

## SUPPLEMENTAL MATERIALS

### Supplemental Tables

**Table S1. Sphingolipid absolute concentrations with standard deviations**

	Mean	SD	Minimum	Maximum
Cer-14	0.01	0.002	0.001	0.013
Cer-16	0.26	0.06	0.11	0.91
Cer-18	0.18	0.07	0.04	0.88
Cer-20	0.09	0.03	0.01	0.25
Cer-22	0.62	0.19	0.18	1.90
Cer-24	4.5	1.1	1.5	10.0
SM-14	36	11	6	100
SM-16	125	19	49	227
SM-18	38	10	13	129
SM-20	18	4	6	36
SM-22	27	6	10	63
SM-24	14	3	5	33
HexCer-16	0.19	0.07	0.05	0.69
HexCer-22	0.19	0.05	0.07	0.52
HexCer-24	0.17	0.05	0.05	0.50
LacCer-16	0.75	0.23	0.20	2.67
LacCer-24	0.09	0.03	0.02	0.45

All sphingolipid concentrations are given in  $\mu\text{M}$  units.

**Table S2. Baseline characteristics (ceramides)**

	Mean (SD)	Cer-14		Cer-16		Cer-18		Cer-20		Cer-22		Cer-24	
		Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4
Age, years	77 (5)		76, 77 +		76, 77		76, 77		76, 77 -		77, 76 -		77, 76
Sex, % male	41%	-	43, 36 -	-	43, 36 -	-	52, 31 -	-	49, 35	-	44, 39	-	39, 42
Race, % White	84%		82, 85 +		81, 86 -		93, 73 -		91, 78		85, 84		84, 85
Height, cm	165 (9)	-	165, 164 -	-	166, 164 -	-	167, 163 -	-	167, 163 -	-	166, 164	-	165, 165
Weight, lbs	167 (81)		171, 161		170, 165		163, 173		167, 169		165, 166		166, 167
HDL, mg/dL	53 (14)	+	51, 57 +	-	56, 51 -	-	55, 51 -	-	55, 51 -	-	57, 49 -	-	56, 50
LDL, mg/dL	128 (33)	+	120, 137 +	+	115, 139 +	+	119, 137 +	+	116, 137 +	+	112, 139 +	+	113, 141
Alcohol consumption, drinks/wk	2 (5)		2, 2		3, 2 -		3, 1 -		3, 1 -		3, 1		2, 2
Prevalent diabetes, %	19%	-	23, 15 +	+	16, 24 +	+	12, 27 +	+	14, 27 +	+	12, 28 +	+	14, 24
Never smoker, %	46%		44, 47		45, 45		44, 48		46, 46		47, 45 -		51, 44
Past smoker, %	44%		46, 42		46, 44 -		47, 41		45, 42		45, 44		41, 44
Current smoker, %	9%		8, 9 +	+	7, 10		8, 11		7, 11		6, 10 +	+	7, 10

+ indicates a significant positive trend across quartiles of sphingolipid levels. - indicates a significant negative trend across quartiles of sphingolipid levels. A blue line indicates a statistically significant positive trend in univariate analyses. A red line indicates a statistically significant negative trend in univariate analyses. A grey line indicates no significant trend.

