Supplementary Material

Title: Serum proteins associated with LDL-C and non-HDL-C reduction in response to dietary interventions in the DASH and DASH-Sodium trials

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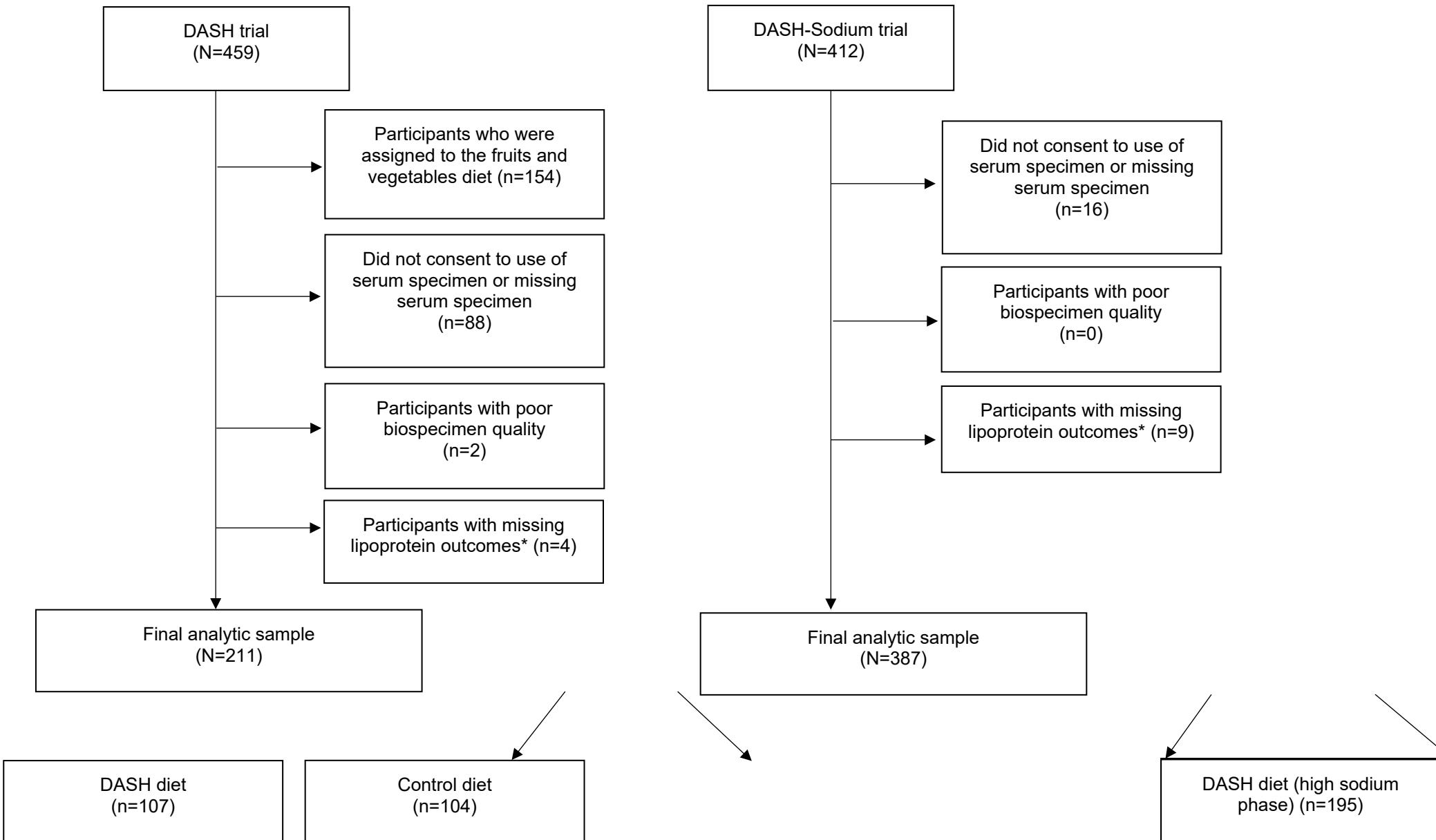
Supplemental Figure 1. Flow diagram of study participants in the DASH and the DASH-Sodium trials. *Lipid outcomes include low-density lipoprotein-cholesterol and non-high-density lipoprotein (HDL)-C levels.
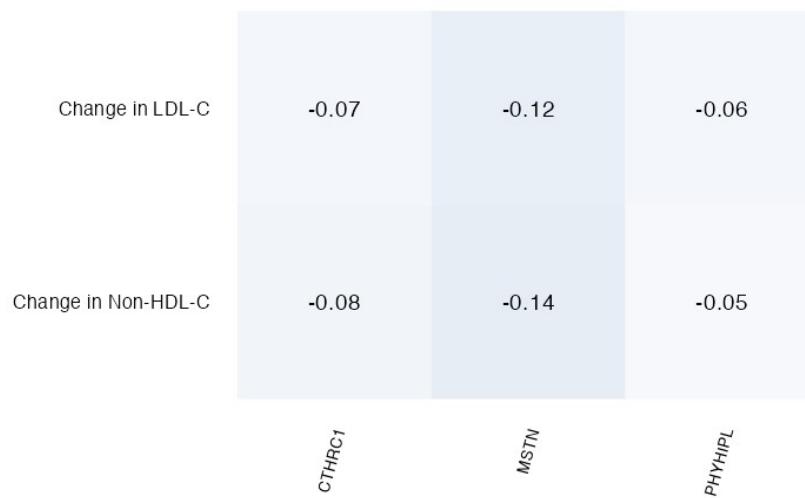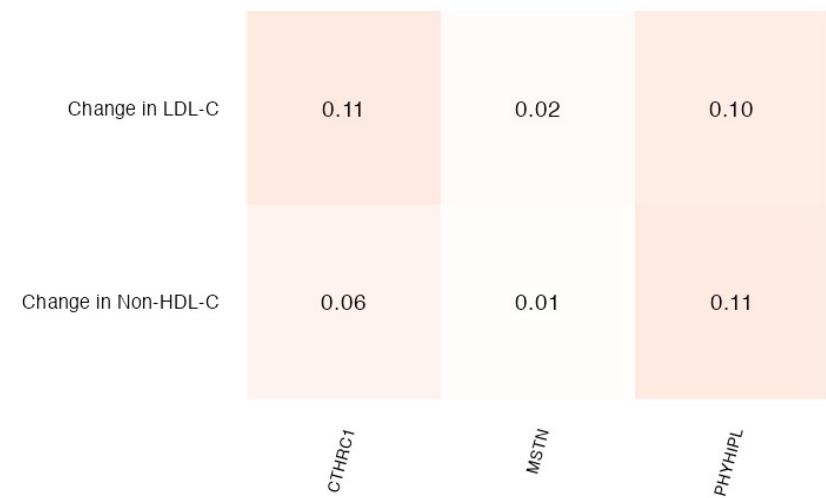
