**Supplementary Table S2:** Phospholipid measures from the paired cohort (Cohort A) that were associated with sample malignancy (p<0.01).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Lipid ID** | **Est [95%CI]** | **p-value** |
| Lipid abundance | PI 38:6 | -0.35 [-0.36, -0.33] | 6.52E-19 |
|  | PI 40:6 | 0.19 [0.18, 0.21] | 1.78E-14 |
|  | PS 40:8 | 1.10 [1.00, 1.20] | 6.40E-14 |
|  | PC 36:4 | -0.56 [-0.64, -0.49] | 3.51E-11 |
|  | PC 34:1 | 0.17 [0.14, 0.20] | 5.81E-10 |
|  | PC 40:4 | -0.45 [-0.57, -0.33] | 1.18E-06 |
|  | PI 38:5 | -0.68 [-0.89, -0.48] | 4.51E-06 |
|  | PS 42:8 | 0.70 [0.50, 0.90] | 2.20E-05 |
|  | PS 42:2 | -0.26 [-0.35, -0.16] | 4.08E-05 |
|  | PS 42:4 | -0.23 [-0.32, -0.14] | 8.25E-05 |
|  | PE 42:6 | 0.75 [0.44, 1.06] | 0.000149 |
|  | PI 36:4 | -0.68 [-0.96, -0.39] | 0.000203 |
|  | PE 42:5 | 0.51 [0.29, 0.74] | 0.000255 |
|  | PS 38:4 | -0.66 [-0.96, -0.36] | 0.000399 |
|  | PC 38:4 | -0.52 [-0.77, -0.27] | 0.000693 |
|  | PS 36:2 | -0.32 [-0.48, -0.16] | 0.000753 |
|  | PS 36:1 | -0.46 [-0.68, -0.23] | 0.000789 |
|  | PC 32:0 | -0.66 [-0.98, -0.33] | 0.000832 |
|  | PS 38:3 | -0.72 [-1.08, -0.36] | 0.000942 |
|  | PC 40:6 | -0.36 [-0.55, -0.18] | 0.001045 |
|  | PS 38:6 | -0.82 [-1.24, -0.40] | 0.001116 |
|  | PE 40:4 | 0.042 [0.02, 0.065] | 0.001414 |
|  | PC 38:5 | -0.38 [-0.59, -0.18] | 0.001489 |
|  | PE 38:7 | 0.36 [0.17, 0.56] | 0.001681 |
|  | PI 38:4 | -0.50 [-0.80, -0.20] | 0.001944 |
|  | PC 36:5 | -0.40 [-0.60, -0.20] | 0.002105 |
|  | PS 44:6 | 0.52 [0.23, 0.81] | 0.002306 |
|  | PI 36:1 | 0.51 [0.22, 0.80] | 0.00274 |
|  | PS 42:9 | 0.47 [0.19, 0.75] | 0.003707 |
|  | PS 40:4 | -0.48 [-0.77, -0.20] | 0.003719 |
|  | PE 42:9 | 0.45 [0.16, 0.73] | 0.005855 |
|  | PE 40:6 | 0.36 [0.13, 0.60] | 0.006456 |
|  | PE 40:8 | 0.28 [0.10, 0.46] | 0.006487 |
|  | PC 40:5 | -0.30 [-0.50, -0.10] | 0.008872 |
| Mean Chain Length | PE 3 | -0.13 [-0.14, -0.12] | 7.43E-14 |
|  | PS 1 | 0.13 [0.07, 0.18] | 0.000187 |
|  | PE 6 | 0.11 [0.06, 0.15] | 0.000209 |
|  | PI 1 | 0.19 [0.11, 0.27] | 0.000231 |
|  | PS 3 | 0.096 [0.048, 0.144] | 0.000948 |
| Saturation Abundance | PC 6 | -0.0021 [-0.0024, -0.0017] | 6.10E-10 |
|  | PI 2 | 0.013 [0.01, 0.015] | 2.16E-08 |
|  | PE 3 | 0.0029 [0.0022, 0.0037] | 9.74E-07 |
|  | PS 8 | 0.0036 [0.0026, 0.0046] | 1.82E-06 |
|  | PS 9 | 0.00078 [0.00048, 0.00108] | 6.25E-05 |
|  | PC 4 | -0.038 [-0.056, -0.021] | 0.00046 |
|  | PC 1 | 0.066 [0.033, 0.098] | 0.000959 |
|  | PC 5 | -0.0071 [-0.0107, -0.0034] | 0.001172 |
|  | PI 5 | -0.0016 [-0.0025, -7e-04] | 0.002608 |
|  | PS 3 | -0.0088 [-0.0139, -0.0036] | 0.003266 |
|  | PC 0 | -0.013 [-0.021, -0.005] | 0.004081 |
|  | PS 4 | -0.0079 [-0.0133, -0.0025] | 0.009611 |

