**Mitochondrial Redox Opto-Lipidomics Reveals Mono-Oxygenated Cardiolipins as Pro-Apoptotic Death Signals**

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**Supporting information table S1.** Lipid composition in all groups. Data was presented as mean±standard deviation, pmol/nmol PL, n=3.

| Lipids | Control | | | NAO+Light 0.5h | | | NAO+Light 6h | | | NAO+Light 48h | | | NAO+Light+FCCP 0.5h | | | NAO+Light+FCCP 48h | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CL(16:1/16:1/20:4/18:2) | 4.3E-02 | ± | 9.5E-04 | 5.3E-F02 | ± | 3.3E-03 | 6.1E-02 | ± | 1.9E-03 | 5.0E-02 | ± | 6.8E-04 | 4.3E-02 | ± | 2.1E-03 | 5.6E-02 | ± | 3.7E-03 |
| CL(16:1/18:1/18:2/18:1) | 1.5E+00 | ± | 3.3E-02 | 2.0E+00 | ± | 5.7E-02 | 2.2E+00 | ± | 1.8E-01 | 1.2E+00 | ± | 4.5E-02 | 1.5E+00 | ± | 9.5E-02 | 1.5E+00 | ± | 4.4E-02 |
| CL(16:1/18:2/18:2/18:1) | 1.0E+00 | ± | 5.3E-02 | 1.2E+00 | ± | 3.6E-02 | 1.2E+00 | ± | 2.2E-02 | 8.3E-01 | ± | 2.4E-02 | 1.0E+00 | ± | 2.8E-02 | 9.9E-01 | ± | 2.2E-02 |
| CL(16:1/18:2/18:2/18:2) | 2.7E-01 | ± | 1.5E-02 | 3.4E-01 | ± | 1.7E-03 | 3.3E-01 | ± | 2.1E-02 | 1.9E-01 | ± | 1.3E-02 | 2.8E-01 | ± | 6.5E-03 | 2.6E-01 | ± | 1.8E-02 |
| CL(18:0/18:1/18:2/18:1) | 6.5E-01 | ± | 2.4E-02 | 8.4E-01 | ± | 1.8E-02 | 7.9E-01 | ± | 3.1E-02 | 5.6E-01 | ± | 1.8E-02 | 6.6E-01 | ± | 3.9E-02 | 6.6E-01 | ± | 9.2E-02 |
| CL(18:0/18:1/18:2/18:1)-OH | N.D. | | | 1.6E-03 | ± | 3.3E-04 | 4.4E-04 | ± | 1.2E-04 | 5.5E-04 | ± | 5.0E-04 | 4.9E-05 | ± | 8.4E-05 | 9.1E-05 | ± | 1.6E-04 |
| CL(18:1/18:1/18:2/20:1) | 6.6E-02 | ± | 5.8E-03 | 1.4E-01 | ± | 4.8E-02 | 9.4E-02 | ± | 5.7E-03 | 6.8E-02 | ± | 9.9E-03 | 7.5E-02 | ± | 5.0E-03 | 6.6E-02 | ± | 6.8E-03 |
| CL(18:1/18:2/16:0/16:1) | 4.7E-01 | ± | 1.3E-02 | 5.6E-01 | ± | 2.7E-02 | 5.6E-01 | ± | 3.3E-02 | 4.5E-01 | ± | 3.4E-02 | 4.3E-01 | ± | 2.6E-02 | 4.6E-01 | ± | 5.3E-03 |
| CL(18:1/18:2/18:1/18:1) | 9.1E-01 | ± | 4.5E-02 | 1.1E+00 | ± | 8.2E-02 | 1.1E+00 | ± | 6.8E-02 | 8.1E-01 | ± | 4.1E-02 | 9.0E-01 | ± | 5.0E-02 | 1.0E+00 | ± | 5.4E-02 |
| CL(18:1/18:1/18:1/18:2-OH) | 4.3E-05 | ± | 7.4E-05 | 1.9E-04 | ± | 3.0E-05 | 2.1E-04 | ± | 4.6E-05 | 3.4E-04 | ± | 2.9E-04 | 4.2E-04 | ± | 4.8E-04 | 4.4E-04 | ± | 2.5E-04 |
| CL(18:1/18:2/18:1/18:2) | 2.5E+00 | ± | 1.5E-01 | 3.1E+00 | ± | 1.6E-02 | 2.9E+00 | ± | 3.5E-01 | 2.2E+00 | ± | 1.5E-01 | 2.3E+00 | ± | 1.3E-01 | 2.6E+00 | ± | 1.7E-01 |
| CL(18:1/18:2/18:1/18:2-OH) | 4.8E-04 | ± | 1.3E-04 | 2.4E-02 | ± | 2.8E-03 | 1.1E-02 | ± | 1.4E-03 | N.D. | ± | N.D. | 9.4E-04 | ± | 9.0E-04 | 2.8E-04 | ± | 2.7E-04 |
| CL(18:1/18:2/18:2/18:2) | 1.6E+00 | ± | 1.2E-01 | 1.9E+00 | ± | 4.8E-02 | 1.8E+00 | ± | 5.0E-02 | 1.3E+00 | ± | 9.7E-02 | 1.6E+00 | ± | 7.2E-02 | 1.4E+00 | ± | 7.3E-02 |
| CL(18:1/18:2/18:2/18:2-OH) | N.D. | | | 5.0E-04 | ± | 5.1E-04 | 4.0E-04 | ± | 7.9E-05 | 1.4E-03 | ± | 6.4E-04 | 1.3E-04 | ± | 1.3E-04 | 2.6E-04 | ± | 2.5E-04 |
| CL(16:1/18:2/16:1/16:1) | 3.9E-02 | ± | 3.7E-03 | 4.5E-02 | ± | 7.2E-04 | 4.2E-02 | ± | 4.2E-03 | 2.0E-02 | ± | 5.1E-04 | 3.4E-02 | ± | 2.4E-03 | 4.5E-02 | ± | 2.2E-03 |
| CL(16:1/18:2/18:2/16:1) | 8.1E-03 | ± | 2.0E-03 | 1.1E-02 | ± | 1.2E-03 | 1.4E-02 | ± | 2.3E-03 | 7.9E-03 | ± | 1.7E-03 | 9.7E-03 | ± | 1.9E-03 | 1.4E-02 | ± | 2.2E-03 |
| CL(18:1/18:2/16:1/14:0) | 9.7E-02 | ± | 4.1E-03 | 1.2E-01 | ± | 5.7E-03 | 1.3E-01 | ± | 6.2E-03 | 7.9E-02 | ± | 7.4E-03 | 1.1E-01 | ± | 8.3E-03 | 1.2E-01 | ± | 2.0E-02 |
| CL(18:1/18:2/18:0/20:3) | 2.4E-01 | ± | 5.8E-03 | 3.3E-01 | ± | 2.3E-02 | 2.9E-01 | ± | 1.2E-02 | 2.6E-01 | ± | 6.7E-02 | 2.2E-01 | ± | 2.0E-02 | 2.1E-01 | ± | 9.3E-03 |
| CL(18:1/18:2/18:0/20:3)-OH | 8.2E-05 | ± | 1.4E-04 | 2.9E-04 | ± | 4.5E-05 | 2.4E-04 | ± | 6.1E-05 | N.D. | ± | N.D. | 1.6E-04 | ± | 2.7E-04 | 2.1E-04 | ± | 1.8E-04 |
| CL(18:1/18:2/18:1/20:3) | 6.0E-01 | ± | 6.2E-02 | 8.7E-01 | ± | 1.8E-02 | 8.3E-01 | ± | 5.7E-02 | 4.7E-01 | ± | 1.3E-02 | 6.8E-01 | ± | 4.0E-02 | 6.1E-01 | ± | 8.7E-03 |
| CL(18:1/18:2/18:1/20:3)-OH | N.D. | | | 1.6E-03 | ± | 2.6E-04 | 2.4E-04 | ± | 2.8E-04 | 2.0E-04 | ± | 3.5E-04 | 1.6E-04 | ± | 3.8E-05 | N.D. | ± | N.D. |
| CL(18:1/18:2/18:2/20:3) | 6.8E-01 | ± | 2.5E-02 | 8.8E-01 | ± | 5.6E-02 | 8.3E-01 | ± | 1.3E-02 | 4.6E-01 | ± | 2.0E-02 | 7.5E-01 | ± | 4.5E-02 | 6.3E-01 | ± | 4.0E-02 |
| CL(18:1/18:2/18:2/20:3)-OH | N.D. | | | 5.3E-03 | ± | 1.3E-03 | 1.5E-03 | ± | 1.2E-04 | 1.8E-04 | ± | 3.0E-04 | 1.7E-04 | ± | 1.5E-04 | N.D. | ± | N.D. |
| CL(18:1/18:2/18:2/20:4) | 2.2E-01 | ± | 1.9E-02 | 2.4E-01 | ± | 1.6E-02 | 2.8E-01 | ± | 1.1E-02 | 2.6E-01 | ± | 1.1E-02 | 2.1E-01 | ± | 2.1E-02 | 2.9E-01 | ± | 2.1E-02 |
| CL(18:1/18:2/18:2/20:4)-OH | N.D. | | | 4.4E-03 | ± | 9.1E-04 | 9.9E-04 | ± | 5.7E-04 | N.D. | ± | N.D. | N.D. | ± | N.D. | N.D. | ± | N.D. |
| CL(18:1/18:2/18:2/20:4)-OOH | 1.9E-04 | ± | 1.9E-04 | 2.0E-04 | ± | 6.0E-06 | 5.8E-04 | ± | 1.2E-04 | 4.1E-04 | ± | 3.6E-04 | 2.2E-04 | ± | 2.6E-04 | 1.2E-04 | ± | 2.1E-04 |
| CL(18:1/18:2/18:2/22:4) | 1.8E-01 | ± | 2.8E-03 | 2.4E-01 | ± | 2.3E-02 | 2.3E-01 | ± | 1.1E-03 | 1.3E-01 | ± | 4.3E-03 | 1.9E-01 | ± | 3.3E-03 | 1.7E-01 | ± | 1.4E-02 |
| CL(18:1/18:2/18:2/22:4)-OOH | 6.1E-05 | ± | 1.1E-04 | 2.2E-04 | ± | 1.4E-04 | 2.2E-04 | ± | 4.4E-05 | 1.9E-04 | ± | 3.2E-04 | 5.4E-05 | ± | 9.3E-05 | 5.5E-05 | ± | 9.5E-05 |
| CL(18:2/18:2/18:2/18:2) | 8.1E-01 | ± | 4.0E-02 | 1.1E+00 | ± | 5.5E-02 | 1.0E+00 | ± | 9.2E-02 | 7.0E-01 | ± | 4.1E-02 | 7.9E-01 | ± | 3.0E-02 | 8.1E-01 | ± | 4.7E-02 |
| CL(18:2/18:2/18:2/20:4) | 1.6E-01 | ± | 1.2E-02 | 2.2E-01 | ± | 2.7E-02 | 2.4E-01 | ± | 2.6E-02 | 1.9E-01 | ± | 3.6E-03 | 1.8E-01 | ± | 1.9E-02 | 2.0E-01 | ± | 6.7E-03 |
| CL(18:2/18:2/18:2/20:4)-OOH | 6.3E-04 | ± | 3.1E-04 | 1.3E-03 | ± | 2.1E-04 | 1.8E-03 | ± | 7.3E-04 | 1.6E-04 | ± | 2.8E-04 | 1.5E-03 | ± | 1.7E-04 | 1.5E-03 | ± | 1.1E-03 |
| CL(18:2/20:3/18:2/20:4) | 6.0E-02 | ± | 1.2E-02 | 5.4E-02 | ± | 9.4E-03 | 6.5E-02 | ± | 2.2E-03 | 4.6E-02 | ± | 6.3E-03 | 4.5E-02 | ± | 1.1E-02 | 6.2E-02 | ± | 9.7E-03 |
| CL(18:2/20:3/18:2/20:4)-OOH | 4.0E-03 | ± | 6.2E-04 | 5.3E-03 | ± | 1.9E-03 | 5.6E-03 | ± | 2.5E-03 | 9.4E-04 | ± | 9.5E-04 | 4.3E-03 | ± | 9.6E-04 | 6.4E-03 | ± | 3.0E-03 |

