

**Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham
Heart Study
Walker et al**

Online Supplementary Material

Supplementary Figure 1. Participant flow diagram

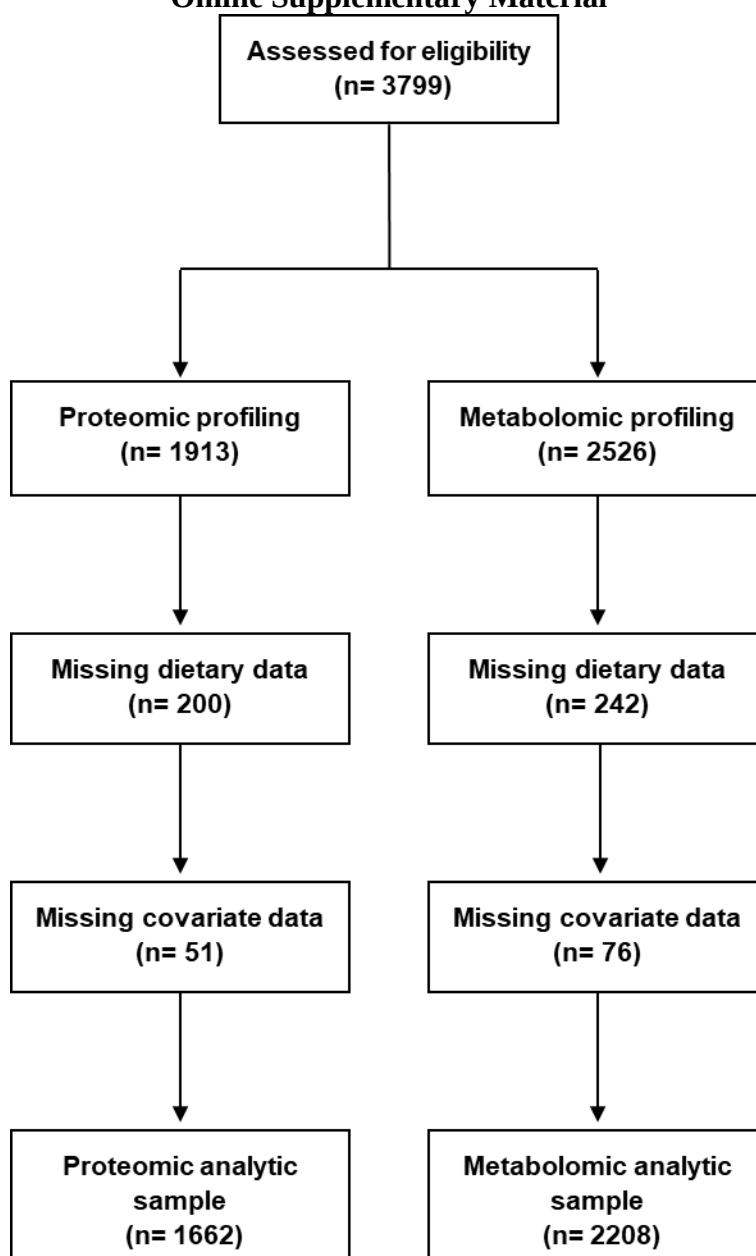
Supplementary Table 1. Statistically significant associations of dietary patterns with plasma protein concentrations

Supplementary Table 2. Statistically significant associations of dietary patterns with plasma metabolite concentrations

Supplementary Table 3. Pathway over representation analysis of protein markers associated with the AHEI and DASH dietary pattern indices

Supplementary Table 4. KEGG pathway mapping of metabolites associated with dietary pattern indices

**Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham
Heart Study
Walker et al
Online Supplementary Material**



Supplementary Figure 1. Participant flow diagram of the study sample. Among the 3799 participants who attended the fifth examination cycle of the Framingham Offspring Cohort, 1913 participants had blood proteomic profiling completed and 2526 participants had metabolomic profiling completed and were considered eligible for the present investigation. We excluded participants with missing dietary data from each respective analytical sample.