*For Mean Chain Length and Saturation Abundance, lipids are named by subclass and total number of unsaturations.*

**Supplementary Table S3:** Phospholipid measures from the un-paired cohort (Cohort B) associated with sample malignancy (p<0.01).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Lipid ID** | **Est [95%CI]** | **p-value** |
| Lipid Abundance | Cer(d18:1/26:5) | -0.59 [-0.71, -0.48] | 2.99E-13 |
|  | PI 38:4 | -0.77 [-0.95, -0.60] | 1.52E-11 |
|  | Cer(d18:1/26:3) | -0.79 [-0.99, -0.60] | 1.94E-10 |
|  | Cer(d18:1/18:8) | -0.73 [-0.94, -0.51] | 2.64E-08 |
|  | PC 42:7 | 0.60 [0.40, 0.80] | 2.67E-08 |
|  | PE 42:6 | 0.84 [0.55, 1.12] | 5.49E-07 |
|  | Cer(d18:1/24:7) | 0.97 [0.61, 1.32] | 2.12E-06 |
|  | PC 42:8 | 0.31 [0.19, 0.42] | 2.13E-06 |
|  | Cer(d18:1/22:7) | 1.10 [0.60, 1.60] | 7.02E-05 |
|  | Cer(d18:1/26:7) | 0.61 [0.33, 0.90] | 8.04E-05 |
|  | PC 42:6 | 0.32 [0.17, 0.48] | 0.000142 |
|  | PE 42:7 | 0.46 [0.24, 0.69] | 0.000174 |
|  | Cer(d18:1/22:2) | -0.40 [-0.60, -0.20] | 0.000199 |
|  | PC 40:1 | 0.36 [0.18, 0.54] | 0.000212 |
|  | SM d18:2/24:1 | -0.21 [-0.31, -0.10] | 0.000236 |
|  | PC 40:5 | 0.21 [0.10, 0.32] | 0.000296 |
|  | PI 38:5 | -0.49 [-0.74, -0.23] | 0.000429 |
|  | PC 40:7 | 0.30 [0.10, 0.50] | 0.00044 |
|  | PE 32:1 | 0.27 [0.13, 0.41] | 0.000492 |
|  | PC L 22:1 | -0.37 [-0.57, -0.17] | 0.000571 |
|  | Cer(d18:1/26:2) | -0.97 [-1.51, -0.44] | 0.000646 |
|  | PE 32:2 | 0.55 [0.24, 0.87] | 0.001055 |
|  | PC 42:3 | 0.34 [0.14, 0.53] | 0.001414 |
|  | PE 36:2 | 0.51 [0.21, 0.81] | 0.001584 |
|  | PE L 14:5 | 1.10 [0.40, 1.70] | 0.001594 |
|  | PC L 18:0 | -0.47 [-0.76, -0.19] | 0.001872 |
|  | Cer(d18:1/16:8) | -0.71 [-1.14, -0.28] | 0.001924 |
|  | Cer(d18:1/16:9) | 0.46 [0.18, 0.74] | 0.002174 |
|  | PE 36:3 | 0.51 [0.19, 0.82] | 0.002183 |
|  | PE 38:0 | -0.51 [-0.82, -0.19] | 0.002252 |
|  | PC 28:0 | 0.60 [0.20, 1.00] | 0.003476 |
|  | PC L 22:3 | -0.35 [-0.58, -0.12] | 0.003681 |
|  | PC 42:5 | 0.28 [0.09, 0.46] | 0.003975 |
|  | PC 40:4 | 0.23 [0.08, 0.38] | 0.004354 |
|  | PC 42:4 | 0.33 [0.11, 0.56] | 0.004794 |
|  | PC 36:1 | 0.36 [0.12, 0.61] | 0.005118 |
|  | PE 36:0 | -0.41 [-0.69, -0.13] | 0.005191 |
|  | PI 36:4 | -0.40 [-0.70, -0.10] | 0.005688 |
|  | PI 40:3 | 0.98 [0.30, 1.65] | 0.005736 |
|  | PS 34:0 | -0.90 [-1.50, -0.30] | 0.006216 |
|  | PS 38:6 | -0.68 [-1.17, -0.19] | 0.008117 |
|  | PC 34:1 | 0.47 [0.13, 0.82] | 0.008694 |
|  | SM d18:1/24:1 | -0.11 [-0.20, -0.03] | 0.008839 |
|  | PS 36:1 | -0.46 [-0.80, -0.12] | 0.009917 |
| Mean Chain Length | PE 7 | 0.12 [0.07, 0.16] | 2.05E-06 |
|  | PS 4 | 0.12 [0.07, 0.16] | 3.64E-06 |
|  | Cer 1-1 | -0.038 [-0.06, -0.015] | 0.001637 |
|  | PS 6 | 0.078 [0.031, 0.125] | 0.001773 |
|  | PS 1 | 0.076 [0.029, 0.124] | 0.002483 |
|  | PE 6 | 0.088 [0.029, 0.146] | 0.004439 |
|  | Cer 1-7 | 0.15 [0.05, 0.25] | 0.004768 |
|  | PI 2 | 0.16 [0.05, 0.27] | 0.005542 |
|  | PE 1 | -0.086 [-0.146, -0.025] | 0.007031 |
|  | PI 1 | 0.12 [0.03, 0.21] | 0.00791 |
| Saturation Abundance | Cer 1-4 | -0.012 [-0.015, -0.009] | 5.61E-09 |
|  | PS 4 | -0.012 [-0.018, -0.006] | 0.000292 |
|  | Cer 1-7 | 0.012 [0.006, 0.018] | 0.000354 |
|  | PE 0 | -0.0051 [-0.0078, -0.0023] | 0.000654 |
|  | PC 9 | -0.00034 [-0.00056, -0.00013] | 0.002216 |
|  | PC 1 | 0.06 [0.02, 0.10] | 0.004828 |
|  | PI 4 | -0.036 [-0.061, -0.012] | 0.005076 |
|  | PC 12 | -0.00071 [-0.0012, -0.00023] | 0.005235 |
|  | PI 1 | 0.019 [0.005, 0.032] | 0.008837 |
|  | PC 4 | -0.037 [-0.064, -0.009] | 0.009926 |

