

Supplemental Table S1. Comparison of plasma sphingolipids levels in baseline plasma specimens from participants who progressed or did not progress to prediabetes during 5 years of follow-up

| Sphingolipids | All Mean ± SD | Non- progressors Mean ± SD | Progressors Mean ± SD | P value |
|--|--------------------------|---|----------------------------------|----------------|
| Total SPL (nmol/ml) | 98.2 ± 28.3 | 102 ± 25.2 | 94.0 ± 30.6 | 0.08 |
| Ceramides (pmol/ml) | | | | |
| C14:0 | 12.6 ± 5.69 | 13.1 ± 5.97 | 12.2 ± 5.40 | 0.36 |
| C16:0 | 56.8 ± 21.8 | 56.9 ± 23.0 | 56.8 ± 20.5 | 0.98 |
| C18:1 | 6.40 ± 3.61 | 7.03 ± 3.46 | 5.77 ± 3.66 | 0.04 |
| C18:0 | 38.4 ± 21.7 | 37.2 ± 18.4 | 39.6 ± 24.6 | 0.50 |
| C20:0 | 68.0 ± 34.2 | 65.5 ± 31.9 | 70.5 ± 36.5 | 0.38 |
| C22:0 | 521 ± 286 | 467 ± 235 | 574 ± 323 | 0.03 |
| C24:1 | 458 ± 224 | 453 ± 222 | 462 ± 227 | 0.80 |
| C24:0 | 1526 ± 818 | 1395 ± 692 | 1657 ± 913 | 0.06 |
| C26:1 | 7.62 ± 4.56 | 7.24 ± 4.21 | 8.00 ± 4.87 | 0.32 |
| C26:0 | 13.6 ± 7.53 | 11.4 ± 4.38 | 15.8 ± 9.23 | 0.0005 |
| C28:1 | 0.75 ± 0.84 | 0.66 ± 0.54 | 0.84 ± 1.05 | 0.19 |
| C28:0 | 0.94 ± 1.64 | 0.93 ± 1.57 | 0.95 ± 1.72 | 0.94 |
| C30:1 | 0.46 ± 0.51 | 0.43 ± 0.54 | 0.49 ± 0.47 | 0.46 |
| C30:0 | 0.06 ± 0.16 | 0.05 ± 0.14 | 0.07 ± 0.18 | 0.53 |
| C32:1 | 1.44 ± 2.29 | 1.34 ± 2.19 | 1.53 ± 2.41 | 0.62 |
| C32:0 | 0.32 ± 0.51 | 0.29 ± 0.44 | 0.35 ± 0.58 | 0.50 |
| C34:1 | 0.67 ± 1.00 | 0.61 ± 0.94 | 0.74 ± 1.05 | 0.44 |
| C34:0 | 0.13 ± 0.29 | 0.11 ± 0.20 | 0.16 ± 0.36 | 0.30 |
| Total ceramides | 2713 ± 1238 | 2518 ± 1061 | 2907 ± 1373 | 0.06 |
| Total VLC ceramides | 4.79 ± 6.19 | 4.43 ± 5.61 | 5.14 ± 6.73 | 0.49 |
| Ceramide ratios | | | | |
| C16:0/C18:0 | 1.83 ± 1.05 | 1.90 ± 1.19 | 1.76 ± 0.90 | 0.43 |
| C18:0/C18:1 | 7.35 ± 5.38 | 5.83 ± 2.87 | 8.88 ± 6.74 | 0.0008 |
| C24:0/C24:1 | 3.72 ± 1.84 | 3.47 ± 1.76 | 3.97 ± 1.90 | 0.10 |
| C26:0/C26:1 | 2.02 ± 0.92 | 1.84 ± 0.81 | 2.20 ± 0.99 | 0.017 |
| %Cer of SPL | 2.99 ± 1.72 | 2.51 ± 1.02 | 3.46 ± 2.12 | 0.001 |
| Monohexosyl ceramides (pmol/ml) | | | | |
| C14:0 | 8.19 ± 5.31 | 7.76 ± 4.58 | 8.62 ± 5.95 | 0.33 |
| C16:0 | 901 ± 623 | 898 ± 541 | 905 ± 699 | 0.95 |

