

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Spearman's correlation matrix among plasma ceramides, plasma LRG1 and other clinical/metabolic parameters.

	Cer(d18:1/16:0)	Cer(d18:1/18:0)	Cer(d18:1/20:0)	Cer(d18:1/22:0)	Cer(d18:1/24:0)	Cer(d18:1/24:1)	LRG1	Age	BMI	Cholesterol	HOMA-IR	HbA1c	PAS	hsCRP	NEFA
Cer(d18:1/16:0)	1.00														
Cer(d18:1/18:0)	0.63**	1.00													
Cer(d18:1/20:0)	0.67**	0.87**	1.00												
Cer(d18:1/22:0)	0.62**	0.48**	0.64**	1.00											
Cer(d18:1/24:0)	0.57**	0.32**	0.47**	0.86**	1.00										
Cer(d18:1/24:1)	0.67**	0.54**	0.65**	0.47**	0.37**	1.00									
LRG1	0.29**	0.25**	0.22*	0.10	0.06	0.43**	1.00								
Age	-0.05	-0.14	-0.07	-0.22*	-0.15	0.09	0.11	1.00							
BMI	0.09	0.11	0.10	0.06	-0.05	0.16	0.13	-0.12	1.00						
Cholesterol	0.45**	0.30**	0.28**	0.45**	0.52**	0.34**	0.12	-0.14	0.10	1.00					
HOMA-IR	-0.01	0.13	0.18	0.26**	0.14	0.03	0.05	0.01	0.37**	0.05	1.00				
HbA1c	-0.18	-0.07	-0.09	0.08	0.03	-0.19	-0.14	0.01	0.11	-0.16	0.30**	1.00			
PAS	0.10	0.03	0.03	-0.07	-0.11	0.16	0.22*	0.23*	0.16	0.12	-0.03	0.09	1.00		
hs-CRP	0.36**	0.23*	0.22*	0.26**	0.23*	0.37**	0.22*	-0.19	0.27**	0.23*	0.18	0.08	0.02	1.00	
NEFA	0.05	0.03	0.01	0.07	0.02	0.10	0.04	0.17	0.15	0.12	0.04	0.18	0.16	0.01	1.00

Sample size, $n=99$. Data are expressed as Spearman's rho correlation coefficients. For the sake of clarity, significant p-values are highlighted in bold.

* P -value <0.05 ; ** P -value <0.01

Supplementary Table S2. Forward stepwise linear regression analyses: independent predictors of different plasma ceramide concentrations in post-menopausal women with T2DM.

Forward stepwise linear regression analysis	β coefficients (95% confidence intervals)	P-values
Log Cer(d18:1/16:0)		
Forward-stepwise selection procedure $p = 0.0001$ (<0.05) adding total cholesterol $p = 0.0076$ (<0.05) adding LRG1		
Total cholesterol (mg/dl)	0.003 (0.002-0.004)	<0.001
LRG1 (1 st tertile vs. 2 nd and 3 rd tertiles combined)	0.101 (0.027-0.175)	0.008
Log Cer(d18:1/18:0)		
Forward-stepwise selection procedure $p = 0.0022$ (<0.05) adding LRG1 $p = 0.0057$ (<0.05) adding total cholesterol		
LRG1 (1 st tertile vs. 2 nd and 3 rd tertiles combined)	0.214 (0.068-0.359)	0.004
Total cholesterol (mg/dl)	0.003 (0.001-0.005)	0.006
Log Cer(d18:1/20:0)		
Forward-stepwise selection procedure $p = 0.0036$ (<0.05) adding total cholesterol $p = 0.0193$ (<0.05) adding LRG1		
Total cholesterol (mg/dl)	0.002 (0.001-0.005)	0.007
LRG1 (1 st tertile vs. 2 nd and 3 rd tertiles combined)	0.167 (0.027-0.306)	0.019
Log Cer(d18:1/22:0)		
Forward-stepwise selection procedure $p = 0.0001$ (<0.05) adding total cholesterol $p = 0.0023$ (<0.05) adding HOMA-IR score		
Total cholesterol (mg/dl)	0.005 (0.004-0.007)	<0.001
Log HOMA-IR score	0.115 (0.04-0.187)	0.002
Log Cer(d18:1/24:0)		
Forward-stepwise selection procedure $p = 0.0001$ (<0.05) adding total cholesterol $p = 0.0147$ (<0.05) adding HbA1c		
Total cholesterol (mg/dl)	0.004 (0.003-0.006)	<0.001
HbA1c (%)	0.084 (0.017-0.151)	0.015
Log Cer(d18:1/24:1)		
Forward-stepwise selection procedure $p = 0.0002$ (<0.05) adding total cholesterol $p = 0.0011$ (<0.05) adding LRG1		
Total cholesterol (mg/dl)	0.004 (0.002-0.006)	<0.001
LRG1 (1 st tertile vs. 2 nd and 3 rd tertiles combined)	0.241 (0.099-0.382)	0.001

Sample size, $n=99$. Data are expressed as beta coefficients and 95% confidence intervals (in parenthesis) as tested by forward-stepwise selection linear regression analysis. Each plasma ceramide (logarithmically transformed before statistical analysis) was the dependent variable in each forward-stepwise selection linear regression model. The significance level for addition to the model was p -value <0.05. Covariates included in the forward-stepwise selection linear regression models were: LRG1 (1st tertile vs. 2nd and 3rd tertiles combined), age, BMI, HbA1c, total cholesterol level, HOMA-estimated insulin resistance, systolic blood pressure and statin use.

Abbreviations: Cer, ceramides; HOMA-IR, homeostasis model assessment-insulin resistance; Log, logarithmic; LRG1, leucine-rich- α 2 glycoprotein 1.