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al

Online Supplementary Material

Supplementary Table 1. Statistically significant associations of dietary patterns with plasma protein concentrations¹

		AHEI			DASH			MDS		
Label	Diet ²	β^3	SE	FDR ⁴	β	SE	FDR	β	SE	FDR
14-3-3	AHEI	-0.078	0.024	0.044	-0.044	0.025	0.321	-0.046	0.026	0.534
AK1A1	AHEI, DASH	-0.090	0.024	0.013	-0.092	0.025	0.008	-0.045	0.026	0.570
AMPM2	DASH	-0.060	0.023	0.131	-0.074	0.024	0.032	-0.047	0.025	0.490
Antithrombin III	AHEI	0.093	0.021	0.001	0.063	0.022	0.053	0.053	0.023	0.379
Apoptosis regulator Bcl-W	AHEI	-0.111	0.033	0.034	-0.082	0.033	0.107	-0.063	0.035	0.529
ATS13	DASH	0.065	0.024	0.105	0.089	0.024	0.009	0.056	0.025	0.395
bFGF-R	AHEI, DASH	0.092	0.023	0.004	0.107	0.023	0.001	0.076	0.024	0.125
BMPR1A	DASH	0.065	0.024	0.111	0.086	0.024	0.013	0.044	0.025	0.555
C1s	DASH	-0.049	0.022	0.194	-0.073	0.022	0.024	-0.047	0.023	0.446
C3a	AHEI	-0.082	0.023	0.020	-0.032	0.023	0.488	-0.035	0.025	0.682
Cadherin-5	DASH	0.034	0.024	0.478	0.081	0.025	0.024	0.042	0.026	0.605
Calpastatin	DASH	0.045	0.023	0.280	0.069	0.023	0.050	0.035	0.024	0.683
Carbonic anhydrase 6	AHEI, DASH	0.095	0.023	0.004	0.108	0.023	0.001	0.085	0.025	0.069
Cathepsin D	AHEI, DASH	-0.103	0.031	0.042	-0.097	0.031	0.040	-0.072	0.033	0.410
Cathepsin S	MDS	-0.067	0.025	0.114	-0.073	0.026	0.058	-0.099	0.027	0.046
CDC37	DASH	-0.058	0.024	0.178	-0.078	0.025	0.035	-0.067	0.026	0.276
CNDP1	AHEI, DASH	0.137	0.024	0.000	0.105	0.025	0.002	0.085	0.026	0.100
contactin-1	DASH	0.053	0.023	0.178	0.092	0.023	0.003	0.084	0.024	0.068
Contactin-4	DASH	0.051	0.024	0.230	0.112	0.024	0.001	0.075	0.025	0.158
CRP	DASH	-0.056	0.023	0.167	-0.075	0.023	0.027	-0.056	0.024	0.379
Cyclophilin A	AHEI	-0.077	0.024	0.048	-0.061	0.025	0.121	-0.055	0.026	0.427

