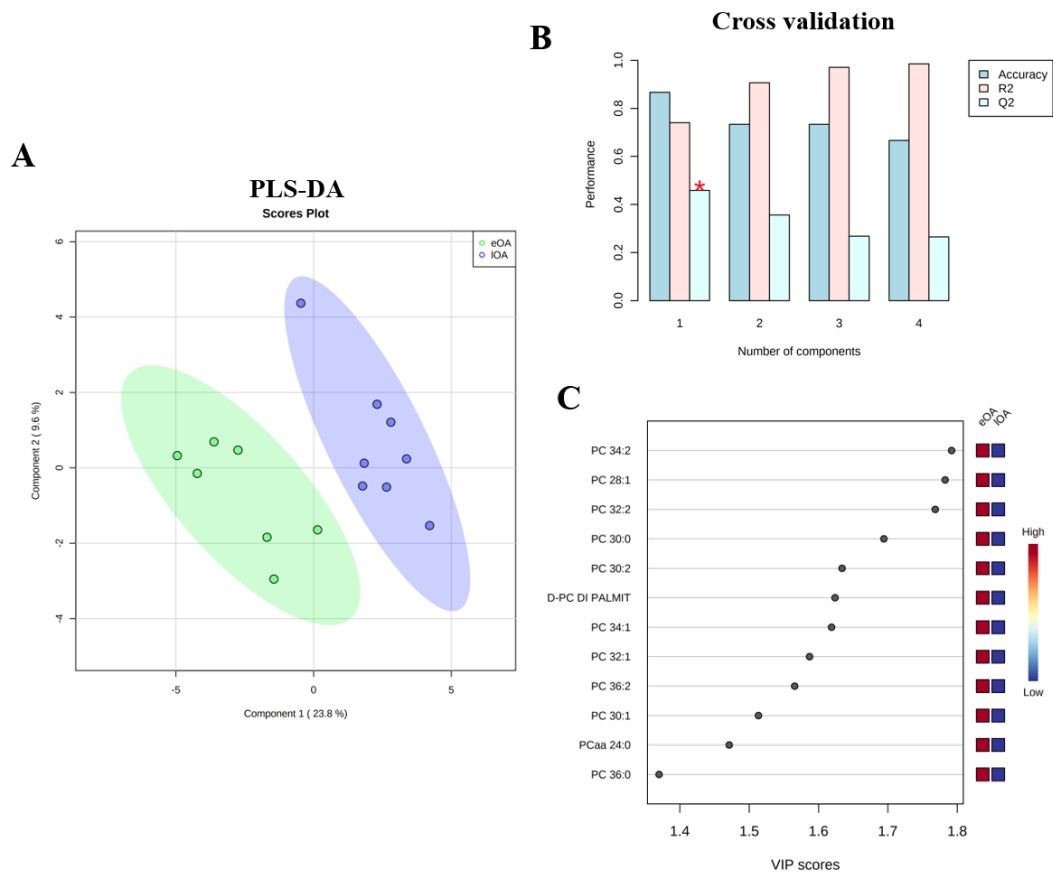
**Supplementary Table 6.** Correlation of specific phospholipid species with cartilage damage in OA patients.