Supplemental Figure 2. Correlation matrix for the association between relative abundances of collagen triple helix repeat-containing protein 1 (CTHRC1), growth differentiation factor 8 (MSTN), and phytanoyl-CoA hydroxylase-interacting protein-like (PHYHIPL), measured at the end of the diet interventions (DASH or control diets) and change in low-density lipoprotein (LDL)-cholesterol (C) and non-high-density lipoprotein (HDL)-C from baseline to end-of-study after pooling data the DASH and DASH-Sodium trials. The correlation matrices are stratified by diet interventions (DASH vs. control diets). No covariate was adjusted.
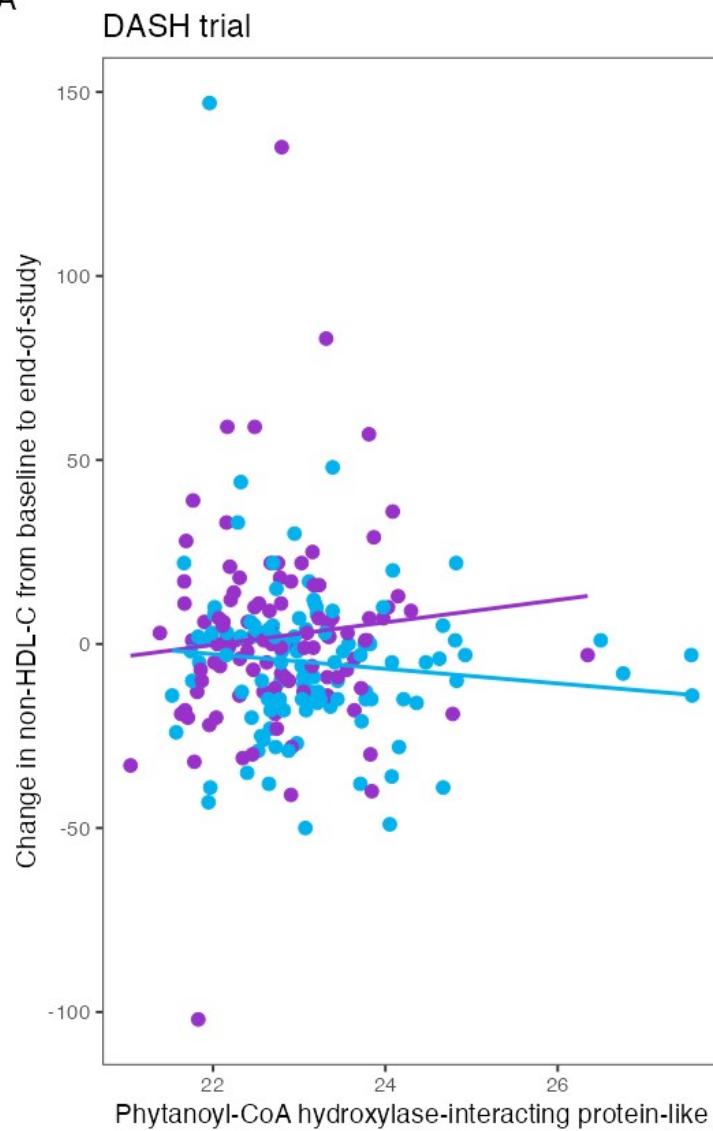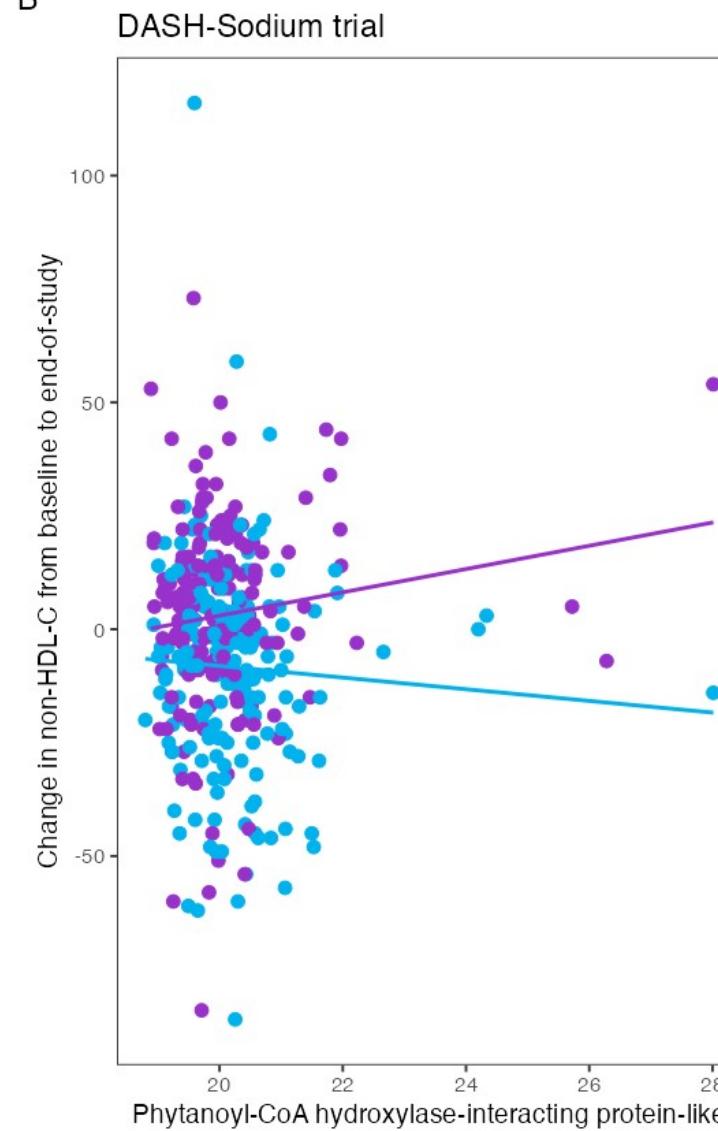
Supplemental Figure 3. Scatterplots for the association between relative abundances of phytanoyl-CoA hydroxylase-interacting protein-like (PHYHIPL) measured at the end of the diet interventions (DASH or control diets) and non-high-density lipoprotein (HDL)-cholesterol (C) from baseline to end-of-study, stratified by DASH and DASH-Sodium trials. Trend lines were added to visually describe the association between PHYHIPL and change in non-HDL-C by diet interventions. Covariates were not adjusted.