| Lipids | Control | | | NAO+Light 0.5h | | | NAO+Light 6h | | | NAO+Light 48h | | | NAO+Light+FCCP 0.5h | | | NAO+Light+FCCP 48h | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CL(18:2/20:4/18:2/16:1) | 1.1E-01 | ± | 1.0E-02 | 1.2E-01 | ± | 6.6E-03 | 1.5E-01 | ± | 6.0E-03 | 1.2E-01 | ± | 8.2E-03 | 1.2E-01 | ± | 5.7E-03 | 1.4E-01 | ± | 9.6E-03 |
| CL(18:1/20:3/18:1/20:3) | 5.9E-02 | ± | 5.0E-03 | 9.4E-02 | ± | 2.3E-02 | 8.0E-02 | ± | 2.2E-02 | 4.8E-02 | ± | 1.3E-02 | 8.3E-02 | ± | 3.1E-02 | 6.0E-02 | ± | 1.7E-02 |
| CL(18:1/22:5/18:2/18:2) | 3.1E-02 | ± | 3.9E-03 | 3.4E-02 | ± | 1.6E-03 | 3.7E-02 | ± | 4.6E-03 | 3.3E-02 | ± | 2.2E-03 | 3.0E-02 | ± | 1.0E-03 | 3.6E-02 | ± | 1.9E-03 |
| CL(18:1/22:5/18:2/18:2)-OOH | 1.4E-03 | ± | 8.4E-04 | 9.5E-04 | ± | 7.3E-04 | 6.3E-04 | ± | 5.8E-04 | 2.1E-04 | ± | 3.7E-04 | 4.4E-04 | ± | 2.9E-04 | 1.0E-03 | ± | 8.5E-04 |
| PC(16:0/18:2) | 3.0E+01 | ± | 1.7E+00 | 3.2E+01 | ± | 2.2E+00 | 3.2E+01 | ± | 6.7E-01 | 3.3E+01 | ± | 2.8E+00 | 2.9E+01 | ± | 9.3E-02 | 2.7E+01 | ± | 2.5E+00 |
| PC(16:0/18:2)-OH | 9.2E-02 | ± | 1.0E-02 | 4.1E-01 | ± | 4.1E-02 | 1.4E-01 | ± | 6.8E-03 | N.D. | | | 1.8E-02 | ± | 4.2E-03 | 1.1E-01 | ± | 6.9E-03 |
| PC(16:0/18:2)-OOH | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | | 3.3E-03 | ± | 3.0E-03 |
| PC(16:0/20:4) | 5.2E+01 | ± | 5.2E+00 | 5.4E+01 | ± | 1.4E+00 | 6.5E+01 | ± | 7.4E-01 | 4.7E+01 | ± | 1.7E+00 | 5.9E+01 | ± | 2.3E+00 | 2.5E+01 | ± | 4.5E-01 |
| PC(16:0/20:4)-OH | N.D. | | | 1.6E-01 | ± | 6.3E-03 | 1.1E-01 | ± | 1.1E-02 | N.D. | | | 3.5E-02 | ± | 1.6E-02 | 9.9E-02 | ± | 1.2E-02 |
| PC(16:0/20:4)-OOH | N.D. | | | 2.8E-03 | ± | 7.8E-04 | 1.9E-02 | ± | 3.3E-03 | N.D. | | | 1.9E-03 | ± | 1.7E-03 | 4.0E-03 | ± | 2.1E-03 |
| PC(16:0/20:5) | 8.9E+00 | ± | 8.5E-01 | 9.2E+00 | ± | 9.0E-02 | 8.3E+00 | ± | 2.7E-01 | 8.2E+00 | ± | 1.3E+00 | 8.4E+00 | ± | 5.4E-01 | 6.3E+00 | ± | 2.6E-01 |
| PC(16:0/20:5)-OH | N.D. | | | 1.8E-02 | ± | 7.4E-03 | 5.3E-03 | ± | 3.9E-03 | N.D. | | | 1.7E-03 | ± | 1.4E-03 | 6.5E-03 | ± | 1.8E-03 |
| PC(16:0/20:5)-OOH | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | | 6.0E-04 | ± | 5.7E-04 |
| PC(16:0/22:6) | 1.1E+01 | ± | 9.9E-01 | 1.2E+01 | ± | 4.1E-01 | 9.1E+00 | ± | 4.5E-01 | 8.3E+00 | ± | 3.6E-01 | 8.8E+00 | ± | 3.2E-01 | 9.0E+00 | ± | 8.9E-01 |
| PC(16:0/22:6)-OH | N.D. | | | 2.4E-02 | ± | 2.7E-03 | 7.6E-03 | ± | 2.6E-03 | N.D. | | | 2.7E-03 | ± | 9.7E-04 | 4.9E-03 | ± | 2.4E-03 |
| PC(16:0/22:6)-OOH | N.D. | | | N.D. | | | 7.8E-04 | ± | 6.8E-04 | N.D. | | | N.D. | | | 6.0E-04 | ± | 5.7E-04 |
| PC(16:1/18:2) | 2.6E+00 | ± | 4.8E-02 | 2.6E+00 | ± | 2.0E-01 | 2.8E+00 | ± | 2.0E-01 | 2.8E+00 | ± | 3.0E-01 | 2.8E+00 | ± | 1.3E-01 | 2.3E+00 | ± | 1.7E-01 |
| PC(16:1/18:2)-OH | 2.3E-02 | ± | 1.1E-02 | 3.3E-03 | ± | 2.2E-03 | 1.4E-03 | ± | 4.0E-04 | N.D. | | | 8.9E-04 | ± | 1.5E-03 | 1.1E-02 | ± | 4.5E-03 |
| PC(16:1/18:2)-OOH | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | |
| PC(18:0/18:2) | 3.9E+01 | ± | 1.2E+00 | 4.3E+01 | ± | 2.0E+00 | 4.0E+01 | ± | 2.1E+00 | 3.4E+01 | ± | 1.8E+00 | 3.6E+01 | ± | 1.9E+00 | 5.5E+01 | ± | 7.1E+00 |
| PC(18:0/18:2)-OH | 5.6E-03 | ± | 5.0E-03 | 1.3E-01 | ± | 1.6E-02 | 3.9E-02 | ± | 3.0E-03 | N.D. | | | 2.7E-03 | ± | 2.9E-03 | 4.1E-02 | ± | 3.6E-03 |
| PC(18:0/18:2)-OOH | N.D. | | | 6.7E-04 | ± | 6.0E-04 | 3.2E-03 | ± | 1.6E-03 | N.D. | | | N.D. | | | 2.3E-03 | ± | 1.5E-03 |
| PC(18:0/20:3) | 3.7E+00 | ± | 2.2E-01 | 4.8E+00 | ± | 4.4E-01 | 4.2E+00 | ± | 3.0E-01 | 2.6E+00 | ± | 8.5E-02 | 3.7E+00 | ± | 2.3E-01 | 4.9E+00 | ± | 1.5E-01 |
| PC(18:0/20:3)-OH | N.D. | | | 6.7E-04 | ± | 5.8E-04 | 1.3E-03 | ± | 4.0E-04 | N.D. | | | N.D. | | | 2.0E-03 | ± | 4.5E-04 |
| PC(18:0/20:3)-OOH | N.D. | | | N.D. | | | 2.4E-04 | ± | 4.2E-04 | N.D. | | | N.D. | | | N.D. | | |
| PC(18:0/20:4) | 3.3E+01 | ± | 2.1E+00 | 3.7E+01 | ± | 1.3E+00 | 3.8E+01 | ± | 2.0E+00 | 3.2E+01 | ± | 2.4E+00 | 3.6E+01 | ± | 2.4E+00 | 2.1E+01 | ± | 9.5E-01 |
| PC(18:0/20:4)-OH | N.D. | | | 8.9E-02 | ± | 1.3E-02 | 5.4E-02 | ± | 3.2E-03 | N.D. | | | 4.9E-03 | ± | 3.4E-03 | 7.3E-02 | ± | 5.7E-03 |
| PC(18:0/20:4)-OOH | N.D. | | | 1.7E-03 | ± | 6.7E-04 | 1.3E-02 | ± | 1.4E-03 | N.D. | | | 5.6E-04 | ± | 9.8E-04 | 4.4E-03 | ± | 2.5E-03 |
| PC(18:0/22:4) | 1.9E+00 | ± | 1.7E-01 | 2.3E+00 | ± | 7.8E-02 | 2.3E+00 | ± | 5.9E-02 | 2.3E+00 | ± | 5.8E-01 | 2.4E+00 | ± | 1.3E-01 | 2.5E+00 | ± | 1.3E-01 |
| PC(18:0/22:4)-OOH | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | |
| PC(18:0/22:6) | 7.0E+00 | ± | 6.7E-01 | 7.1E+00 | ± | 2.8E-01 | 6.3E+00 | ± | 4.6E-01 | 5.8E+00 | ± | 2.2E-01 | 5.9E+00 | ± | 2.8E-01 | 6.3E+00 | ± | 1.9E-01 |
| PC(18:0/22:6)-OH | N.D. | | | 5.1E-03 | ± | 5.3E-03 | 2.2E-03 | ± | 1.6E-03 | N.D. | | | N.D. | | | 1.6E-03 | ± | 1.5E-03 |
| PC(18:0/22:6)-OOH | N.D. | | | N.D. | | | N.D. | | | N.D. | | | N.D. | | | 2.3E-04 | ± | 4.0E-04 |
| PC(18:1/18:2) | 1.7E+01 | ± | 3.8E-01 | 1.9E+01 | ± | 9.8E-01 | 1.9E+01 | ± | 1.5E-01 | 1.5E+01 | ± | 1.8E+00 | 1.7E+01 | ± | 8.4E-01 | 1.4E+01 | ± | 1.2E+00 |
| PC(18:1/18:2)-OH | N.D. | | | 4.4E-02 | ± | 9.8E-03 | 2.3E-02 | ± | 5.9E-03 | N.D. | | | 3.9E-03 | ± | 1.7E-03 | 3.8E-02 | ± | 5.8E-03 |
| PC(18:1/18:2)-OOH | N.D. | | | 8.2E-04 | ± | 7.7E-04 | 1.9E-03 | ± | 1.6E-03 | N.D. | | | 1.1E-03 | ± | 1.9E-03 | 3.8E-04 | ± | 3.4E-04 |
| PC(18:1/20:4) | 3.4E+01 | ± | 2.1E+00 | 3.6E+01 | ± | 9.4E-01 | 4.0E+01 | ± | 2.1E+00 | 2.6E+01 | ± | 1.4E+00 | 3.5E+01 | ± | 2.3E+00 | 2.1E+01 | ± | 7.1E-01 |