	<b>Pearson r</b>	<b>95% CI</b>	<b>p-value</b>
<b>D-<math>\alpha</math>-PC dipalmitoyl</b>	-0.777	-0.9261 to -0.4204	0.001
<b>PC 28:1</b>	-0.722	-0.9009 to -0.3322	0.002
<b>PC 30:0</b>	-0.794	-0.9319 to -0.4546	0.001
<b>PC 30:1</b>	-0.613	-0.8562 to -0.1464	0.015
<b>PC 30:2</b>	-0.711	-0.9014 to -0.2894	0.004
<b>PC 32:1</b>	-0.758	-0.919 to -0.3808	0.002
<b>PC 32:2</b>	-0.850	-0.9515 to -0.5818	0
<b>PC 34:1</b>	-0.747	-0.9149 to -0.3584	0.002
<b>PC 34:2</b>	-0.781	-0.9273 to -0.4274	0.001
<b>PC 36:0</b>	-0.555	-0.8309 to -0.05928	0.032
<b>PC 36:1</b>	-0.054	-0.6331 to 0.5644	0.876
<b>PC 36:2</b>	-0.634	-0.8652 to -0.18	0.011
<b>PC aa 24:0</b>	-0.596	-0.8489 to -0.1199	0.019
<b>PA 28:0</b>	-0.137	-0.6065 to 0.4038	0.627
<b>PA 30:0</b>	0.254	-0.297 to 0.6779	0.361
<b>PA 34:1</b>	-0.086	-0.5731 to 0.4459	0.760
<b>PA 36:1</b>	0.138	-0.4027 to 0.6074	0.624
<b>PE 30:0</b>	-0.156	-0.6187 to 0.3873	0.579
<b>PE 32:1</b>	-0.295	-0.7011 to 0.2563	0.286
<b>PE 34:1</b>	0.270	-0.2812 to 0.6872	0.331
<b>PE 36:2</b>	0.135	-0.4054 to 0.6053	0.632
<b>PE 36:1</b>	-0.063	-0.5571 to 0.4645	0.824
<b>PG 32:1</b>	0.068	-0.4605 to 0.5606	0.810
<b>PG 34:2</b>	0.275	-0.2762 to 0.6901	0.321
<b>PG 34:1</b>	0.215	-0.3343 to 0.655	0.442
<b>PS 32:1</b>	-0.271	-0.6877 to 0.2803	0.329
<b>PS 32:0</b>	0.033	-0.4874 to 0.5363	0.907
<b>PS 36:0</b>	0.106	-0.4298 to 0.5863	0.708
<b>PI 26:0</b>	0.012	-0.5033 to 0.5212	0.966
<b>PI 28:1</b>	-0.163	-0.6229 to 0.3815	0.563
<b>PI 28:0</b>	0.060	-0.4667 to 0.5551	0.832
<b>PI 30:2</b>	0.490	-0.02952 to 0.8012	0.064
<b>PI 30:1</b>	0.060	-0.4669 to 0.555	0.833
<b>PI 30:0</b>	0.309	-0.2417 to 0.7089	0.263
<b>PI 32:1</b>	0.052	-0.4729 to 0.5496	0.854
<b>PI 32:0</b>	0.493	-0.0255 to 0.8027	0.062
<b>PI 34:1</b>	0.073	-0.4561 to 0.5644	0.795
<b>PI 36:2</b>	0.458	-0.0713 to 0.7857	0.086
<b>PI 36:1</b>	0.024	-0.4941 to 0.53	0.931
<b>PI 36:0</b>	0.051	-0.4734 to 0.5491	0.856