Supplemental Table 1. Associations between DASH diet and non-high-density lipoprotein (HDL)-C levels [1]

	Mean (standard deviation) of non-HDL-C					
	DASH (N=305)			DASH-Sodium (N=412)		
	DASH diet (N=151)	Control diet (N=154)	P value	DASH-high Na (N=208)	Control-high Na (N=204)	P value
Non-HDL-C	-5.98 (21.4)	3.37 (23.6)	<0.001	-8.57 (23.3)	3.12 (21.1)	<0.001

[1] In the full DASH and DASH-Sodium trial participants, two-way analysis of variance was conducted, adjusting for clinical site as an indicator variable according to intention-to-treat analysis. This analysis method is the same as what was reported in the original trials[1,2]

[1] Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER, Lin PH, Karanja NM, Most-Windhauser MM, Moore TJ, Swain JF, Bales CW, Proschan MA, DASH Research Group. Effects on blood lipids of a blood pressure-lowering diet: the Dietary Approaches to Stop Hypertension (DASH) Trial. *Am J Clin Nutr*. 2001;74:80–89.
[2] Harsha DW, Sacks FM, Obarzanek E, Svetkey LP, Lin P-H, Bray GA, Aickin M, Conlin PR, Miller ER, Appel LJ. Effect of Dietary Sodium Intake on Blood Lipids. *Hypertension*. 2004;43:393–398.

Supplemental Table 2. Participant characteristics of the DASH and DASH-Sodium trials, stratified by low-density lipoprotein (LDL)-cholesterol levels[1]

	DASH trial			DASH-Sodium trial		
	LDL-C <130 mg/dL (N=126)	LDL-C ≥130 mg/dL (N=85)	P-value	LDL-C <130 mg/dL (N=190)	LDL-C ≥130 mg/dL (N=197)	P-value
Age, %			0.07			0.008
≤30 y	17 (13.5%)	9 (10.6%)		9 (4.7%)	3 (1.5%)	
31-50 y	75 (59.5%)	40 (47.1%)		121 (63.7%)	105 (53.3%)	
≥51 y	34 (27.0%)	36 (42.4%)		60 (31.6%)	89 (45.2%)	
Women, %	64 (50.8%)	36 (42.4%)	0.29	112 (58.9%)	110 (55.8%)	0.61
Race or ethnicity, %			0.90			0.99
African American	72 (57.1%)	47 (55.3%)		109 (57.4%)	113 (57.4%)	
Income, %			0.84			
<$29,999	42 (33.3%)	27 (31.8%)		57 (30.0%)	66 (33.5%)	0.40
$30,000-$59,999	58 (46.0%)	36 (42.4%)		75 (39.5%)	66 (33.5%)	
≥$60,000	26 (20.6%)	20 (23.5%)		52 (27.4%)	62 (31.5%)	
Not Answered	0 (0%)	2 (2.4%)		6 (3.2%)	3 (1.5%)	
Education, %			0.34			0.37
High school graduate or less	18 (14.3%)	13 (15.3%)		26 (13.7%)	39 (19.8%)	
Some College	43 (34.1%)	34 (40.0%)		75 (39.5%)	66 (33.5%)	
College graduate	41 (32.5%)	18 (21.2%)		45 (23.7%)	45 (22.8%)	
Post graduate work/degree	24 (19.0%)	20 (23.5%)		44 (23.2%)	46 (23.4%)	
Current smoker, %	11 (8.7%)	5 (5.9%)	0.45	20 (10.5%)	20 (10.2%)	0.94
Weight (kg)	81.5 (15.0)	84.5 (14.6)	0.15	83.9 (15.2)	84.1 (15.4)	0.87
Height (kg)	170 (8.73)	172 (9.46)	0.16	170 (8.63)	169 (9.74)	0.20
Body mass index, kg/m^2	28.0 (3.92)	28.5 (3.88)	0.33	28.9 (4.74)	29.4 (4.79)	0.29
Systolic blood pressure, mm Hg	130 (10.8)	131 (10.2)	0.50	135 (10.1)	134 (8.96)	0.54
Diastolic blood pressure, mm Hg	84.8 (4.84)	84.3 (3.78)	0.37	85.5 (4.69)	85.7 (4.29)	0.65
Hypertension, %	63 (50.0%)	33 (38.8%)	0.15	92 (48.4%)	83 (42.1%)	0.25
Total cholesterol, mg/dL	170.5 (27.4)	221.4 (21.5)	<0.001	175.6 (23.2)	225.8 (24.5)	<0.001
Low-density lipoprotein-cholesterol, mg/dL	99.3 (22.5)	149.0 (16.4)	<0.001	106.6 (16.7)	155.1 (19.2)	<0.001
High-density lipoprotein-cholesterol, mg/dL	49.5 (16.3)	47.8 (15.6)	0.433	49.5 (14.4)	47.9 (11.1)	0.23

Non-high-density lipoprotein-cholesterol, mg/dL	121.0 (26.0)	174.0 (18.2)	<0.001	126.0 (21.7)	178.0 (23.0)	<0.001
Triacylglycerols, mg/dL	108.4 (56.9)	121.1 (55.6)	0.11	97.8 (59.0)	114.0 (54.9)	0.005

[1] Values are mean (standard deviation) for continuous variables and n (proportions) for categorical variables.