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|---------------------------|-------------|-------------|-------------|-------|
| C18:1 | 75.8 ± 56.7 | 74.8 ± 38.3 | 6.89 ± 70.7 | 0.82 |
| C18:0 | 43.3 ± 31.9 | 43.7 ± 25.8 | 42.9 ± 37.2 | 0.88 |
| C20:0 | 81.4 ± 66.7 | 80.2 ± 56.3 | 82.6 ± 76.1 | 0.83 |
| C22:0 | 1076 ± 756 | 1066 ± 654 | 1085 ± 850 | 0.88 |
| C24:1 | 706 ± 568 | 677 ± 417 | 736 ± 689 | 0.54 |
| C24:0 | 1153 ± 811 | 1077 ± 614 | 1230 ± 968 | 0.26 |
| C26:1 | 14.1 ± 11.5 | 13.0 ± 8.79 | 15.3 ± 13.6 | 0.24 |
| C26:0 | 5.89 ± 4.50 | 5.83 ± 4.29 | 5.94 ± 4.72 | 0.88 |
| C28:1 | 1.68 ± 1.20 | 1.69 ± 1.15 | 1.68 ± 1.26 | 0.96 |
| C28:0 | 0.88 ± 0.70 | 0.91 ± 0.71 | 0.84 ± 0.69 | 0.55 |
| C30:1 | 1.09 ± 0.95 | 1.06 ± 0.83 | 1.12 ± 1.06 | 0.72 |
| C30:0 | 6.54 ± 4.43 | 6.10 ± 3.64 | 6.98 ± 5.08 | 0.24 |
| C32:1 | 1.71 ± 1.60 | 1.59 ± 1.31 | 1.84 ± 1.85 | 0.35 |
| C32:0 | 0.19 ± 0.44 | 0.15 ± 0.41 | 0.23 ± 0.47 | 0.32 |
| C34:1 | 0.43 ± 0.33 | 0.39 ± 0.28 | 0.46 ± 0.38 | 0.22 |
| C34:0 | 0.17 ± 0.15 | 0.16 ± 0.14 | 0.18 ± 0.16 | 0.42 |
| Total MHC | 4078 ± 2574 | 3955 ± 2095 | 4201 ± 2988 | 0.57 |
| Total VLC MHC | 12.7 ± 6.58 | 12.1 ± 5.05 | 13.3 ± 7.80 | 0.25 |
| MHC ratios | | | | |
| C16:0/C18:0 | 23.9 ± 15.2 | 22.6 ± 12.0 | 25.2 ± 17.8 | 0.30 |
| C18:0/C18:1 | 0.82 ± 0.74 | 0.64 ± 0.33 | 1.00 ± 0.96 | 0.004 |
| C24:0/C24:1 | 1.89 ± 0.95 | 1.78 ± 0.83 | 1.99 ± 1.05 | 0.19 |
| C26:0/C26:1 | 0.49 ± 0.30 | 0.51 ± 0.34 | 0.46 ± 0.26 | 0.28 |
| %MHC of SPL | 3.95 ± 1.71 | 3.70 ± 1.19 | 4.21 ± 2.09 | 0.08 |
| Sphingomyelins | | | | |
| C14:0 (nmol/ml) | 6.42 ± 2.16 | 6.42 ± 2.37 | 6.42 ± 1.94 | 0.99 |
| C16:0 (nmol/ml) | 24.9 ± 7.76 | 26.6 ± 6.09 | 23.3 ± 8.85 | 0.009 |
| C18:1 (nmol/ml) | 6.66 ± 2.66 | 7.40 ± 2.30 | 5.93 ± 2.81 | 0.009 |
| C18:0 (nmol/ml) | 7.86 ± 2.79 | 8.41 ± 2.39 | 7.31 ± 3.07 | 0.019 |
| C20:0 (nmol/ml) | 7.21 ± 2.53 | 7456 ± 2357 | 6957 ± 2679 | 0.24 |
| C22:0 (nmol/ml) | 12.3 ± 4.34 | 12.6 ± 3.95 | 12.0 ± 4.70 | 0.43 |
| C24:1 (nmol/ml) | 16.3 ± 5.56 | 17.1 ± 4.97 | 15.5 ± 6.02 | 0.09 |
| C24:0 (nmol/ml) | 8.92 ± 3.50 | 9.10 ± 3.66 | 8.73 ± 3.34 | 0.54 |
| C26:1 (pmol/ml) | 135 ± 54.9 | 137 ± 57.3 | 133 ± 52.7 | 0.66 |
| C26:0 (pmol/ml) | 44.7 ± 20.0 | 40.5 ± 18.4 | 49.0 ± 20.8 | 0.01 |
| C28:1 (pmol/ml) | 19.5 ± 7.90 | 20.7 ± 8.31 | 18.3 ± 7.32 | 0.07 |
| C28:0 (pmol/ml) | 40.7 ± 18.6 | 42.7 ± 20.3 | 38.7 ± 16.6 | 0.21 |
| C30:1 (pmol/ml) | 10.4 ± 4.16 | 10.9 ± 4.60 | 9.85 ± 3.62 | 0.12 |
| C30:0 (pmol/ml) | 8.14 ± 3.50 | 8.65 ± 3.46 | 7.62 ± 3.48 | 0.08 |
| C32:1 (pmol/ml) | 1.32 ± 0.66 | 1.43 ± 0.68 | 1.21 ± 0.62 | 0.04 |
| C32:0 (pmol/ml) | 2.37 ± 1.25 | 2.56 ± 1.17 | 2.18 ± 1.30 | 0.07 |
| C34:1 (pmol/ml) | 0.86 ± 0.40 | 0.86 ± 0.40 | 0.86 ± 0.41 | 0.95 |
| C34:0 (pmol/ml) | 1.08 ± 0.58 | 1.05 ± 0.62 | 1.11 ± 0.54 | 0.54 |
| Total SM (nmol/ml) | 90.8 ± 26.3 | 95.3 ± 23.0 | 86.3 ± 28.6 | 0.04 |