| Lipids | Control | NAO+Light 0.5h | NAO+Light 6h | NAO+Light 48h | NAO+Light+FCCP 0.5h | NAO+Light+FCCP 48h |
|---|---|---|---|---|---|---|
| PC(18:1/20:4)-OH | 3.1E-03 ± 5.4E-03 | 1.1E-01 ± 3.6E-03 | 5.8E-02 ± 6.4E-03 | N.D. | 1.5E-02 ± 6.7E-03 | 5.7E-02 ± 1.1E-02 |
| PC(18:1/20:4)-OOH | N.D. | 1.1E-03 ± 1.1E-03 | 9.8E-03 ± 1.8E-03 | N.D. | N.D. | 1.9E-03 ± 1.7E-03 |
| PC(18:1/22:6) | 4.5E+00 ± 4.0E-01 | 4.7E+00 ± 1.9E-01 | 4.2E+00 ± 1.6E-01 | 2.6E+00 ± 1.5E-01 | 4.5E+00 ± 1.2E-01 | 3.9E+00 ± 2.6E-01 |
| PC(18:1/22:6)-OH | N.D. | 1.5E-03 ± 1.4E-03 | N.D. | N.D. | N.D. | 3.9E-04 ± 6.7E-04 |
| PC(18:1/22:6)-OOH | N.D. | 2.2E-04 ± 3.9E-04 | N.D. | N.D. | N.D. | 3.8E-04 ± 6.5E-04 |
| PC(18:2/20:5) | 5.1E-01 ± 1.4E-02 | 6.2E-01 ± 1.8E-02 | 5.7E-01 ± 3.1E-02 | N.D. | 6.2E-01 ± 2.4E-02 | 4.7E-01 ± 4.5E-02 |
| PC(20:0/20:5) | 6.0E+00 ± 3.6E-01 | 7.5E+00 ± 1.5E-01 | 7.5E+00 ± 1.7E-01 | 5.1E+00 ± 6.3E-01 | 6.2E+00 ± 5.8E-01 | 5.6E+00 ± 5.6E-01 |
| PC(20:0/20:5)-OH | N.D. | 1.3E-03 ± 1.3E-03 | 2.3E-03 ± 6.8E-04 | N.D. | 1.2E-03 ± 2.0E-03 | 1.3E-03 ± 1.2E-03 |
| PC(20:0/20:5)-OOH | N.D. | N.D. | N.D. | N.D. | N.D. | 2.7E-04 ± 4.7E-04 |
| PC(20:3/22:6) | 1.4E+00 ± 4.3E-02 | 1.9E+00 ± 1.5E-01 | 2.8E+00 ± 1.3E-01 | 1.2E-01 ± 8.0E-02 | 2.7E+00 ± 2.4E-02 | 3.6E-01 ± 9.1E-03 |
| PC(20:4/20:4) | 8.3E-01 ± 6.6E-02 | 1.6E+00 ± 1.2E-01 | 2.1E+00 ± 6.5E-02 | 1.4E-01 ± 5.6E-02 | 2.5E+00 ± 2.6E-01 | 4.1E-01 ± 2.6E-02 |
| PC(20:4/22:4) | 9.3E-01 ± 1.9E-01 | 1.3E+00 ± 4.3E-02 | 1.9E+00 ± 5.2E-02 | 7.7E-02 ± 6.4E-02 | 1.9E+00 ± 3.1E-02 | 2.7E-01 ± 2.4E-02 |
| PC(20:4/22:4)-OH | 3.2E-02 ± 2.9E-02 | 8.0E-04 ± 1.4E-03 | 1.2E-03 ± 9.0E-04 | 1.8E-01 ± 5.2E-02 | 2.2E-03 ± 2.3E-03 | 2.3E-03 ± 1.3E-03 |
| PC(20:5/22:5) | 5.2E-01 ± 8.6E-02 | 1.1E+00 ± 1.3E-01 | 1.2E+00 ± 1.0E-01 | 1.5E-02 ± 2.6E-02 | 1.6E+00 ± 1.2E-01 | 3.6E-01 ± 1.1E-02 |
| PC(O-16:0/18:2) | 3.9E+00 ± 2.1E-01 | 4.1E+00 ± 3.7E-01 | 4.2E+00 ± 1.9E-01 | 1.8E+00 ± 1.2E-02 | 3.6E+00 ± 1.2E-01 | 5.7E+00 ± 3.0E-01 |
| PC(O-16:0/18:2)-OOH | 7.2E-02 ± 2.5E-02 | 1.2E-01 ± 2.2E-03 | 1.4E-01 ± 2.3E-02 | 3.2E-02 ± 2.8E-02 | 1.9E-01 ± 4.2E-02 | 3.9E-01 ± 2.2E-02 |
| PC(O-16:0/20:3) | 1.6E+00 ± 1.1E-01 | 1.9E+00 ± 8.1E-02 | 1.8E+00 ± 8.2E-02 | 1.9E-01 ± 5.6E-02 | 1.6E+00 ± 9.0E-02 | 3.3E+00 ± 6.9E-02 |
| PC(O-16:0/20:3)-OOH | 5.7E-03 ± 5.1E-03 | 1.4E-01 ± 1.7E-02 | 3.9E-02 ± 3.3E-03 | N.D. | 2.6E-03 ± 2.8E-03 | 4.1E-02 ± 2.7E-03 |
| PC(O-16:0/20:4) | 3.5E+00 ± 2.8E-01 | 4.6E+00 ± 2.4E-01 | 5.5E+00 ± 4.2E-01 | 3.8E+00 ± 6.9E-01 | 4.7E+00 ± 2.9E-01 | 3.6E+00 ± 3.1E-01 |
| PC(O-16:0/20:4)-OOH | N.D. | 4.4E-02 ± 8.8E-03 | 2.2E-02 ± 4.1E-03 | N.D. | 3.5E-03 ± 1.5E-03 | 3.8E-02 ± 6.0E-03 |
| PC(O-18:0/20:4) | 2.7E+00 ± 3.7E-01 | 4.1E+00 ± 1.6E-01 | 5.0E+00 ± 5.0E-01 | 2.5E+00 ± 2.7E-01 | 3.7E+00 ± 2.2E-01 | 3.5E+00 ± 3.0E-01 |
| PC(O-18:0/20:4)-OOH | N.D. | 6.3E-04 ± 5.5E-04 | 1.4E-03 ± 4.6E-04 | N.D. | N.D. | 2.0E-03 ± 5.2E-04 |
| PC(O-18:1/20:4) | 6.4E+00 ± 4.1E-01 | 5.8E+00 ± 1.1E-01 | 6.2E+00 ± 3.2E-01 | 7.3E+00 ± 5.9E-01 | 5.6E+00 ± 4.8E-01 | 6.9E+00 ± 7.5E-01 |
| PC(O-18:1/20:4)-OOH | N.D. | 8.4E-02 ± 9.3E-03 | 5.5E-02 ± 4.3E-03 | N.D. | 3.6E-03 ± 9.4E-04 | 7.6E-02 ± 5.2E-03 |
| PC(P-16:0/20:4) | 3.6E+00 ± 6.1E-01 | 3.9E+00 ± 2.4E-01 | 4.1E+00 ± 9.8E-02 | 4.3E+00 ± 5.0E-01 | 3.9E+00 ± 1.6E-01 | 3.8E+00 ± 1.5E-01 |
| PC(P-18:0/20:5) | 4.0E+00 ± 3.0E-01 | 4.0E+00 ± 1.2E-01 | 3.8E+00 ± 4.1E-01 | 3.7E+00 ± 1.9E-01 | 3.5E+00 ± 6.5E-02 | 4.7E+00 ± 4.0E-01 |
| PC(P-18:0/20:5)-OOH | 2.7E-03 ± 4.6E-03 | 1.2E-01 ± 4.0E-03 | 5.9E-02 ± 6.7E-03 | N.D. | 1.5E-02 ± 7.1E-03 | 5.7E-02 ± 5.0E-03 |
| PC(P-18:0/22:4) | 1.5E+00 ± 7.2E-02 | 2.0E+00 ± 9.0E-03 | 1.7E+00 ± 1.4E-01 | 1.3E-01 ± 1.3E-01 | 1.5E+00 ± 1.1E-01 | 2.1E+00 ± 1.4E-01 |
| PC(P-18:0/22:4)-OH | N.D. | N.D. | N.D. | N.D. | N.D. | 7.0E-03 ± 5.0E-03 |
| PE(16:0/22:6) | 3.1E+00 ± 2.0E-01 | 3.0E+00 ± 3.3E-01 | 2.5E+00 ± 1.3E-01 | 2.7E+00 ± 4.8E-01 | 3.1E+00 ± 2.5E-01 | 3.1E+00 ± 1.5E-01 |
| PE(16:0/22:6)-OH | 9.3E-03 ± 1.3E-03 | 5.3E-02 ± 1.5E-03 | 6.7E-02 ± 9.7E-03 | N.D. | 3.3E-02 ± 5.0E-03 | 2.8E-02 ± 5.4E-03 |
| PE(16:0/22:6)-OOH | 1.2E-03 ± 2.1E-03 | 7.4E-04 ± 6.6E-04 | 1.1E-03 ± 1.1E-03 | N.D. | N.D. | 5.7E-04 ± 7.1E-04 |
| PE(18:0/18:1) | 9.2E-03 ± 1.1E-03 | 5.0E-02 ± 4.0E-03 | 6.9E-02 ± 3.1E-03 | N.D. | 3.3E-02 ± 6.6E-03 | 2.7E-02 ± 6.7E-03 |
| PE(18:0/18:2)-OH | 2.8E-02 ± 1.1E-02 | 3.5E-02 ± 1.2E-02 | 5.3E-02 ± 5.6E-03 | 9.5E-03 ± 1.6E-02 | 2.0E-02 ± 6.7E-03 | 2.6E-02 ± 7.4E-03 |
| PE(18:0/20:4) | 7.3E+01 ± 2.0E+00 | 6.9E+01 ± 4.3E+00 | 7.0E+01 ± 1.1E+00 | 7.5E+01 ± 3.4E+00 | 6.1E+01 ± 4.5E+00 | 6.5E+01 ± 2.3E+00 |
| PE(18:0/20:4)-OH | 1.3E-01 ± 2.4E-02 | 2.0E-01 ± 1.0E-02 | 2.2E-01 ± 7.7E-03 | 5.2E-02 ± 2.8E-02 | 4.0E-02 ± 2.1E-02 | 7.5E-02 ± 7.1E-03 |
| PE(18:0/20:4)-OOH | N.D. | 1.5E-03 ± 7.6E-04 | 6.2E-03 ± 3.7E-03 | N.D. | N.D. | 4.6E-03 ± 1.6E-03 |