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Discoidin domain receptor	AHEI, DASH	0.076	0.024	0.049	0.075	0.025	0.044	0.056	0.026	0.408
DKK3	DASH	0.062	0.023	0.109	0.090	0.023	0.005	0.067	0.024	0.202
dopa decarboxylase	AHEI	0.078	0.024	0.042	0.055	0.025	0.174	0.034	0.026	0.728
eIF-5A-1	DASH	-0.063	0.025	0.145	-0.092	0.025	0.010	-0.061	0.026	0.379
Elafin	DASH	-0.055	0.024	0.197	-0.083	0.025	0.020	-0.085	0.026	0.100
ERBB1	AHEI, DASH, MDS	0.133	0.022	0.000	0.127	0.023	0.000	0.111	0.024	0.004
Esterase D	DASH	-0.058	0.025	0.184	-0.090	0.025	0.011	-0.039	0.026	0.659
FABPE	AHEI	-0.078	0.024	0.042	-0.062	0.025	0.101	-0.039	0.026	0.649
Factor H	DASH	-0.042	0.021	0.280	-0.066	0.022	0.042	-0.043	0.023	0.483
FAM107B	DASH	-0.041	0.023	0.344	-0.080	0.023	0.018	-0.031	0.025	0.741
Ferritin	DASH	-0.083	0.030	0.106	-0.121	0.030	0.003	-0.059	0.032	0.511
FETUB	DASH	0.065	0.024	0.106	0.084	0.024	0.014	0.049	0.025	0.483
Galectin-3	AHEI, DASH	0.101	0.023	0.001	0.073	0.024	0.039	0.076	0.025	0.142
GAPDH, liver	DASH	-0.047	0.025	0.292	-0.081	0.025	0.027	-0.050	0.026	0.488
Glypican 3	DASH	0.057	0.024	0.178	0.109	0.024	0.001	0.070	0.025	0.198
hnRNP A/B	DASH	-0.054	0.023	0.184	-0.099	0.024	0.003	-0.042	0.025	0.605
hnRNP A2/B1	AHEI, DASH	-0.082	0.024	0.032	-0.099	0.025	0.003	-0.056	0.026	0.408
HSP 90a/b	AHEI, DASH	-0.092	0.024	0.013	-0.090	0.025	0.011	-0.056	0.026	0.408
iC3b	AHEI	-0.071	0.023	0.048	-0.029	0.023	0.536	-0.052	0.024	0.410
IgD	DASH	-0.050	0.025	0.267	-0.087	0.025	0.018	-0.061	0.027	0.379
IGFBP-1	DASH	0.024	0.021	0.593	0.086	0.021	0.003	0.042	0.022	0.487
IL-5 Ra	AHEI, DASH	0.079	0.025	0.047	0.077	0.026	0.044	0.077	0.027	0.167
JAG1	DASH	0.036	0.024	0.436	0.090	0.024	0.008	0.055	0.025	0.408

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

KYNU	AHEI, DASH, MDS	-0.127	0.024	0.000	-0.153	0.024	0.000	-0.112	0.026	0.005
LRIG3	AHEI, DASH	0.114	0.024	0.001	0.087	0.025	0.013	0.069	0.026	0.238
LSAMP	DASH	0.052	0.020	0.146	0.069	0.021	0.022	0.046	0.022	0.412
MDHC	DASH	-0.060	0.024	0.158	-0.099	0.025	0.003	-0.055	0.026	0.421
MED-1	AHEI, DASH	0.104	0.032	0.042	0.109	0.032	0.016	0.075	0.025	0.390
MET	AHEI, DASH	0.102	0.023	0.001	0.096	0.024	0.003	0.050	0.025	0.449
MFGM	AHEI, DASH	0.086	0.024	0.021	0.077	0.025	0.039	0.052	0.026	0.473
MIC-1	AHEI, DASH	-0.091	0.028	0.044	-0.087	0.028	0.040	-0.072	0.030	0.346
MIF	AHEI, DASH, MDS	-0.098	0.024	0.004	-0.119	0.024	0.000	-0.106	0.026	0.011
MMP-2	AHEI, DASH	0.076	0.024	0.044	0.117	0.024	0.000	0.074	0.025	0.167
Myokinase, human	DASH	-0.050	0.025	0.262	-0.099	0.025	0.004	-0.049	0.026	0.498
NCAM-120	DASH	0.049	0.022	0.206	0.070	0.022	0.035	0.068	0.023	0.158
NEGR1	DASH	0.066	0.031	0.231	0.094	0.031	0.044	0.075	0.033	0.386
Notch 1	AHEI, DASH	0.098	0.023	0.001	0.113	0.023	0.000	0.069	0.024	0.167
NRX3B	AHEI	0.089	0.024	0.013	0.071	0.024	0.053	0.062	0.026	0.319
PAI-1	DASH	-0.043	0.022	0.282	-0.067	0.023	0.050	-0.014	0.024	0.906
PARC	DASH	-0.071	0.023	0.061	-0.080	0.024	0.019	-0.068	0.025	0.208
PCI	AHEI	0.086	0.023	0.015	0.045	0.024	0.288	0.040	0.025	0.609
PD-L2	AHEI, DASH	0.083	0.024	0.032	0.074	0.025	0.049	0.041	0.026	0.609