*For Mean Chain Length and Saturation Abundance, lipids are named by subclass and total number of unsaturations.*

**Supplementary Table S4:** Phospholipid measures from Cohort B associated with malignant samples Ki67 cell positivity (p<0.01).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Lipid ID** | **Est [95%CI]** | **p-value** |
| Lipid Abundance | PC 38:2 | -0.35 [-0.56, -0.13] | 0.001137415 |
|  | PC L 20:5 | 0.48 [0.16, 0.79] | 0.002488468 |
|  | PC 40:2 | -0.81 [-1.36, -0.26] | 0.00304984 |
|  | Cer(d18:1/22:0) | -0.40 [-0.70, -0.10] | 0.003552997 |
|  | Cer(d18:1/20:0) | -0.34 [-0.57, -0.10] | 0.004787576 |
|  | PC 40:3 | -0.84 [-1.44, -0.24] | 0.004928755 |
|  | SM d18:3/22:1 | -0.68 [-1.17, -0.19] | 0.005400972 |
|  | Cer(d18:1/14:0) | -0.39 [-0.69, -0.09] | 0.008881727 |
| Mean Chain Length | Cer 1-3 | 59.90 [22.70, 97.20] | 0.001286395 |
|  | PE 8 | 84.60 [31.90, 137.30] | 0.001335494 |
|  | PC 6 | 66.50 [23.50, 109.50] | 0.001985756 |
|  | PE 5 | 35.50 [12.40, 58.60] | 0.002132982 |
|  | PC 5 | 33.20 [11.20, 55.20] | 0.002523195 |
|  | Cer 1-4 | 61.90 [19.10, 104.70] | 0.003803916 |
|  | Cer 1-0 | -4.70 [-8.00, -1.40] | 0.004346096 |
|  | Cer 1-2 | 40.70 [11.00, 70.40] | 0.006064642 |
|  | PC 7 | 193.64 [50.55, 336.74] | 0.006798926 |
|  | PC 9 | 850.99 [202.46, 1499.52] | 0.008681164 |

*For Mean Chain Length and Saturation Abundance, lipids are named by subclass and total number of unsaturations.*