| Lipids | Control | | | NAO+Light 0.5h | | | NAO+Light 6h | | | NAO+Light 48h | | | NAO+Light+FCCP 0.5h | | | NAO+Light+FCCP 48h | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PE(18:0/22:2) | 2.5E-01 | ± | 9.1E-02 | 2.2E-01 | ± | 5.1E-02 | 2.8E-01 | ± | 3.9E-02 | 7.6E-03 | ± | 1.3E-02 | 1.9E-01 | ± | 7.2E-02 | 3.0E-01 | ± | 5.8E-02 |
| PE(18:0/22:2)-OH | N.D. | | | N.D. | | | 8.0E-04 | ± | 1.0E-04 | N.D. | | | N.D. | | | N.D. | | |
| PE(18:0/22:6) | 5.0E+00 | ± | 3.9E-01 | 4.8E+00 | ± | 1.4E-01 | 4.8E+00 | ± | 2.0E-01 | 6.0E+00 | ± | 3.6E-01 | 5.2E+00 | ± | 1.3E-01 | 4.7E+00 | ± | 1.8E-01 |
| PE(18:0/22:6)-OOH | 2.3E-02 | ± | 1.0E-02 | 4.2E-03 | ± | 1.0E-03 | 8.7E-03 | ± | 3.8E-03 | N.D. | | | 5.2E-03 | ± | 2.6E-03 | 4.6E-03 | ± | 1.1E-03 |
| PE(18:1/18:2) | 1.5E+00 | ± | 1.3E-01 | 2.3E+00 | ± | 1.0E-01 | 3.2E+00 | ± | 1.5E-01 | 2.4E+00 | ± | 7.8E-01 | 2.5E+00 | ± | 2.9E-01 | 3.1E+00 | ± | 1.4E-01 |
| PE(18:1/18:2)-OH | 1.5E-02 | ± | 1.0E-02 | 1.5E-02 | ± | 2.6E-03 | 2.9E-02 | ± | 2.4E-03 | N.D. | | | 1.4E-02 | ± | 1.4E-03 | 1.6E-02 | ± | 2.1E-03 |
| PE(18:2/18:2) | 7.4E+00 | ± | 2.6E-01 | 7.4E+00 | ± | 1.7E-01 | 7.7E+00 | ± | 8.1E-01 | 8.6E+00 | ± | 7.3E-01 | 7.6E+00 | ± | 2.3E-01 | 6.4E+00 | ± | 3.1E-01 |
| PE(18:2/18:2)-OH | 1.8E-03 | ± | 3.2E-03 | 1.2E-02 | ± | 2.9E-03 | 1.3E-02 | ± | 3.8E-03 | N.D. | | | 1.4E-03 | ± | 2.4E-03 | 8.6E-03 | ± | 1.4E-03 |
| PE(18:2/18:2)-OOH | N.D. | | | N.D. | | | 3.3E-04 | ± | 5.8E-04 | N.D. | | | N.D. | | | 2.3E-04 | ± | 4.0E-04 |
| PE(20:1/20:4) | 5.3E+00 | ± | 6.6E-02 | 5.1E+00 | ± | 2.3E-01 | 6.0E+00 | ± | 2.3E-01 | 7.5E+00 | ± | 6.5E-01 | 6.0E+00 | ± | 3.4E-01 | 4.3E+00 | ± | 1.9E-01 |
| PE(20:1/20:4)-OH | 5.9E-01 | ± | 3.8E-02 | 2.6E-01 | ± | 8.9E-03 | 1.8E-01 | ± | 6.7E-03 | 9.1E-02 | ± | 1.7E-02 | 1.0E-01 | ± | 1.8E-02 | 8.9E-02 | ± | 1.9E-03 |
| PE(20:1/20:4)-OOH | 3.8E-03 | ± | 6.6E-04 | 6.4E-04 | ± | 5.6E-04 | 6.9E-03 | ± | 4.8E-03 | N.D. | | | 6.7E-03 | ± | 5.0E-03 | 6.2E-03 | ± | 3.7E-03 |
| PE(16:1/20:4) | 1.0E+00 | ± | 6.0E-02 | 1.3E+00 | ± | 7.3E-02 | 1.0E+00 | ± | 7.1E-02 | 6.6E-01 | ± | 1.6E-01 | 1.1E+00 | ± | 4.0E-02 | 1.2E+00 | ± | 5.8E-02 |
| PE(16:1/20:4)-OH | N.D. | | | 1.8E-03 | ± | 2.7E-04 | 1.8E-02 | ± | 2.6E-03 | N.D. | | | 2.5E-03 | ± | 2.4E-03 | 1.9E-03 | ± | 5.8E-04 |
| PE(16:1/20:4)-OOH | N.D. | | | N.D. | | | N.D. | ± | N.D. | N.D. | | | N.D. | | | N.D. | | |
| PE(18:1/20:4) | 2.3E+01 | ± | 2.1E+00 | 2.3E+01 | ± | 1.1E+00 | 2.3E+01 | ± | 1.1E+00 | 2.5E+01 | ± | 1.8E+00 | 2.4E+01 | ± | 5.8E-01 | 2.3E+01 | ± | 1.1E+00 |
| PE(18:1/20:4)-OH | 2.6E-01 | ± | 5.4E-02 | 2.3E-01 | ± | 1.3E-02 | 2.6E-01 | ± | 1.1E-02 | N.D. | | | 1.9E-01 | ± | 2.1E-02 | 1.4E-01 | ± | 2.8E-03 |
| PE(18:1/20:4)-OOH | N.D. | | | 1.4E-03 | ± | 1.5E-03 | 8.2E-03 | ± | 1.7E-03 | N.D. | | | N.D. | | | 2.7E-03 | ± | 2.2E-03 |
| PE(22:0/20:4) | 2.4E-01 | ± | 4.8E-02 | 2.9E-01 | ± | 4.5E-02 | 3.1E-01 | ± | 3.2E-02 | N.D. | | | 2.4E-01 | ± | 2.3E-02 | 4.1E-01 | ± | 5.2E-03 |
| PE(22:0/20:4)-OOH | N.D. | | | 7.7E-04 | ± | 2.9E-04 | 7.5E-04 | ± | 8.0E-04 | N.D. | | | N.D. | | | N.D. | | |
| PE(18:0/22:4) | 3.0E+00 | ± | 2.8E-01 | 3.0E+00 | ± | 1.2E-01 | 3.7E+00 | ± | 1.2E-01 | 4.8E+00 | ± | 8.1E-01 | 3.6E+00 | ± | 3.0E-02 | 3.4E+00 | ± | 1.6E-01 |
| PE(18:0/22:4)-OOH | N.D. | | | N.D. | | | 1.9E-03 | ± | 1.0E-03 | 2.8E-02 | ± | 4.8E-02 | 1.1E-02 | ± | 2.9E-03 | 5.9E-04 | ± | 7.9E-05 |
| PE(18:1/22:6) | 1.5E+00 | ± | 2.2E-02 | 1.5E+00 | ± | 6.8E-02 | 1.5E+00 | ± | 6.5E-02 | 9.6E-01 | ± | 3.3E-01 | 1.9E+00 | ± | 1.1E-01 | 1.7E+00 | ± | 5.3E-02 |
| PE(18:1/22:6)-OH | 5.7E-03 | ± | 1.8E-03 | 1.5E-02 | ± | 5.0E-03 | 1.1E-02 | ± | 1.3E-03 | N.D. | | | 3.0E-03 | ± | 2.0E-03 | 3.8E-03 | ± | 1.3E-03 |
| PE(P-16:0/20:4) | 1.3E+01 | ± | 1.9E-01 | 1.2E+01 | ± | 2.6E-01 | 1.1E+01 | ± | 7.7E-01 | 2.0E+01 | ± | 1.9E+00 | 1.4E+01 | ± | 7.3E-01 | 1.6E+01 | ± | 6.4E-01 |
| PE(P-16:0/20:5) | 1.5E+00 | ± | 1.8E-01 | 1.3E+00 | ± | 6.3E-02 | 1.1E+00 | ± | 2.1E-02 | 1.2E+00 | ± | 2.0E-01 | 1.5E+00 | ± | 4.3E-02 | 2.8E+00 | ± | 1.4E-02 |
| PE(P-16:0/20:5)-OH | 1.1E+00 | ± | 5.0E-02 | 1.2E+00 | ± | 3.5E-02 | 9.9E-01 | ± | 6.5E-02 | 6.9E-01 | ± | 2.2E-01 | 1.1E+00 | ± | 5.3E-02 | 1.3E+00 | ± | 6.5E-02 |
| PE(P-16:0/20:5)-OOH | N.D. | | | 1.7E-03 | ± | 6.4E-04 | 1.8E-02 | ± | 2.1E-03 | N.D. | | | 3.6E-03 | ± | 3.1E-03 | 2.1E-03 | ± | 9.0E-04 |
| PE(P-16:0/22:6) | 3.3E+00 | ± | 2.6E-01 | 2.9E+00 | ± | 1.6E-01 | 2.4E+00 | ± | 3.0E-02 | 2.8E+00 | ± | 3.6E-01 | 2.9E+00 | ± | 1.0E-01 | 4.7E+00 | ± | 2.1E-01 |
| PE(P-16:0/22:6)-OH | 1.1E-02 | ± | 1.1E-03 | 7.0E-02 | ± | 9.1E-03 | 8.7E-02 | ± | 1.4E-02 | N.D. | | | 4.0E-02 | ± | 1.0E-02 | 3.7E-02 | ± | 1.1E-02 |
| PE(P-16:0/22:6)-OOH | 9.0E-03 | ± | 8.7E-04 | 5.2E-02 | ± | 2.5E-03 | 7.1E-02 | ± | 6.8E-03 | N.D. | | | 3.3E-02 | ± | 6.4E-03 | 2.8E-02 | ± | 5.0E-03 |
| PE(P-18:0/18:2) | 1.1E+00 | ± | 3.3E-01 | 1.4E+00 | ± | 1.0E-01 | 1.4E+00 | ± | 1.2E-01 | 1.4E+00 | ± | 2.1E-01 | 1.4E+00 | ± | 1.9E-01 | 2.1E+00 | ± | 5.4E-02 |
| PE(P-18:0/18:2)-OOH | 2.6E-02 | ± | 1.3E-02 | 2.8E-02 | ± | 1.0E-02 | 4.5E-02 | ± | 1.7E-02 | 1.1E-02 | ± | 1.9E-02 | 2.1E-02 | ± | 9.7E-03 | 2.2E-02 | ± | 6.3E-03 |
| PE(P-18:0/20:3) | 1.6E-01 | ± | 1.3E-01 | 2.7E-01 | ± | 1.0E-01 | 4.3E-01 | ± | 8.8E-02 | 3.5E-01 | ± | 1.9E-01 | 2.4E-01 | ± | 8.2E-02 | 1.0E+00 | ± | 8.9E-02 |
| PE(P-18:0/20:3)-OH | 6.8E-01 | ± | 2.8E-02 | 1.7E+00 | ± | 1.8E-01 | 2.2E+00 | ± | 1.6E-01 | 8.2E-01 | ± | 5.3E-01 | 1.2E+00 | ± | 1.6E-01 | 1.9E+00 | ± | 4.9E-02 |
| PE(P-18:0/20:3)-OOH | 6.1E-02 | ± | 1.9E-02 | 3.5E-02 | ± | 9.2E-03 | 1.7E-02 | ± | 2.6E-03 | N.D. | | | 7.5E-04 | ± | 1.3E-03 | 3.6E-03 | ± | 1.5E-03 |
| PE(P-18:0/20:4) | 2.3E+01 | ± | 1.2E+00 | 2.1E+01 | ± | 5.2E-01 | 2.0E+01 | ± | 1.5E+00 | 3.1E+01 | ± | 2.3E+00 | 2.6E+01 | ± | 1.2E+00 | 2.6E+01 | ± | 2.1E+00 |