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Peroxiredoxin-1	DASH	-0.068	0.024	0.099	-0.113	0.025	0.001	-0.077	0.026	0.158
Peroxiredoxin-6	AHEI	-0.078	0.024	0.044	-0.067	0.025	0.071	-0.052	0.026	0.449
PGCB	AHEI, DASH	0.071	0.022	0.044	0.075	0.023	0.021	0.053	0.024	0.386
PGM1	AHEI	-0.116	0.033	0.021	-0.025	0.033	0.761	-0.050	0.035	0.683
P-Selectin	MDS	-0.044	0.024	0.317	-0.060	0.025	0.124	-0.094	0.026	0.048
PLPP	AHEI, DASH	-0.079	0.025	0.047	-0.094	0.025	0.008	-0.065	0.027	0.323
PolyUbiquitin K48	DASH	-0.034	0.031	0.604	-0.104	0.030	0.018	-0.073	0.033	0.386
prostatic binding protein	DASH	-0.046	0.024	0.288	-0.101	0.024	0.003	-0.042	0.026	0.605
PSA1	AHEI	-0.074	0.023	0.044	-0.063	0.024	0.081	-0.031	0.025	0.744
Rab GDP dissociation inhi	DASH	-0.072	0.024	0.065	-0.089	0.025	0.011	-0.054	0.026	0.429
RBP	DASH	0.087	0.032	0.112	0.095	0.032	0.050	0.084	0.034	0.318
RGMA	AHEI, DASH	0.103	0.031	0.042	0.098	0.031	0.035	0.067	0.033	0.449
RGMB	DASH	0.059	0.024	0.156	0.073	0.024	0.044	0.049	0.025	0.483
RGM-C	AHEI, DASH	0.090	0.024	0.013	0.105	0.025	0.002	0.088	0.026	0.070
SCF sR	AHEI	0.079	0.022	0.021	0.058	0.023	0.106	0.047	0.024	0.482
sE-Selectin	DASH	-0.063	0.024	0.117	-0.089	0.024	0.009	-0.082	0.025	0.100
sICAM-5	MDS	-0.040	0.023	0.364	-0.057	0.024	0.125	-0.089	0.025	0.048
SLAF6	DASH	-0.072	0.023	0.055	-0.076	0.024	0.028	-0.080	0.025	0.107
SNAA	DASH	-0.058	0.025	0.184	-0.081	0.025	0.028	-0.035	0.026	0.726
Stanniocalcin-1	AHEI, DASH, MDS	-0.108	0.024	0.001	-0.103	0.024	0.002	-0.111	0.025	0.005
STAT6	AHEI	-0.107	0.033	0.044	-0.052	0.034	0.407	-0.064	0.036	0.526
sTie-1	DASH	0.075	0.024	0.055	0.099	0.025	0.003	0.066	0.026	0.291
sTie-2	DASH	0.062	0.025	0.150	0.081	0.025	0.027	0.066	0.026	0.311
TAFI	AHEI	0.083	0.024	0.028	0.037	0.025	0.420	0.060	0.026	0.361
TECK	DASH	-0.020	0.025	0.713	-0.099	0.025	0.004	-0.070	0.026	0.250