**Table S3. Baseline characteristics (sphingomyelins)**

	Mean (SD)	SM-14		SM-16		SM-18		SM-20		SM-22		SM-24	
		Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4
Age, years	77 (5)		77, 76		76, 77 -		77, 76 -		78, 75 -		78, 75 -		78, 75
Sex, % male	41%	-	58, 29 -	-	52, 31 -	-	59, 24 -	-	56, 28 -	-	50, 30 -	-	43, 38
Race, % White	84%	+	75, 91 +		91, 72 -		95, 63 -		86, 80 -		89, 76 -		87, 79
Height, cm	165 (9)	-	167, 163 -	-	167, 163 -	-	167, 162 -	-	167, 163 -	-	166, 164	-	165, 165
Weight, lbs	167 (81)		172, 161		174, 163		169, 170		171, 165		168, 165		170, 165
HDL, mg/dL	53 (14)	+	49, 57 +	+	48, 59 +	+	50, 56 +	+	50, 57 +	+	51, 55 +	+	51, 56
LDL, mg/dL	128 (33)	+	113, 143 +	+	111, 143 +	+	114, 143 +	+	109, 144 +	+	109, 145 +	+	112, 143
Alcohol consumption, drinks/wk	2 (5)		2, 3		2, 2		2, 2		2, 2 -		2, 2 +		2, 2
Prevalent diabetes, %	19%	-	23, 17 -	-	24, 15		18, 20		21, 17		20, 19		22, 18
Never smoker, %	46%		45, 47		43, 47 +		43, 49		45, 47		47, 47		49, 44
Past smoker, %	44%		44, 43 -	-	49, 40 -	-	47, 40		45, 42		44, 42		43, 43
Current smoker, %	9%		10, 9		8, 11		9, 10		9, 9		7, 10 +	+	7, 11

+ indicates a significant positive trend across quartiles of sphingolipid levels. - indicates a significant negative trend across quartiles of sphingolipid levels. A blue line indicates a statistically significant positive trend in univariate analyses. A red line indicates a statistically significant negative trend in univariate analyses. A grey line indicates no significant trend.

**Table S4. Baseline characteristics (other sphingolipids)**

	Mean (SD)	GluCer-16		GluCer-22		GluCer-24		LacCer-16		LacCer-24	
		Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4	Trend	Q1, Q4
Age, years	77 (5)	+	76, 77		76, 77		76, 77 +		76, 77		77, 76
Sex, % male	41%	-	46, 38 -	+	39, 47 +	+	34, 48		43, 39		39, 39
Race, % White	84%	-	96, 68 -	-	88, 78 -	-	86, 79 -	-	91, 74 +	+	81, 86
Height, cm	165 (9)	-	166, 164 +	+	164, 166 +	+	164, 166		165, 165		165, 165
Weight, lbs	167 (81)		162, 171		168, 166		170, 169		165, 169		171, 162
HDL, mg/dL	53 (14)	+	52, 55		52, 53 +		52, 54 +		52, 55 +		50, 56
LDL, mg/dL	128 (33)	+	122, 136 +	+	118, 137 +	+	119, 136 +	+	121, 135 +	+	120, 134
Alcohol consumption, drinks/wk	2 (5)		2, 2		2, 2 +		2, 2 -		3, 2		2, 2
Prevalent diabetes, %	19%		19, 18		21, 16 -	-	22, 16		20, 17		20, 19
Never smoker, %	46%		46, 47		48, 43		48, 42		45, 49		47, 46
Past smoker, %	44%		45, 41		44, 45		43, 45		46, 41		44, 43
Current smoker, %	9%		8, 11		8, 11 +	+	8, 11		8, 9		9, 10

+ indicates a significant positive trend across quartiles of sphingolipid levels. - indicates a significant negative trend across quartiles of sphingolipid levels. A blue line indicates a statistically significant positive trend in univariate analyses. A red line indicates a statistically significant negative trend in univariate analyses. A grey line indicates no significant trend.

**Table S5. Sphingolipid association with FEV<sub>1</sub>**

	FEV <sub>1</sub> Difference	Lower 95%	Upper 95%	P-value
Cer-14	-0.042	-0.088	0.004	0.076
Cer-16	-0.071	-0.130	-0.012	0.018
Cer-18	-0.064	-0.098	-0.029	<0.001
Cer-20	-0.037	-0.078	0.004	0.074
Cer-22	-0.028	-0.076	0.019	0.245
Cer-24	-0.001	-0.058	0.057	0.986
SM-14	0.004	-0.047	0.054	0.886
SM-16	-0.138	-0.235	-0.041	0.006
SM-18	-0.094	-0.153	-0.035	0.002
SM-20	0.033	-0.039	0.106	0.370
SM-22	-0.050	-0.118	0.017	0.144
SM-24	-0.033	-0.092	0.025	0.266
HexCer-16	-0.007	-0.045	0.031	0.715
HexCer-22	0.004	-0.043	0.051	0.862
HexCer-24	0.007	-0.042	0.055	0.793
LacCer-16	0.009	-0.033	0.052	0.664
LacCer-24	-0.019	-0.059	0.022	0.370

Association of two-fold higher sphingolipid levels with FEV<sub>1</sub> (in liters). Analyses adjusted for age, race, sex, clinic site, height and weight, LDL and HDL cholesterol, weekly alcohol intake, diabetic status, smoker status, and pack-years smoked.