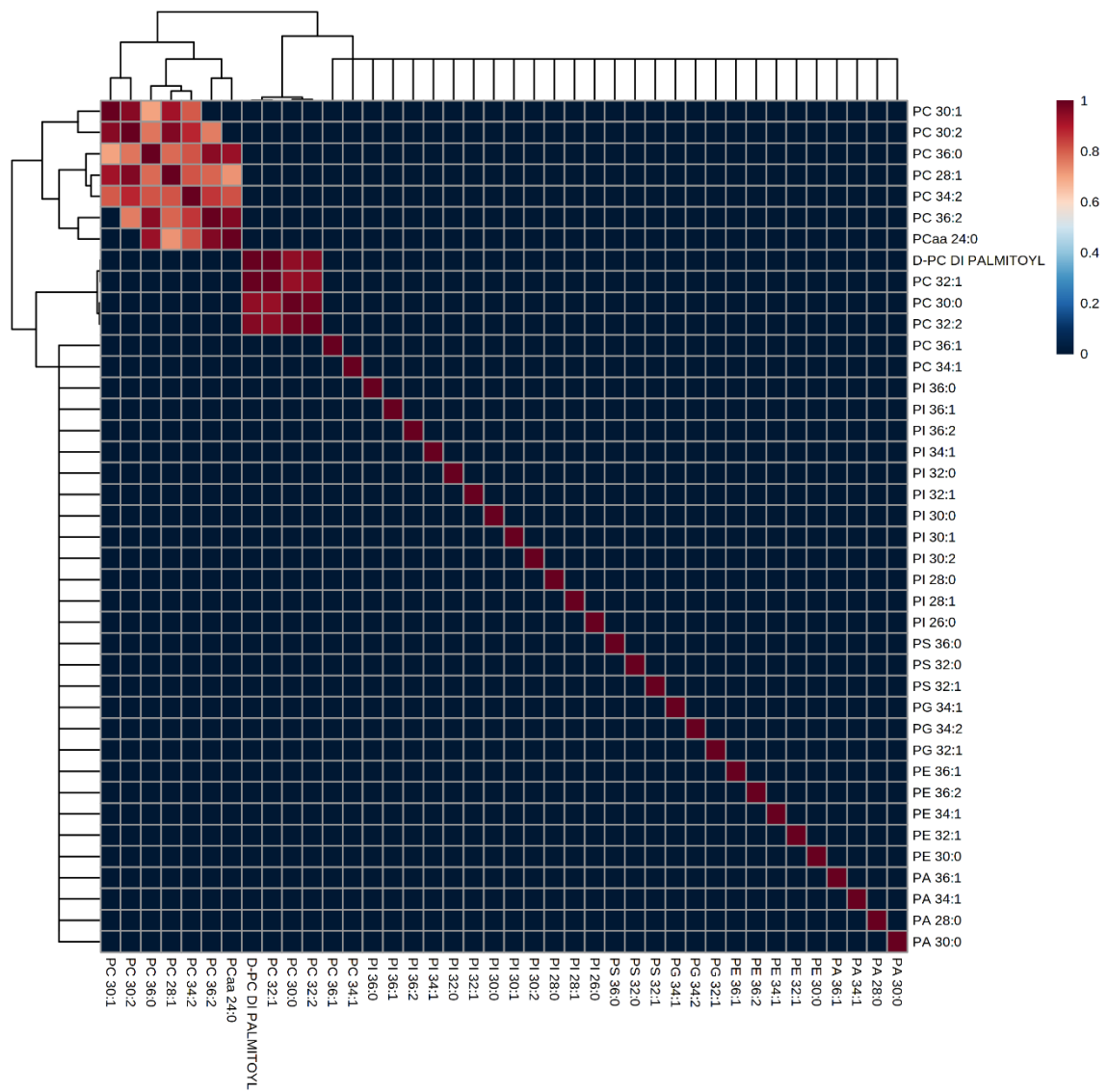
Data were analysed by Pearson's correlation test. Pearson's correlation coefficients, 95% confidence interval and *p*-values are indicated.



**Supplementary Figure 1. PLS-DA loadings and VIP scores of first discriminant function.** A) Loading values show the top ten phospholipid species selected by the PLS-DA for component 1 (non OA-control vs OA). B) VIP scores show the top ten phospholipid species selected by the PLS-DA for component 1 (non OA-control vs OA). Each phospholipid is ranked by the absolute values of their loadings.



**Supplementary Figure 2. PLS-DA displayed differences in phospholipid profiles between eOA and IOA patients.** A) PLS-DA revealed clear separation with minimum overlap between eOA and IOA. 95% confidence ellipses illustrate sample separation. B) PLS-DA shows a good prediction (with  $Q2=0.46$ ,  $R2=0.74$  and  $accuracy=0.87$ ). C) VIP scores show the top twelve phospholipid species selected by the PLS-DA for component 1 (eOA vs IOA). Each phospholipid is ranked by the absolute values of their loadings.



**Supplementary Figure 3.** Heatmap showing highly positive correlations among PC concentrations in OA SF. Correlation coefficient was obtained by the Pearson's correlation method. Correlation cut-off: 0.7.