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

TIG2	DASH	-0.068	0.022	0.055	-0.090	0.022	0.003	-0.081	0.023	0.069
tPA	DASH	-0.048	0.022	0.206	-0.101	0.022	0.001	-0.068	0.023	0.158
Transferrin	AHEI, DASH	0.127	0.022	0.000	0.083	0.023	0.011	0.068	0.024	0.181
Transketolase	DASH	-0.070	0.025	0.089	-0.084	0.025	0.020	-0.043	0.026	0.605
TrATPase	DASH	-0.048	0.021	0.203	-0.067	0.022	0.040	-0.036	0.023	0.609
Triosephosphate isomerase	DASH	-0.065	0.025	0.117	-0.083	0.025	0.024	-0.042	0.026	0.609
TrkB	DASH	0.068	0.024	0.101	0.090	0.025	0.010	0.061	0.026	0.370
TrkC	AHEI, DASH	0.073	0.023	0.048	0.076	0.024	0.029	0.061	0.025	0.318
TSP2	AHEI, DASH	-0.112	0.024	0.001	-0.087	0.025	0.014	-0.077	0.026	0.158
TWEAK	AHEI	0.086	0.024	0.016	0.070	0.024	0.053	0.057	0.025	0.386
TYK2	DASH	-0.043	0.024	0.317	-0.086	0.024	0.011	-0.062	0.025	0.318
UBC9	AHEI, DASH	-0.079	0.025	0.044	-0.088	0.025	0.014	-0.067	0.026	0.304
UBE2N	DASH	-0.075	0.025	0.064	-0.099	0.025	0.004	-0.049	0.027	0.512
Ubiquitin+1	DASH	-0.059	0.024	0.170	-0.101	0.025	0.003	-0.051	0.026	0.473
WFKN2	AHEI, DASH, MDS	0.095	0.023	0.003	0.097	0.023	0.002	0.099	0.024	0.011

¹Multivariable regression models with proteins as the dependent variable and dietary pattern scores as the independent variable (separate model for each dietary pattern and protein). Models are adjusted for age, sex, total caloric intake, current smoking, physical activity index, lipid lowering medication, anti-hypertensive medication, and body mass index.

²Diets with a statistically significant association.

³ β estimates represent the change in protein concentrations per standardized unit increase in the respective dietary pattern indices.

⁴False discovery rate p value. Statistically significant (FDR $q \leq 0.05$) values are in bold.

Abbreviations: AHEI, Alternative Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension; MDS, Mediterranean Diet-style Score.

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al

Online Supplementary Material

Supplementary Table 2. Statistically significant associations of dietary patterns with plasma metabolite concentrations¹

		AHEI			DASH			MDS		
Label	Diet ²	β^3	SE	FDR ⁴	β	SE	FDR	β	SE	FDR
3-OH-anthranilic acid	DASH	0.022	0.010	0.130	0.032	0.011	0.015	0.017	0.011	0.295
Aconitate	AHEI, DASH, MDS	-0.025	0.006	0.001	-0.025	0.006	0.001	-0.019	0.007	0.021
Adenosine diphosphate (ADP)	AHEI, MDS	-0.092	0.034	0.038	-0.064	0.034	0.170	-0.068	0.036	0.181
Adenosine monophosphate (AMP)	MDS	-0.356	0.156	0.088	-0.340	0.158	0.111	-0.496	0.168	0.018
betaine	DASH, MDS	0.004	0.004	0.529	0.012	0.004	0.014	0.014	0.004	0.005
Cholesterol ester (C20:5)	AHEI, DASH, MDS	0.049	0.015	0.015	0.044	0.016	0.024	0.054	0.017	0.009
Cholesterol ester (C22:6)	AHEI, DASH, MDS	0.059	0.015	0.002	0.048	0.016	0.014	0.080	0.017	0.000
choline	AHEI, DASH	-0.012	0.004	0.045	-0.014	0.005	0.012	-0.006	0.005	0.353
cis/trans-hydroxyproline	AHEI, DASH, MDS	-0.033	0.012	0.039	-0.070	0.012	0.000	-0.054	0.013	0.000
cotinine	AHEI, DASH, MDS	-2.094	0.723	0.031	-3.075	0.734	0.000	-3.097	0.772	0.001
Deoxycholates	AHEI, DASH, MDS	-0.088	0.031	0.031	-0.092	0.031	0.018	-0.055	0.033	0.237
Fructose-1-phosphate + fructose-6-phosphate + glucose-1-phosphate + glucose-6-phosphate	AHEI	-0.033	0.011	0.031	-0.001	0.012	0.976	-0.004	0.012	0.856
Glyco deoxycholates	DASH	-0.089	0.034	0.050	-0.113	0.034	0.009	-0.086	0.037	0.073