| Lipids | Control | NAO+Light 0.5h | NAO+Light 6h | NAO+Light 48h | NAO+Light+FCCP 0.5h | NAO+Light+FCCP 48h |
|---|---|---|---|---|---|---|
| PE(P-18:0/20:4)-OH | 1.6E-01 ± 4.0E-02 | 2.5E-01 ± 5.4E-02 | 2.7E-01 ± 9.7E-03 | 5.8E-02 ± 1.3E-02 | 4.9E-02 ± 1.9E-02 | 9.6E-02 ± 2.2E-02 |
| PE(P-18:0/20:4)-OOH | 1.2E-01 ± 1.7E-02 | 2.0E-01 ± 8.5E-03 | 2.1E-01 ± 1.1E-02 | 4.8E-02 ± 2.3E-02 | 4.3E-02 ± 1.9E-02 | 7.8E-02 ± 1.4E-02 |
| PE(P-18:0/20:5) | 1.4E+01 ± 8.5E-01 | 1.4E+01 ± 5.3E-01 | 1.4E+01 ± 1.3E-01 | 2.1E+01 ± 1.8E+00 | 1.6E+01 ± 1.8E-01 | 1.5E+01 ± 3.1E-01 |
| PE(P-18:0/20:5)-OH | 2.9E-01 ± 6.2E-02 | 2.3E-01 ± 4.2E-02 | 2.6E-01 ± 3.7E-02 | N.D. | 2.5E-01 ± 4.1E-02 | 1.7E-01 ± 1.4E-02 |
| PE(P-18:0/20:5)-OOH | 2.5E-01 ± 4.0E-02 | 1.9E-01 ± 7.1E-03 | 2.2E-01 ± 3.0E-02 | N.D. | 2.0E-01 ± 2.9E-02 | 1.3E-01 ± 1.1E-02 |
| PE(P-18:0/22:4) | 7.6E+00 ± 1.0E+00 | 6.4E+00 ± 4.3E-01 | 7.1E+00 ± 3.1E-01 | 8.3E+00 ± 1.5E-01 | 7.8E+00 ± 5.4E-01 | 6.9E+00 ± 2.0E-01 |
| PE(P-18:0/22:4)-OH | 2.3E-03 ± 3.9E-03 | 2.5E-03 ± 1.8E-03 | 1.3E-02 ± 7.0E-03 | 1.6E-01 ± 6.1E-02 | 2.1E-03 ± 1.9E-03 | 4.4E-03 ± 1.9E-03 |
| PE(P-18:0/22:4)-OOH | 1.5E-03 ± 2.7E-03 | 1.8E-03 ± 1.1E-03 | 8.8E-03 ± 3.3E-03 | 1.3E-01 ± 6.4E-02 | 1.5E-03 ± 1.4E-03 | 3.5E-03 ± 8.6E-04 |
| PE(P-18:0/22:6) | 5.6E+00 ± 6.1E-01 | 4.9E+00 ± 3.6E-01 | 4.2E+00 ± 3.5E-02 | 4.2E+00 ± 3.7E-01 | 5.0E+00 ± 2.8E-01 | 5.4E+00 ± 1.9E-01 |
| PE(P-18:0/22:6)-OH | 3.9E-01 ± 3.1E-02 | 1.5E-01 ± 1.5E-02 | 1.1E-01 ± 1.3E-02 | N.D. | 5.0E-02 ± 7.6E-03 | 5.3E-02 ± 1.3E-02 |
| PE(P-18:0/22:6)-OOH | 2.9E-01 ± 3.9E-02 | 1.2E-01 ± 7.9E-03 | 8.3E-02 ± 3.3E-03 | N.D. | 4.1E-02 ± 9.7E-03 | 4.2E-02 ± 4.3E-03 |
| PE(P-18:1/22:6) | 1.1E+00 ± 1.2E-01 | 1.1E+00 ± 6.6E-02 | 8.9E-01 ± 4.7E-02 | 4.3E-01 ± 1.4E-01 | 1.1E+00 ± 2.0E-02 | 1.6E+00 ± 5.6E-02 |
| PE(P-18:1/22:6)-OH | 1.3E-03 ± 2.3E-03 | 1.6E-03 ± 1.4E-03 | 1.2E-02 ± 2.6E-03 | 3.4E-02 ± 6.0E-02 | N.D. | N.D. |
| PE(P-20:0/20:5) | 1.2E+01 ± 8.6E-01 | 1.1E+01 ± 6.5E-01 | 9.9E+00 ± 4.2E-01 | 1.0E+01 ± 1.0E+00 | 1.1E+01 ± 2.4E-01 | 8.9E+00 ± 4.8E-01 |
| PE(P-20:0/20:5)-OH | 7.7E-01 ± 8.6E-02 | 3.5E-01 ± 1.5E-02 | 2.2E-01 ± 2.6E-02 | 1.2E-01 ± 2.3E-02 | 1.2E-01 ± 3.2E-02 | 1.2E-01 ± 7.3E-03 |
| PE(P-20:0/20:5)-OOH | 5.8E-01 ± 8.9E-03 | 2.6E-01 ± 8.6E-03 | 1.8E-01 ± 6.0E-03 | 9.5E-02 ± 2.3E-02 | 9.9E-02 ± 1.7E-02 | 9.0E-02 ± 6.5E-03 |
| PE(P-20:0/22:4) | 3.8E-01 ± 2.9E-02 | 2.8E-01 ± 7.6E-02 | 3.0E-01 ± 1.0E-01 | N.D. | 3.1E-01 ± 7.9E-02 | 4.2E-01 ± 8.8E-02 |
| PE(P-20:0/22:4)-OH | 2.4E-01 ± 5.1E-02 | 2.9E-01 ± 5.3E-02 | 3.0E-01 ± 4.2E-02 | N.D. | 2.3E-01 ± 2.9E-02 | 4.2E-01 ± 2.8E-02 |
| PI(18:0/20:4) | 3.3E+01 ± 1.2E+01 | 1.5E+01 ± 4.8E-01 | 1.9E+01 ± 8.5E+00 | 3.2E+01 ± 1.3E+01 | 5.5E+01 ± 2.3E+01 | 1.8E+01 ± 5.1E+00 |
| PI(18:0/20:4)-OH | 5.6E-03 ± 8.0E-03 | 1.4E-02 ± 5.9E-03 | 1.2E-02 ± 2.9E-03 | 2.3E-02 ± 1.7E-02 | 1.8E-02 ± 6.7E-03 | 1.5E-02 ± 3.6E-03 |
| PI(18:0/22:6) | 4.0E-01 ± 5.8E-01 | 4.0E-01 ± 4.9E-02 | 4.1E-01 ± 1.6E-01 | 8.3E-01 ± 3.8E-01 | 7.9E-01 ± 2.5E-01 | 8.8E-01 ± 2.5E-01 |
| PI(18:1/22:4) | 6.4E-01 ± 9.1E-01 | 9.6E-01 ± 8.7E-02 | 9.2E-01 ± 3.2E-01 | 1.4E+00 ± 3.4E-01 | 2.5E+00 ± 7.2E-01 | 1.2E+00 ± 4.0E-01 |
| PI(16:0/18:2) | 2.1E-01 ± 2.3E-01 | 7.7E-02 ± 2.6E-02 | 1.0E-01 ± 6.3E-02 | 2.0E-01 ± 1.0E-01 | 7.2E-02 ± 4.3E-02 | 7.3E-02 ± 5.2E-03 |
| PI(18:0/18:2) | 4.4E+00 ± 6.3E+00 | 2.5E+00 ± 4.2E-01 | 2.4E+00 ± 6.5E-01 | 3.1E+00 ± 4.1E-01 | 3.4E+00 ± 1.8E+00 | 2.5E+00 ± 7.7E-01 |
| PI(18:1/18:2) | 2.6E-01 ± 3.5E-01 | 1.2E-01 ± 5.8E-02 | 1.7E-01 ± 6.6E-02 | 2.0E-01 ± 1.2E-01 | 5.6E-01 ± 2.6E-01 | 1.0E-01 ± 4.0E-02 |
| PI(18:0/20:2) | 1.0E-01 ± 1.4E-01 | 8.4E-02 ± 1.9E-02 | 9.9E-02 ± 1.6E-02 | 2.4E-01 ± 8.6E-02 | 2.9E-01 ± 1.2E-01 | 1.3E-01 ± 5.8E-02 |
| PI(16:0/20:4) | 1.7E+00 ± 2.4E+00 | 8.7E-01 ± 2.8E-01 | 9.2E-01 ± 2.8E-01 | 1.2E+00 ± 4.6E-01 | 6.9E-01 ± 5.1E-01 | 6.6E-01 ± 1.3E-01 |
| PI(18:1/20:4) | 1.9E+00 ± 2.8E+00 | 1.5E+00 ± 2.0E-01 | 1.2E+00 ± 1.2E-01 | 2.8E+00 ± 1.2E+00 | 1.7E+00 ± 6.1E-01 | 1.8E+00 ± 4.6E-01 |
| PI(18:1/20:5) | 1.5E-01 ± 2.2E-01 | 8.9E-02 ± 4.9E-02 | 8.7E-02 ± 3.5E-02 | 1.6E-01 ± 8.9E-02 | 2.0E-01 ± 4.5E-02 | 1.5E-01 ± 4.5E-02 |
| PI(18:0/22:4) | 3.7E-01 ± 5.1E-01 | 4.3E-01 ± 8.7E-02 | 4.7E-01 ± 7.6E-02 | 5.6E-01 ± 1.3E-01 | 1.3E+00 ± 3.1E-01 | 5.7E-01 ± 1.8E-01 |
| PS(16:1/20:3) | 2.1E+00 ± 3.6E-01 | 2.2E+00 ± 4.5E-01 | 3.5E+00 ± 7.6E-01 | 2.1E+00 ± 8.1E-02 | 4.0E+00 ± 3.7E-01 | 1.3E+00 ± 6.9E-02 |
| PS(18:0/18:2) | 2.0E-03 ± 3.4E-03 | 1.8E-03 ± 3.2E-03 | 6.2E-03 ± 5.5E-03 | 6.8E-03 ± 5.0E-04 | 2.7E-01 ± 3.7E-01 | 4.5E+00 ± 9.5E-01 |
| PS(18:0/18:2)-OH | 7.6E-02 ± 4.8E-02 | 7.5E-02 ± 4.8E-02 | 9.4E-03 ± 2.1E-03 | 3.0E-03 ± 2.1E-04 | 4.6E-03 ± 4.0E-03 | 1.0E-03 ± 2.7E-04 |
| PS(18:0/18:2)-OOH | 9.4E-03 ± 4.2E-03 | 1.0E-02 ± 5.3E-03 | 7.1E-04 ± 1.2E-03 | N.D. | N.D. | N.D. |
| PS(18:0/20:4) | 2.4E+01 ± 3.1E+00 | 2.3E+01 ± 4.0E+00 | 2.4E+01 ± 2.4E+00 | 1.7E+01 ± 4.9E-01 | 2.7E+01 ± 8.9E-01 | 1.4E+01 ± 5.7E-01 |
| PS(18:0/20:4)-OH | 2.4E-01 ± 2.6E-02 | 2.4E-01 ± 4.2E-02 | 1.2E-02 ± 2.6E-03 | 3.8E-02 ± 4.9E-03 | 2.6E-02 ± 2.2E-02 | 5.2E-03 ± 2.5E-03 |
| PS(18:1/22:4) | 6.6E-01 ± 1.9E-01 | 6.5E-01 ± 1.9E-01 | 4.7E-01 ± 1.7E-01 | 3.5E-01 ± 2.7E-02 | 1.4E+00 ± 1.4E-01 | 4.3E+00 ± 1.2E-01 |

| Lipids | Control | | | NAO+Light 0.5h | | | NAO+Light 6h | | | NAO+Light 48h | | | NAO+Light+FCCP 0.5h | | | NAO+Light+FCCP 48h | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PS(22:0/18:2) | 2.9E-02 | ± | 1.0E-02 | 2.9E-02 | ± | 1.2E-02 | 1.6E-02 | ± | 7.9E-03 | 1.4E-02 | ± | 4.8E-04 | 1.0E-01 | ± | 5.4E-02 | 6.4E-02 | ± | 2.4E-02 |
| PS(20:1/22:4) | 1.9E+00 | ± | 3.9E-01 | 1.8E+00 | ± | 5.3E-01 | 1.5E+00 | ± | 3.2E-01 | 1.0E+00 | ± | 3.5E-02 | 2.7E+00 | ± | 2.2E-01 | 5.9E-01 | ± | 1.7E-02 |
| PS(18:0/20:2) | 1.4E-01 | ± | 3.5E-02 | 1.3E-01 | ± | 2.8E-02 | 2.3E-01 | ± | 1.2E-02 | 7.6E-02 | ± | 4.6E-03 | 1.6E-01 | ± | 1.4E-01 | 1.1E-01 | ± | 2.8E-02 |
| PS(18:0/20:2)-OH | 4.6E-03 | ± | 2.6E-03 | 4.4E-03 | ± | 2.7E-03 | 7.7E-04 | ± | 1.3E-03 | 3.6E-03 | ± | 2.1E-04 | N.D. | | | 5.4E-04 | ± | 4.7E-04 |
| PS(18:0/20:2)-OOH | 5.6E-04 | ± | 9.6E-04 | 5.6E-04 | ± | 9.6E-04 | 9.1E-04 | ± | 1.6E-03 | 3.5E-03 | ± | 1.8E-04 | 2.0E-03 | ± | 3.4E-03 | 2.1E-03 | ± | 1.8E-03 |
| PS(20:2/22:6) | 1.6E+00 | ± | 2.8E-01 | 1.5E+00 | ± | 4.0E-01 | 4.3E+00 | ± | 5.2E-01 | 2.4E+00 | ± | 7.5E-02 | 4.1E+00 | ± | 2.5E-01 | 1.5E+00 | ± | 9.2E-02 |
| PS(20:3/20:4) | 5.9E+00 | ± | 1.6E+00 | 6.1E+00 | ± | 1.6E+00 | 4.7E+00 | ± | 1.6E-01 | 3.7E+00 | ± | 6.5E-02 | 8.2E+00 | ± | 5.8E-01 | 2.7E+00 | ± | 1.5E-01 |
| PS(20:3/20:4)-OH | 6.4E-02 | ± | 1.4E-02 | 6.9E-02 | ± | 1.3E-02 | 9.1E-04 | ± | 1.6E-03 | 1.8E-03 | ± | 1.8E-04 | N.D. | | | 6.4E-04 | ± | 5.5E-04 |
| PS(20:3/20:4)-OOH | 6.8E-01 | ± | 6.9E-02 | 6.5E-01 | ± | 1.1E-01 | 8.2E-01 | ± | 1.2E-01 | 5.6E-01 | ± | 9.5E-03 | 8.1E-01 | ± | 1.2E-01 | 2.5E-01 | ± | 2.9E-02 |
| PS(20:3/22:4) | 2.4E+00 | ± | 4.8E-01 | 2.3E+00 | ± | 5.8E-01 | 3.5E+00 | ± | 5.3E-01 | 2.3E+00 | ± | 6.6E-02 | 4.9E+00 | ± | 5.7E-01 | 1.3E+00 | ± | 4.6E-02 |
| PS(20:3/22:6) | 1.6E+00 | ± | 3.2E-01 | 1.6E+00 | ± | 2.2E-01 | 3.2E+00 | ± | 7.4E-01 | 1.8E+00 | ± | 5.5E-02 | 2.4E+00 | ± | 3.7E-01 | 1.0E+00 | ± | 7.3E-02 |
| PS(18:1/20:4) | 5.1E+00 | ± | 1.1E+00 | 4.9E+00 | ± | 1.4E+00 | 5.5E+00 | ± | 7.7E-01 | 3.7E+00 | ± | 6.4E-02 | 7.5E+00 | ± | 7.8E-01 | 2.6E+00 | ± | 9.9E-02 |
| PS(18:1/20:4)-OOH | 1.5E-02 | ± | 2.3E-03 | 1.4E-02 | ± | 1.2E-03 | 2.0E-03 | ± | 4.6E-04 | N.D. | | | N.D. | | | 8.6E-04 | ± | 7.8E-04 |
| PS(22:1/20:5) | 6.4E-01 | ± | 1.4E-01 | 6.3E-01 | ± | 1.3E-01 | 7.9E-01 | ± | 1.6E-01 | 5.2E-01 | ± | 4.0E-02 | 1.3E+00 | ± | 1.6E-01 | 3.4E-01 | ± | 4.6E-02 |
| PS(18:0/22:4) | 7.3E-01 | ± | 6.9E-01 | 7.1E-01 | ± | 6.6E-01 | 9.7E-01 | ± | 9.9E-01 | 2.0E+00 | ± | 4.9E-02 | 1.7E+00 | ± | 1.2E+00 | 4.8E+00 | ± | 3.6E-01 |