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|-----------------------------|-------------|-------------|-------------|---------|
| Total VLC (pmol/ml) | 84.4 ± 33.7 | 88.9 ± 36.6 | 79.9 ± 30.2 | 0.11 |
| SM ratios | | | | |
| C16:0/C18:0 | 3.30 ± 0.74 | 3.31 ± 0.79 | 3.29 ± 0.69 | 0.85 |
| C18:0/C18:1 | 1.22 ± 0.19 | 1.16 ± 0.17 | 1.28 ± 0.19 | 0.0002 |
| C24:0/C24:1 | 0.55 ± 0.12 | 0.53 ± 0.12 | 0.58 ± 0.12 | 0.008 |
| C26:0/C26:1 | 0.34 ± 0.10 | 0.30 ± 0.09 | 0.38 ± 0.10 | <0.0001 |
| %SM of SPL | 92.4 ± 2.56 | 93.2 ± 1.40 | 91.6 ± 3.15 | 0.0002 |
| Sphingosine(pmol/ml) | | | | |
| Dh-So (pmol/ml) | 89.9 ± 46.5 | 72.3 ± 37.5 | 108 ± 48.2 | <0.0001 |
| S1P (pmol/ml) | 10.8 ± 25.4 | 9.11 ± 9.85 | 12.5 ± 34.7 | 0.43 |
| S1P (pmol/ml) | 400 ± 171 | 398 ± 157 | 402 ± 186 | 0.88 |
| Dh-S1P (pmol/ml) | 65.5 ± 29.2 | 67.0 ± 31.4 | 64.1 ± 27.0 | 0.56 |

Cer, ceramides; Dh-So, dihydrosphingosine; MHC, monohexosyl ceramide (gluco- or galactosyl ceramide); S1P, sphingosine 1-phosphate; Dh-S1P, dihydrosphingosine 1-phosphate; SM, sphingomyelins; SPL, sphingolipids; VLC, very long chain species (C28-C34).