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Glycocholate	AHEI, DASH, MDS	-0.080	0.029	0.038	-0.095	0.029	0.011	-0.084	0.031	0.033
Hippurate	AHEI, DASH, MDS	0.364	0.079	0.000	0.430	0.080	0.000	0.354	0.085	0.000
Indoxylsulfate	DASH	-0.036	0.015	0.075	-0.048	0.015	0.011	-0.034	0.016	0.112
Inositol	DASH, MDS	0.008	0.008	0.547	0.026	0.008	0.015	0.029	0.009	0.010
Isocitrate	AHEI, DASH, MDS	-0.041	0.008	0.000	-0.049	0.008	0.000	-0.041	0.008	0.000
lysine	AHEI	0.019	0.007	0.033	0.015	0.007	0.118	0.016	0.007	0.109
Lysophosphatidylcholine (C18:1)	AHEI, MDS	-0.031	0.011	0.031	-0.024	0.011	0.106	-0.029	0.011	0.044
Lysophosphatidylcholine (C20:5)	AHEI, DASH, MDS	0.079	0.016	0.000	0.069	0.017	0.000	0.062	0.018	0.004
Lysophosphatidylcholine (C22:6)	AHEI, DASH, MDS	0.073	0.010	0.000	0.052	0.011	0.000	0.077	0.011	0.000
Lysophosphatidylethanolamine (C18:1)	MDS	-0.030	0.015	0.138	-0.035	0.015	0.082	-0.045	0.016	0.023
Lysophosphatidylethanolamine (C18:2)	MDS	-0.023	0.010	0.088	-0.025	0.010	0.070	-0.034	0.011	0.011
Lysophosphatidylethanolamine (C20:4)	DASH, MDS	-0.022	0.009	0.075	-0.028	0.009	0.016	-0.045	0.010	0.000
Malate	AHEI, DASH, MDS	-0.021	0.007	0.031	-0.023	0.007	0.012	-0.025	0.008	0.008
ornithine	DASH, MDS	-0.028	0.011	0.059	-0.057	0.011	0.000	-0.039	0.012	0.008
Oxalate	AHEI, DASH, MDS	0.064	0.018	0.004	0.107	0.018	0.000	0.086	0.019	0.000

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Pantothenate	DASH, MDS	0.049	0.022	0.088	0.126	0.022	0.000	0.083	0.023	0.004
Phosphatidylcholine (C32:1)	MDS	-0.020	0.012	0.231	-0.003	0.012	0.892	-0.042	0.013	0.008
Phosphatidylcholine (C34:1)	MDS	-0.005	0.004	0.308	-0.004	0.004	0.503	-0.012	0.004	0.016
Phosphatidylcholine (C36:1)	MDS	-0.015	0.006	0.062	-0.006	0.006	0.565	-0.018	0.007	0.038
Phosphatidylcholine (C36:2)	AHEI, DASH	-0.010	0.003	0.008	-0.009	0.003	0.016	-0.007	0.003	0.086
Phosphatidylcholine (C38:6)	AHEI, DASH, MDS	0.039	0.005	0.000	0.035	0.005	0.000	0.046	0.005	0.000
Phosphatidylcholine (C40:6)	AHEI, DASH, MDS	0.041	0.006	0.000	0.038	0.006	0.000	0.054	0.006	0.000
Phosphoglycerate	AHEI	-0.044	0.016	0.038	-0.035	0.016	0.118	-0.022	0.017	0.405
proline	DASH	-0.007	0.006	0.376	-0.015	0.006	0.037	-0.011	0.006	0.197
serine	DASH	-0.006	0.007	0.577	-0.030	0.007	0.000	-0.018	0.008	0.062
Sphingomyelin (C14:0)	MDS	-0.012	0.006	0.173	-0.010	0.007	0.316	-0.043	0.007	0.000
Sphingomyelin (C16:0)	DASH, MDS	-0.006	0.003	0.088	-0.009	0.003	0.012	-0.008	0.003	0.021
Sphingomyelin (C18:0)	AHEI, DASH, MDS	-0.026	0.006	0.000	-0.028	0.006	0.000	-0.032	0.006	0.000
Sphingomyelin (C18:1)	AHEI, DASH, MDS	-0.044	0.007	0.000	-0.044	0.007	0.000	-0.036	0.007	0.000
thiamine	DASH, MDS	0.067	0.037	0.187	0.150	0.037	0.001	0.101	0.039	0.046
threonine	DASH	-0.005	0.006	0.550	-0.015	0.006	0.043	-0.010	0.006	0.252
Triacylglycerol (C48:1)	MDS	-0.027	0.015	0.175	-0.015	0.015	0.510	-0.043	0.016	0.027
Triacylglycerol (C50:1)	MDS	-0.019	0.009	0.131	-0.011	0.009	0.461	-0.028	0.010	0.025
Triacylglycerol (C50:2)	AHEI, MDS	-0.021	0.007	0.031	-0.015	0.007	0.118	-0.026	0.008	0.007
Triacylglycerol (C52:2)	AHEI, DASH	-0.020	0.006	0.013	-0.017	0.006	0.038	-0.014	0.007	0.112