**Supporting information table S2**

Quantification of phospholipid levels in WT and Cardiolipin Synthase (CLS) knockdown HeLa cells

| Phospholipid | pmol/nmol total phospholipid phosphorous | |
|---|---|---|
| | WT | CLS knockdown |
| CL | 20.8±1.4 | 9.2±1.5* |
| PG | 3.3±0.5 | 5.2±0.1* |
| PE | 241.4±21.6 | 253.8±18.9 |
| PC | 535.5±31.9 | 547.7±42.7 |
| PS | 63.7±5.4 | 65.4±3.9 |
| PI | 79.2±11.0 | 74.1±7.1 |
| Sph | 58.0±6.3 | 49.8±15.0 |

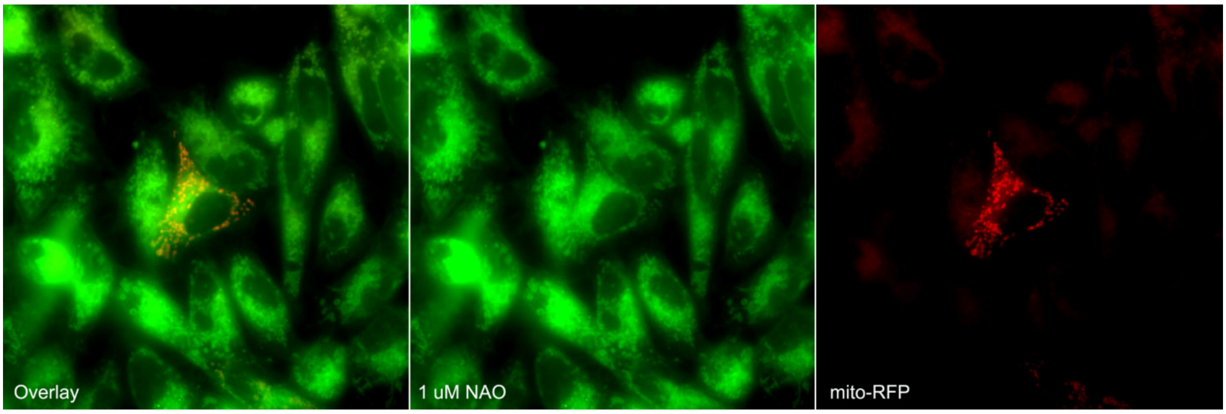
Data presented are means±SD (n=3)

*p<0.01 vs WT HeLa cells

CL: cardiolipin; PG: phosphatidylglycerol; PE: phosphatidylethanolamine; PC: phosphatidylcholine; PS: phosphatidylserine; PI: phosphatidylinositol; Sph: sphingomyelin.

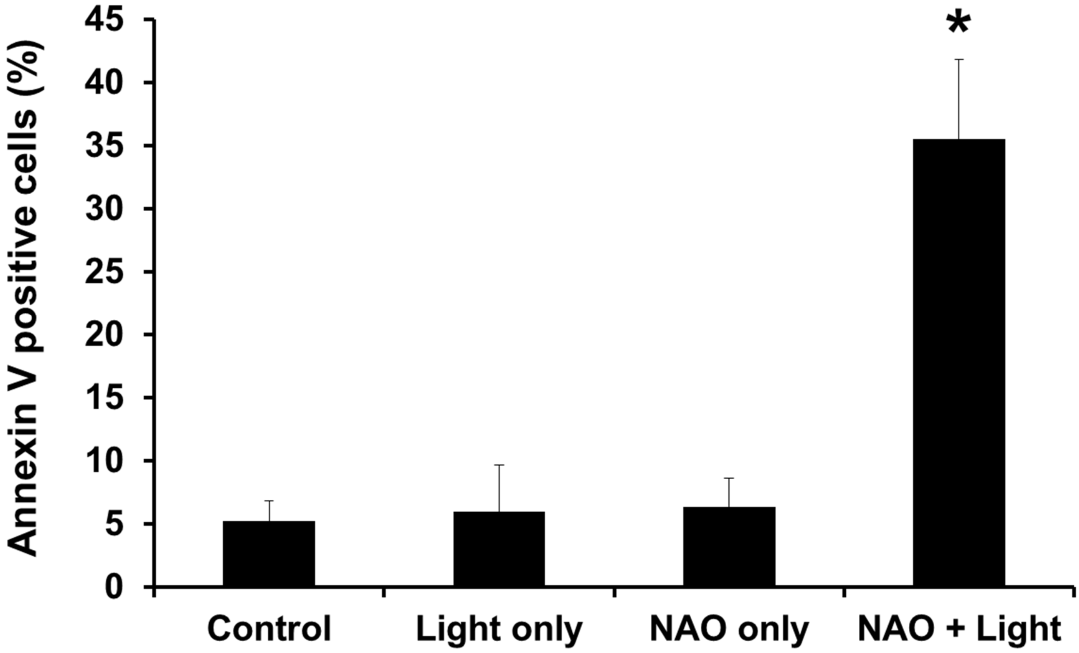
Quoted and modified from Free radical biology & medicine 44, 1935-1944 [1]

**Supporting information figure S1**



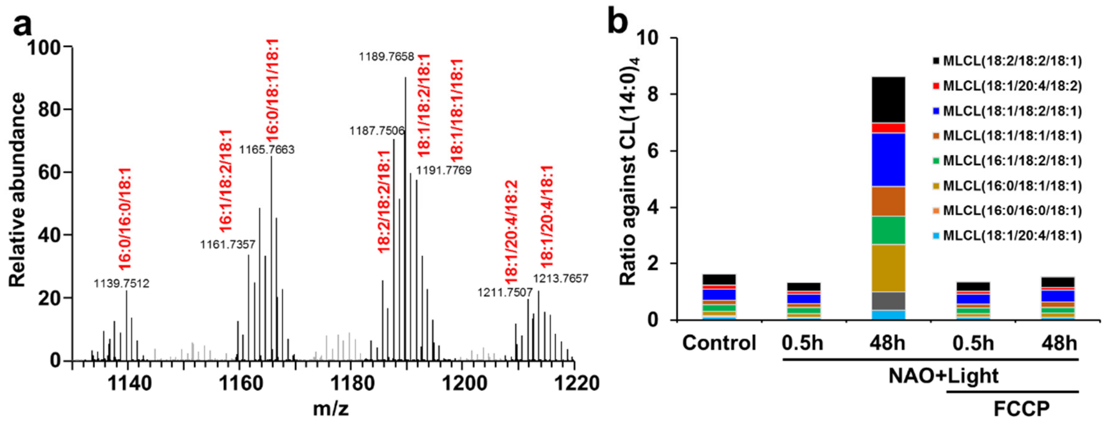

At a high concentration of 1 µM, NAO diffused into extra-mitochondrial compartments (30 min incubation). Mitochondria were visualized using the mFAP technology (in red).

**Supporting information figure S2**




NAO facilitates photo-induced apoptosis in mouse embryonic cells (MECs). MECs were treated with 100 nM NAO for 30 min, washed by medium and exposed to light at the intensity of 11.4 $W/cm^2$ for 30 min. At 24 h after treatment, cells were collected for analysis of phosphatidylserine (PS) externalization indicated by Annexin V binding. Mean ± SD (n=3). *$p < 0.05$ vs. control, NAO only, and light only groups.

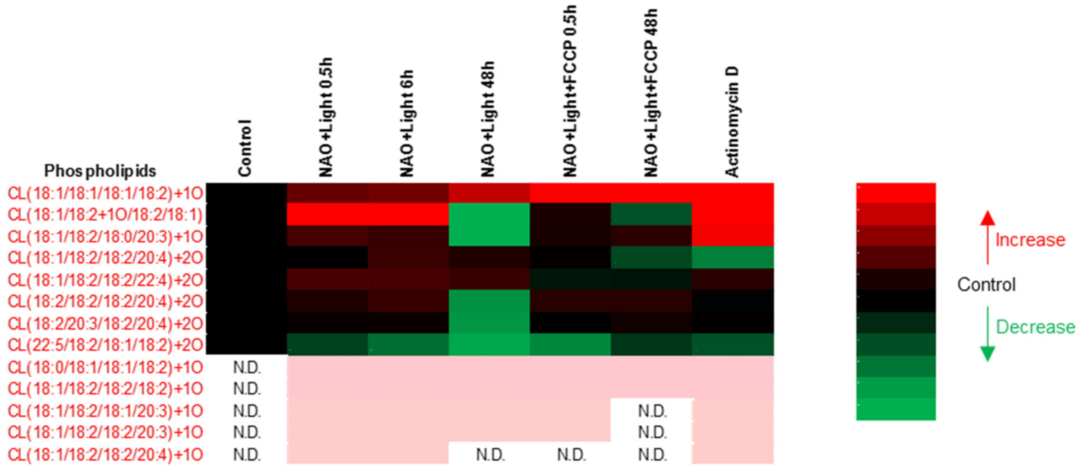
**Supporting information figure S3**




**Monolyso-cardiolipin (MLCL) increased 48 hours after NAO+Light treatment.**

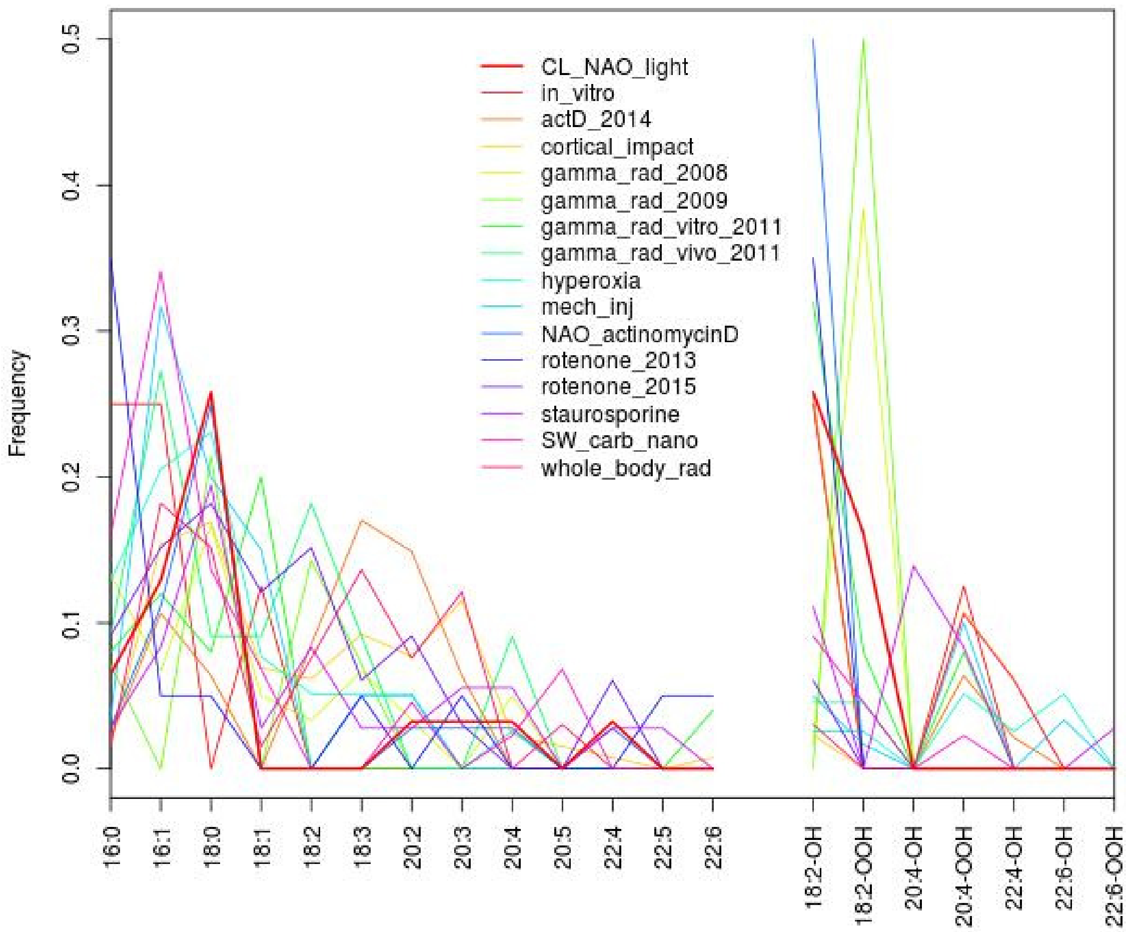
**a.** Eight major species of MLCLs (indicated by red) were identified by accurate m/z value (<5 ppm) and its corresponding MS/MS fragments. **b.** Relative quantitation was achieved by comparing to $CL(14:0)_4$, showing the amount of each MLCL species and total amount in stacked bar-plot.