**Supplementary Table S5:** Phospholipid measures from Cohort B associated with sample ERG status (p<0.01).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Lipid ID** | **Est [95%CI]** | **p-value** |
| Lipid Abundance | Cer(d18:1/24:4) | -0.88 [-1.01, -0.75] | 4.66E-07 |
|  | Cer(d18:1/24:5) | -0.61 [-0.73, -0.50] | 4.84E-06 |
|  | PC 44:8 | -0.58 [-0.80, -0.37] | 8.40E-06 |
|  | PC L 18:0 | 0.25 [0.17, 0.33] | 1.50E-05 |
|  | PC 42:4 | -0.45 [-0.59, -0.32] | 2.17E-05 |
|  | PE 36:1 | 0.57 [0.33, 0.80] | 3.63E-05 |
|  | Cer(d18:1/24:7) | 0.75 [0.47, 1.03] | 4.99E-05 |
|  | Cer(d18:1/26:7) | 0.41 [0.24, 0.58] | 0.0001159 |
|  | PE 34:1 | 0.94 [0.44, 1.43] | 0.000403975 |
|  | PC L 16:0 | 0.39 [0.21, 0.57] | 0.000437926 |
|  | PS 34:0 | -1.50 [-2.40, -0.60] | 0.000905376 |
|  | PE 38:2 | 0.69 [0.27, 1.10] | 0.00148699 |
|  | PC 38:2 | 1.30 [0.50, 2.10] | 0.002281809 |
|  | PE L 20:3 | -0.65 [-0.89, -0.40] | 0.002457796 |
|  | PE 36:2 | 0.69 [0.23, 1.16] | 0.003388082 |
|  | PC 36:5 | -0.53 [-0.90, -0.17] | 0.004195823 |
|  | PI L 16:0 | 1.20 [0.40, 2.00] | 0.004216038 |
|  | PC L 18:1 | 0.57 [0.20, 0.94] | 0.004737572 |
|  | PC 42:5 | -0.30 [-0.50, -0.10] | 0.005471192 |
| Mean Chain Length | PE 4 | -0.092 [-0.135, -0.048] | 0.000784549 |
| Saturation Abundance | PE 1 | 0.056 [0.031, 0.081] | 0.000124795 |
|  | SM 2-1 | -0.016 [-0.023, -0.009] | 0.000142232 |
|  | PC 5 | -0.016 [-0.024, -0.008] | 0.000240119 |
|  | PE 5 | -0.0084 [-0.0126, -0.0042] | 0.000361836 |
|  | PC 9 | -0.00018 [-0.00027, -9e-05] | 0.000404002 |
|  | PS 0 | -0.00074 [-0.00112, -0.00036] | 0.000684119 |
|  | Cer 1-5 | -0.002 [-0.003, -0.001] | 0.000806838 |
|  | Cer 1-4 | -0.0058 [-0.0092, -0.0024] | 0.001361804 |
|  | PE 8 | -0.00071 [-0.00116, -0.00026] | 0.002055687 |
|  | PE.L 3 | -0.0042 [-0.0065, -0.0018] | 0.003138887 |
|  | Cer 1-0 | 0.071 [0.026, 0.117] | 0.005062845 |
|  | PC 6 | -0.0061 [-0.0101, -0.002] | 0.005428866 |

*For Mean Chain Length and Saturation Abundance, lipids are named by subclass and total number of unsaturations.*

**Supplementary Table S6:** Phospholipid measures from PDEs associated with change in KI67 cell positivity in ENZ & vehicle treated samples (p<0.01).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Lipid ID** | **Est [95%CI]** | **p-value** |
| Lipid Abundance | PE 32:0 | 1.0 [0.5, 1.5] | 0.000101448 |
|  | PE L 14:5 | -0.22 [-0.35, -0.09] | 0.000625325 |
|  | PC 44:7 | -0.8 [-1.2, -0.3] | 0.000674426 |
|  | PE L 18:1 | 0.59 [0.24, 0.95] | 0.000794281 |
|  | PS 38:1 | 0.8 [0.3, 1.4] | 0.001499912 |
|  | PC 44:3 | -0.8 [-1.3, -0.3] | 0.002054796 |
|  | PC 34:1 | 1.0 [0.3, 1.6] | 0.002532567 |
|  | PE 36:1 | 1.0 [0.3, 1.7] | 0.002561362 |
|  | PC L 14:0 | 0.8 [0.3, 1.4] | 0.003165986 |
|  | Cer(d18:1/24:0) | 0.50 [0.14, 0.87] | 0.005589286 |
|  | SM d18:1/18:1 | -0.6 [-1.0, -0.2] | 0.007073325 |
|  | Cer(d18:1/22:3) | -0.33 [-0.57, -0.08] | 0.00756436 |
|  | PE 38:4 | 0.8 [0.2, 1.5] | 0.008528304 |
|  | PE 36:2 | 0.7 [0.2, 1.2] | 0.008596447 |
|  | PC 44:2 | -0.48 [-0.84, -0.11] | 0.008750496 |
| Mean Chain Length | PC.L 0 | -2.4 [-4.1, -0.7] | 0.005447759 |
| Saturation Abundance | Cer 1-3 | -90 [-139, -41] | 0.00022117 |
|  | Cer 1-4 | -74 [-121, -27] | 0.00154786 |

*For Mean Chain Length and Saturation Abundance, lipids are named by subclass and total number of unsaturations.*