[2] Hypertension was defined as doctor diagnosis of high blood pressure.

Supplemental Table 2. Associations between DASH diet-related proteins and change in low-density lipoprotein (LDL)-cholesterol (C) and non-high-density lipoprotein (HDL)-C levels [1]

UniProt ID	Entrez gene symbol	Protein name	DASH diets		Control diets		P for interaction
			beta	P value	beta	P value	
LDL-C (n=2)							
Q96CG8	CTHRC1	Collagen triple helix repeat-containing protein 1	-1.758	1.77E-01	3.469	1.70E-02	0.014
O14793	MSTN	Growth/differentiation factor 8	-3.693	1.47E-02	0.201	8.86E-01	0.042
non-HDL-C (n=1)							
Q96FC7	PHYHIPL	Phytanoyl-CoA hydroxylase-interacting protein-like	-2.029	1.40E-01	2.777	3.79E-02	0.049

[1] Multivariable linear regression models with cross-product terms between diet and 71 DASH diet-related proteins (per 1-SD higher) were used to identify proteins that were differentially associated by diet interventions (DASH vs. control). Models were performed in each study and by dietary interventions (DASH vs. control), and were adjusted for age, sex, race/ethnicity and measured baseline body mass index (BMI). Meta-analyses using fixed effects models were conducted across the DASH and DASH-Sodium trials. Only the proteins with P for interaction <0.05 are presented.

Supplemental Table 3. Proteins selected from elastic net linear regression models to predict change in low-density lipoprotein (LDL)-cholesterol (C) and non-high-density lipoprotein (HDL)-C levels[1]

UniProt ID	Entrez gene symbol	Protein name	β	P value
LDL-C (n=3)				
Q99536	VAT1	Synaptic vesicle membrane protein VAT-1 homolog	4.66	1.33E-05
Q9Y279	VSIG4	V-set and immunoglobulin domain-containing protein 4	-4.14	1.20E-04
P04114	APOB	Apolipoprotein B	4.01	2.22E-02
non-HDL-C (n=3)				
Q99536	VAT1	Synaptic vesicle membrane protein VAT-1 homolog	4.81	1.41E-05
Q9Y279	VSIG4	V-set and immunoglobulin domain-containing protein 4	-5.26	1.62E-06
P04114	APOB	Apolipoprotein B	4.86	1.16E-05

[1] A set of proteins that predict change in LDL-C, total cholesterol, and non-HDL was selected from elastic net regression models. As tuning parameters, lambda.1se (sparsity of the model) and α=0.5 (relative weights of ridge and lasso regression models) were selected. All 71 DASH diet-related proteins were considered for elastic net models. β coefficients and P values represent joint associations between the set of proteins for the change in LDL-C and non-HDL-C. No protein was selected for change in LDL-C or non-HDL-C in the DASH trial.

Supplemental Table 4. Associations between DASH diet-related proteins and change in low-density lipoprotein (LDL)-cholesterol (C) and non-high-density lipoprotein (HDL)-C levels, adjusting for corresponding lipids at baseline[1]

UniProt ID	Entrez gene symbol	Protein name	DASH diets		Control diets		P for interaction
			beta	P value	beta	P value	
LDL-C (n=2)							
Q96CG8	CTHRC1	Collagen triple helix repeat-containing protein 1	-1.758	1.77E-01	3.469	1.70E-02	0.066
O14793	MSTN	Growth/differentiation factor 8	-3.693	1.47E-02	0.201	8.86E-01	0.054
non-HDL-C (n=1)							
Q96FC7	PHYHIPL	Phytanoyl-CoA hydroxylase-interacting protein-like	-2.067	9.57E-02	2.414	5.40E-02	0.043

[1] Multivariable linear regression models with cross-product terms between diet and 71 DASH diet-related proteins (per 1-SD higher) were used to identify proteins that were differentially associated by diet interventions (DASH vs. control). Models were performed in each study and by dietary interventions (DASH vs. control), and were adjusted for age, sex, race/ethnicity, measured baseline body mass index (BMI), and corresponding lipoprotein levels at baseline. Meta-analyses using fixed effects models were conducted across the DASH and DASH-Sodium trials.