## Supporting information figure S4




Heat map (fold-change) of oxygenated CL species formed during NAO plus light-induced apoptosis and actinomycin D -induced apoptosis. HeLa cells were treated with 100 nM actinomycin D for 18 h; this resulted in 38% apoptotic cells indicated by externalization of PS. The analysis was performed with three replicates and the color of each box represents the relative content of the corresponding CL species; color coding - black for no change, red for increased content, and green for decreased content). For those CLs that were not detected (N.D.) in control, no color was applied.

**Supporting information figure S5**




Unigram analysis of all CL acyl chains from the current study and other previous ones. Each line represents a different experiment. The extracted n-grams (single acyl chains in the observed CL molecules) are shown on the x-axis and their corresponding frequencies on the y-axis. N-grams containing oxygenated FA species are shown in the right end of the plot, and in Figure 5 of the main manuscript.

## Supporting information figure S6


**Bi-gram analysis of CL acyl chains from the same datasets and details as in Supporting information figure S5.**

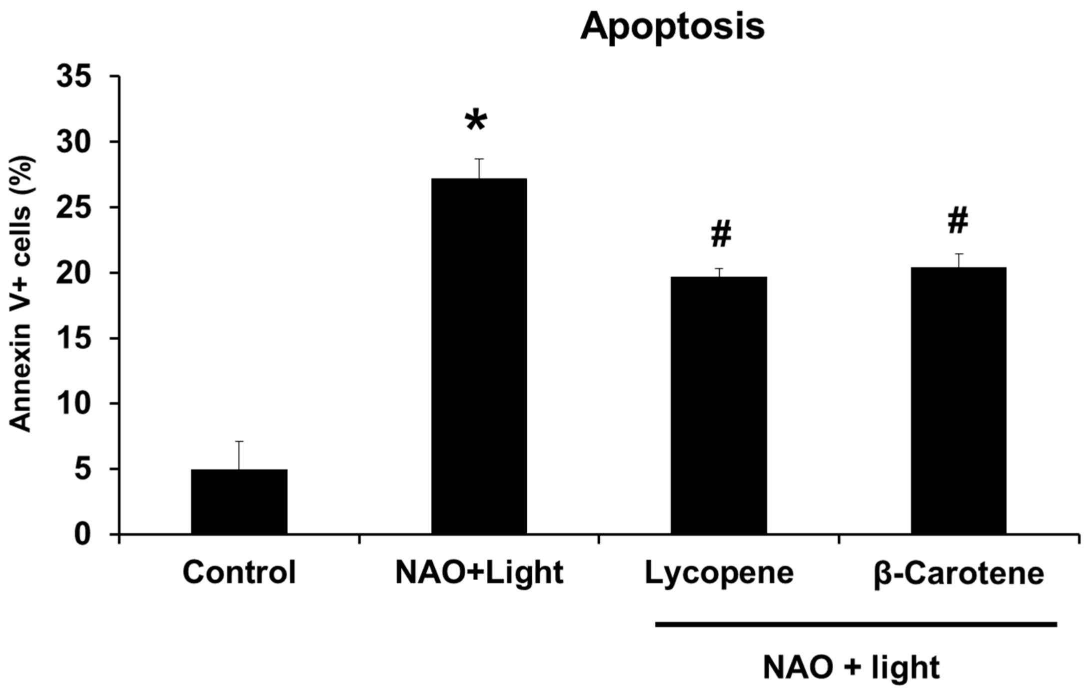
**Supporting information figure S7**

**Trigram analysis of CL acyl chains from the same datasets and details as in Supporting information figure S5.**

## Supporting information figure S8

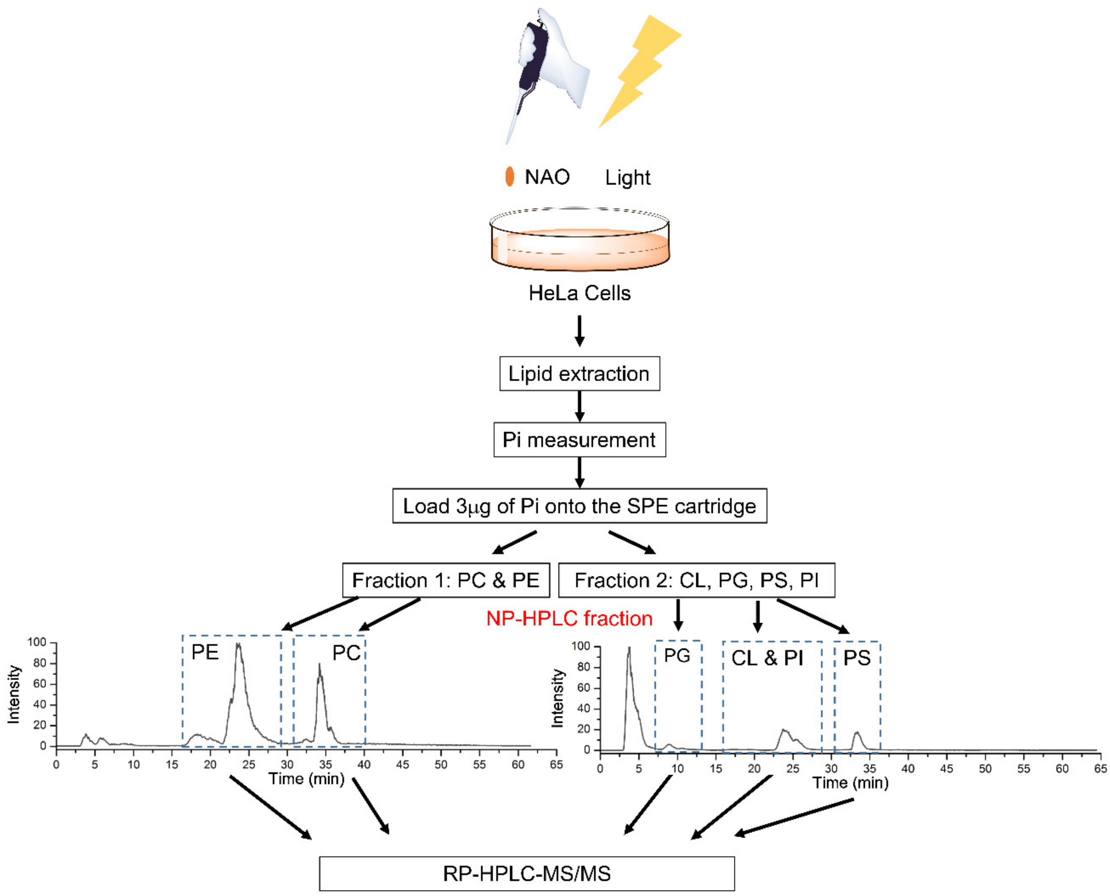
**Tetragram analysis of CL acyl chains from the same datasets and details as in Supporting information figure S5.**

**Supporting information figure S9**



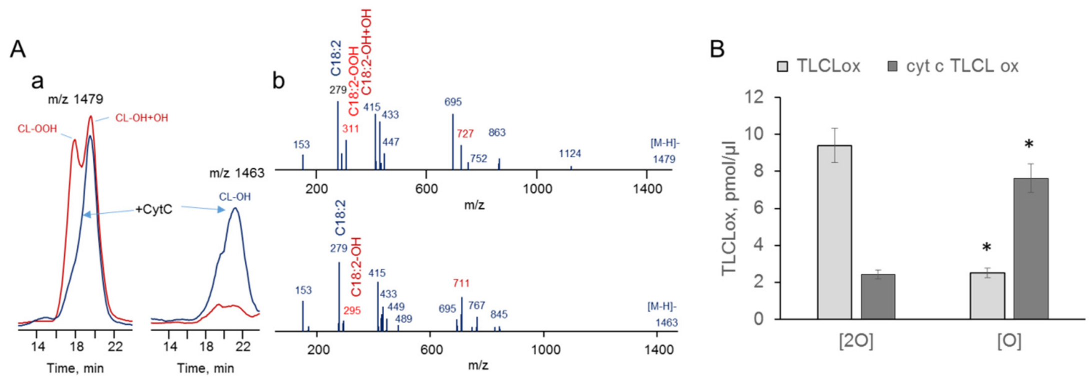

**Singlet oxygen quenchers partially protect cells against apoptosis induced by NAO and light exposure.** Cells were pre-treated with 10 μM Lycopene and 10 μM β-Carotene before NAO staining and light exposure. Cells were collected for analysis of PS externalization by Annexin V binding at 24 h after treatments. Mean ± SD (N=3). *$p$ < 0.05 vs. non-treated controls. $^{\#}p$ < 0.05 vs. NAO and light treatments.

**Supporting information figure S10**



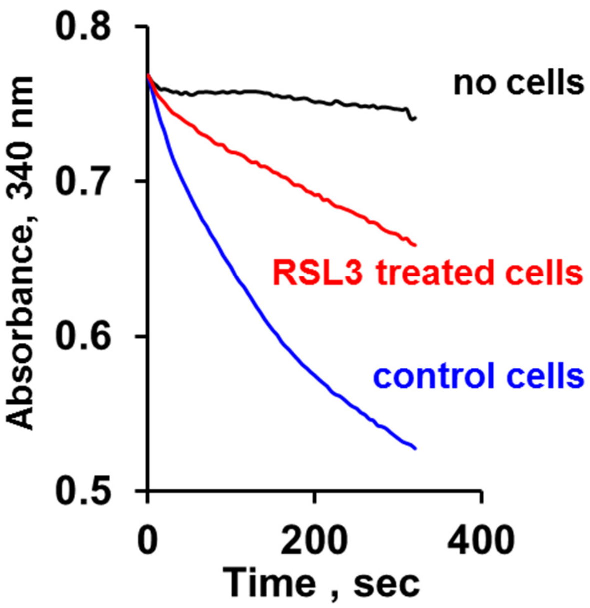

A flow-chart illustrating the LC-MS analytical protocols employed in assessments of phospholipids and their oxygenated species in HeLa cells.