**Table S6. Sphingolipid association with COPD**

	Odds Ratio	Lower 95%	Upper 95%	P-value
Cer-14	1.447	1.039	2.014	0.029
Cer-16	1.300	0.881	1.918	0.187
Cer-18	1.294	1.025	1.632	0.030
Cer-20	1.207	0.923	1.578	0.169
Cer-22	1.226	0.905	1.661	0.188
Cer-24	1.439	0.996	2.077	0.052
SM-14	1.497	1.068	2.098	0.019
SM-16	2.054	1.069	3.949	0.031
SM-18	1.731	1.151	2.602	0.008
SM-20	1.039	0.644	1.677	0.875
SM-22	1.152	0.740	1.794	0.531
SM-24	1.159	0.784	1.715	0.459
HexCer-16	1.117	0.867	1.440	0.393
HexCer-22	1.167	0.859	1.587	0.324
HexCer-24	1.327	0.959	1.836	0.088
LacCer-16	0.953	0.708	1.282	0.751
LacCer-24	0.908	0.685	1.204	0.504

Association of two-fold higher sphingolipid levels with odds of COPD. Analyses adjusted for age, race, sex, clinic site, height and weight, LDL and HDL cholesterol, weekly alcohol intake, diabetic status, smoker status, and pack-years smoked.

**Table S7. Cer-18 and SM-18 co-adjusted model: FEV<sub>1</sub>**

	Association with FEV <sub>1</sub>				Co-adjusted association with FEV <sub>1</sub>			
	Beta	Lower 95%	Upper 95%	P-value	Beta	Lower 95%	Upper 95%	P-value
Cer-18	-0.061	-0.096	-0.026	0.001	-0.046	-0.093	0.002	0.059
SM-18	-0.092	-0.151	-0.033	0.002	-0.036	-0.117	0.045	0.383

Panel on the left shows individual associations of Cer-18 and SM-18 with FEV<sub>1</sub> levels adjusted for age, race, sex, clinic site, height and weight, LDL and HDL cholesterol, weekly alcohol intake, diabetic status, smoker status, and pack-years smoked. Panel on the right shows association of Cer-18 and SM-18 with FEV<sub>1</sub> levels when both sphingolipids are included in the same model.

**Table S8. Interaction of select sphingolipids with smoking, age, race, and sex for association with FEV<sub>1</sub>**

	Interaction with smoking (former vs never), P=	Interaction with smoking (current vs never), P=	Interaction with age, P=	Interaction with race, P=	Interaction with sex, P=
Cer-16	0.547	0.760	0.207	0.324	0.353
Cer-18	0.207	0.153	0.083	0.610	0.092
SM-16	0.349	0.205	0.291	0.537	0.331
SM-18	0.641	0.130	0.115	0.944	0.039

**Table S9. Interaction of select sphingolipids with smoking, age, race, and sex for association with odds of COPD**

	Interaction with smoking (former vs never), P=	Interaction with smoking (current vs never), P=	Interaction with age, P=	Interaction with race, P=	Interaction with sex, P=
Cer-14	0.174	0.224	0.438	0.649	0.013
Cer-18	0.975	0.191	0.386	0.727	0.476
SM-14	0.959	0.459	0.405	0.188	0.479
SM-16	0.203	0.041	0.253	0.311	0.824
SM-18	0.585	0.717	0.822	0.164	0.692

## Supplemental Figures

**Figure S1. Correlation matrix for various sphingolipid species**