**Supporting information figure S11**




**LC-MS/MS analysis and quantitation of TLCL ox reduction by Cyt *C*. (A a)** Typical profiles of singly charged TLCLox molecular species with m/z 1479 and 1463, corresponding to hydroperoxy- , hydroxy-hydroxy-TLCL and mono-hydroxy-TLCL (A a, curves in red color – before incubation with Cyt *C* and A a, curves in dark blue color - after incubation with Cyt C, respectively). **(A b)** MS2 fragmentation of parent ions at m/z 1479 an 1463 resulted in formation of non-oxidized ion fragment with m/z 695 and oxidized ion fragments with m/z 727 and 711, respectively. The major product ion with m/z 279 corresponds to C18:2. Product ions with m/z 311 (C18:2–OOH and C18:2–OH+OH) and 295 (C18:2–OH) were observed in the spectra after fragmentation of the molecular ion with m/z 727 and 711, respectively. **(B)** Quantitative assessment of the reduction of di-oxygenated cardiolipin (TLCL-OOH) to mono-oxygenated cardiolipin (TLCL-OH) after incubation with Cyt *C*. 2.5 μM of Cyt *C* was incubated with liposomes containing 50 μM TLCLox/DOPC in ratio (1:1) for 30 min in room temperature. (* *p*<0.05 vs. samples incubated without Cyt C). Related method was described in Supporting information methods.

**Supporting information figure S12**




**TLCL-OOH can be reduced by Gpx4 from cell homogenate.** As a negative control, TLCL-OOH cannot be reduced where glutathione peroxidase 4 (Gpx4) is inactivated by a chemical compound (100 nM RSL3 for 9 h). GPX4 activities of homogenates of MEF cells were monitored by the disappearance of NADPH absorbance at 340 nm. Homogenates (300 µg of protein per sample) were incubated in buffer containing 0.1 M Tris (pH8.0), 0.5 mM EDTA, 1.25% triton X-100 with 50 µM of TLCLox. Concentration of NADPH was 0.2 mM, concentration of glutathione was 3 mM. Concentration of glutathione peroxidase was 1 u/ml.

**Supplmental Materials and Methods**

**Materials**

MitoTracker Deep Red, tetramethylrhodamine (TMRM), and 5,5',6,6'-tetrachloro1,1',3,3'-tetraethylbenzimidazolyl carbocyanine iodide (JC-1) were purchased from Invitrogen (Carlsbad, CA, USA). All the lipid standards were purchased from Avanti Polar Lipids Inc. (Alabaster, AL, USA). 10-nonylacridine orange bromide was purchased from Life Technology (Grand Island, NY, USA). All other reagents were purchased from Sigma-Aldrich unless indicated.

**Cell lines and cell culture conditions**

Mouse embryonic cells (MECs), HeLa cells, and cardiolipin synthase (CLS) knockdown cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM) with 15% fetal bovine serum (FBS), supplemented with 25 mM Hepes, 50 mg/L uridine, 2mM glutamine, 1× nonessential amino acids, 2'-mercaptoethanol, 100 U/ml penicillin, and 100 µg/ml streptomycin. Cells were grown in incubators with controlled temperature of 37°C, $CO_2$ of 5% and humidity of 95%. Cells were harvested by trypsinization for further analysis.

**Phosphatidylserine externalization**

At the end of incubation, both adherent cells and floating cells in the medium were harvested and incubated with annexin V-FITC conjugate for 5 min in 1× binding buffer for the determination of phosphatidylserine (PS) externalization.

Cells were analyzed by flow cytometry (FACScanto II, BD, NJ, USA) and data were analyzed using FlowJo software (Tree Star, Inc., Ashland, OR).

**Caspase activity**

Caspase activity was evaluated using caspase-Glo 3/7 kit (Promega, Madison, WI) according to the instructions provided by the supplier. Briefly, after 3 freeze-thaw cycles, cells were mixed with assay reagents in a 96-well white walled clear bottom plate and incubated in dark for 30-60 min. Fluorescence values were obtained from each well using a “Fusion α” universal microplate analyzer (PerkinElmer, Shelton, CT).

**TUNEL assay for DNA fragmentation from apoptosis**

The terminal deoxytransferase-mediated dUTP nick end-labeling (TUNEL) assay was performed as previously described [14]. DAPI stain was used to label all nuclei. The total number of cells indicated by DAPI staining and the number of cells undergoing apoptosis indicated by TUNEL staining were counted semiautomatically. Three random fields on each slide were counted and at least 600 cells were counted on each slide.

**Analysis of phospholipids and their oxygenated molecular species by Solid phase extraction (SPE)-2D-LC-MS**

**SPE method**

First, the SPE cartridge (Strata® NH2 (55 μm, 70 Å), 100 mg / 1 mL, purchased from Phenomenex California, USA) was preconditioned with a mixture of 7.5 mL hexane/chloroform/methanol (95:3:2; v/v/v). Then the 0.5mL of lipid extract was loaded on the cartridge and washed with 15 mL hexane/diethyl ether/acetic acid (80:20:3; v/v/v). This washing fraction, containing undesirable components such as non-polar lipids consisting of di- and triacylglycerols, waxes, and cholesterol esters, was collected as fraction 1. Subsequently, the cartridge was eluted with 5 mL of chloroform/methanol (2:1; v/v), resulting in fraction 2 (phosphatidylcholine (PC) and phosphatidylethanolamine (PE)). Further the cartridge was eluted with 10 mL chloroform/methanol/28% ammonium hydroxide (4:1:0.1; v/v/v) and 5 mL chloroform/methanol/ammonium acetate (4:1:0.2M), thereby collecting fraction 3 (phosphatidylglycerol (PG), cardiolipin (CL), phosphatidylserine (PS) and phosphatidylinositol (PI)). Fractions 2 and 3 were dried under gentle nitrogen and re-dissolved in 15 μL of n-propanol/hexane/water/0.5% triethylamine (TEA)/0.01% Formic Acid (57/43/1/0.5/0.01) with 10mM ammonium acetate.

**LC-MS/MS method**

Each fraction from SPE was further loaded onto a normal phase HPLC-MS/MS system. The column was Silica Luna 3 μm, 150×2 mm, (Phenomenex, Torrance, CA). Solvent A consisted of n-propanol/hexane/water/0.5% TEA/0.01% Formic Acid (57/43/1/0.5/0.01; v/v/v/v/v) with 10mM ammonium acetate. Solvent B consisted of n-propanol/hexane/water/0.5% TEA/0.01% Formic Acid (57/43/8/0.5/0.01; v/v/v/v/v) with 10mM ammonium acetate. The gradient is described below (flow rate was 0.2 mL/min unless specified): 0-1 min, 10%B; 1-15 min, 10%-37%B; 15-23 min, 37%-40%B; 23-25min, 40%-100%B, flow rate 0.2 mL/min -0.225 mL/min; 25-47 min, 100%B, flow rate 0.225 mL/min; 47-48 min, 100%-10%B, flow rate 0.225 mL/min - 0.2 mL/min; 48-70 min, 10%B. Two third of the flow was diverted to a fraction collector (Spectra/Chrom CF-1 Fraction Collector, Spectrum Chromatography, Houston, TX US ) while the remainder was used for mass spectrometry (LCQDuo, Thermo-Finnigan) monitoring. Parameters for LCQDuo were as follows: spray voltage, 4.5 kV, negative mode; capillary temp, 250 °C; sheath gas, 30 units. Individual phospholipid classes from the first dimension chromatography were subsequently analyzed in a second dimension system, a reversed phase HPLC (Dionex Ultimate™ 3000 HPLC) coupled to a high resolution mass spectrometry equipped with a heated electrospray ionization probe. A C8 column (1.0 mm×15 cm, 3 μm, Phenomenex, Inc.) was employed to separate non-oxidized and oxidized species. The temperature of column oven was maintained at 35 °C. The solvent system used for reversed phase HPLC was as follows: solvent A: acetonitrile/water/TEA/formic acid (90/10/0.5/0.5; v/v/v/v); solvent B: propanol/water/TEA/formic acid (90/10/0.5/0.5; v/v/v/v). The flow rate was 0.05 mL/min. The gradient was described below: 0-5 min, 50%B; 5-15 min 50%-80%B; 15-30 min, 80%-100%B; 30-35 min, 100%-50%B; 35-40 min, 50%B. Parameters for QEactive were as follows: spray voltage, 3.2 kV; negative mode; capillary temp, 320 °C; sheath gas, 8 units. Other tuning parameters were optimized for each individual lipid class. The QEactive was operated in data-dependent mode, with MS performed at 140,000 full width at half maximum (FWHM) resolution and MS/MS performed at 35,000 FWHM resolution. The five most abundant ions were selected for MS/MS.

**LC-MS/MS Method for measuring monolyso-cardiolipins.**

Total lipid extraction corresponding to 1 µg phosphorus was reconstitute in 20µL solvent A:B (1:9, v/v). Solvent A consisted of n-propanol/hexane/water/0.5% TEA/0.01% Formic Acid (57/43/1/0.5/0.01; v/v/v/v/v) with 10mM ammonium acetate. Solvent B consisted of n-propanol/hexane/water/0.5% TEA/0.01% Formic Acid (57/43/8/0.5/0.01; v/v/v/v/v) with 10mM ammonium acetate. Total lipids were separated on a normal-phase column [Silica Luna 3 µm, 150×2 mm, (Phenomenex, Torrance, CA)] with flow rate of 0.2 mL/min. The gradient is described below: 0-1 min, 10%B; 1-15 min, 10%-37%B; 15-23 min, 37%-40%B; 23-25min, 40%-100%B; 25-47 min, 100%B; 47-48 min, 100%-10%B; 48-70 min, 10%B. Tetra-myristoyl cardiolipin ($CL(14:0)_4$) (Avanti polar lipids, Alabaster, AL, USA) was used as an internal standard. Parameters for QEactive were as follows: spray voltage, 3.2 kV; negative mode; capillary temp, 320 °C; sheath gas, 8 units. Other tuning parameters were optimized for each individual lipid class. The QEactive was operated in data-dependent mode, with MS performed at 140,000 full width at half maximum (FWHM) resolution and MS/MS performed at 35,000 FWHM resolution. The five most abundant ions were selected for MS/MS.

**LC-MS/MS analysis for oxygenated species of TLCL**

Analysis of oxygenated species of TLCL was performed using a Dionex UltimateTM 3000 HPLC system coupled to a linear ion trap mass spectrometer (LXQ, ThermoFisher Scientific, San Jose, CA) using reverse phase column Luna C8 (2) 3 µm 100 Å 1x150 mm (Phenomenex, Torrance, CA). A gradient of solvent A (acetonitrile: water: triethylamine: acetic acid, 45:5:0.25:0.25 v/v, in the presence of 0.01% formic acid) and B (2-propanol: water: triethylamine: acetic acid, 45:5:0.25:0.25, v/v, in the presence of 0.01% formic acid) was used at the flow rate of 60 µl/min as follows: 0-15 min isocratic at 35% solvent B; 15-20 min linear gradient 35-85% solvent B; 20-25 min isocratic at 85% solvent B; 25-28 min linear gradient at 85-35% solvent B; 28-35 min isocratic at 35% solvent B. Spectra were acquired in negative ion mode using a spray voltage of 5.0 kV and a capillary temperature of 150 °C.

**Evaluation of recovery of solid phase extraction**

Mixture of PC(16:0/16:0) and $CL(18:2)_4$ (0.5 µg for each) were dissolved in loading solvent for SPE. After SPE, amount of phosphorus in each fraction was measured by phosphorous measurement using micro method [2]. The result shows that the recovery for PC and CL are 95.0% and 104.9%, respectively.

Hydroperoxyl $CL(18:2)_4$ was prepared and purified. Same amount of hydroperoxyl $CL(18:2)_4$ before and after SPE pretreatment were analyzed by LC-MS/MS. By comparing the peak area of hydroperoxide $CL(18:2)_4$ on base peak chromatogram, the recovery of hydroperoxyl $CL(18:2)_4$ on SPE was 96.1%. Meanwhile, no signal of hydroxyl-$CL(18:2)_4$ was detected.

Above result demonstrates SPE provides satisfying resolution and recovery, prevent hydroperoxyl CL being reduced into hydroxyl counterparts which may artificially increase the amount of hydroxyl products.

**Analysis of Gpx4 activity**

GPX4 activity of homogenates of MEF cells were monitored by disappearance of NADPH. Homogenates (300 μg of protein per sample) were incubated in buffer containing 0.1 M Tris (pH8.0), 0.5 mM EDTA, 1.25% triton X-100 with 50 μM of TLCLox. Concentration of NADPH was 0.2 mM, concentration of glutathione was 3 mM. Concentration of glutathione peroxidase was 1 u/ml.

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