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Triacylglycerol (C54:1)	DASH, MDS	-0.101	0.040	0.060	-0.108	0.040	0.037	-0.118	0.043	0.030
Triacylglycerol (C54:2)	AHEI, DASH, MDS	-0.056	0.019	0.030	-0.055	0.019	0.022	-0.056	0.020	0.030
Triacylglycerol (C54:4)	MDS	-0.003	0.007	0.773	0.001	0.007	0.934	0.019	0.007	0.040
Triacylglycerol (C54:5)	MDS	0.009	0.008	0.416	0.011	0.008	0.350	0.029	0.008	0.005
Triacylglycerol (C54:6)	MDS	0.009	0.008	0.416	0.011	0.008	0.350	0.029	0.008	0.005
Triacylglycerol (C54:7)	AHEI, DASH, MDS	0.036	0.012	0.019	0.037	0.012	0.014	0.050	0.013	0.001
Triacylglycerol (C56:6)	AHEI, DASH, MDS	0.017	0.006	0.034	0.012	0.006	0.144	0.018	0.007	0.029
Triacylglycerol (C56:7)	AHEI, DASH, MDS	0.037	0.007	0.000	0.031	0.007	0.000	0.041	0.008	0.000
Triacylglycerol (C56:8)	AHEI, DASH, MDS	0.043	0.009	0.000	0.040	0.009	0.000	0.054	0.009	0.000
Triacylglycerol (C56:9)	AHEI, MDS	0.033	0.010	0.009	0.022	0.010	0.111	0.034	0.011	0.009
Triacylglycerol (C58:10)	AHEI, DASH, MDS	0.045	0.010	0.000	0.038	0.010	0.001	0.048	0.011	0.000
Triacylglycerol (C58:8)	AHEI, DASH, MDS	0.042	0.008	0.000	0.037	0.008	0.000	0.047	0.008	0.000
Triacylglycerol (C58:9)	AHEI, DASH, MDS	0.050	0.009	0.000	0.045	0.009	0.000	0.057	0.009	0.000
Triacylglycerol (C60:12)	AHEI, MDS	0.043	0.014	0.014	0.030	0.014	0.106	0.045	0.015	0.013
Tryptophan	DASH, MDS	0.009	0.004	0.149	0.014	0.004	0.014	0.015	0.005	0.011

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

Uridine	AHEI, DASH, MDS	0.028	0.005	0.000	0.034	0.005	0.000	0.019	0.005	0.004
Uridine diphosphate-galactose + uridine diphosphate-glucose	AHEI	-0.046	0.017	0.037	-0.033	0.017	0.150	-0.045	0.018	0.055

¹Multivariable regression models with each metabolite as the dependent variable and dietary pattern scores as the independent variable (separate model for each dietary pattern and protein). Models are adjusted for age, sex, total caloric intake, current smoking, physical activity index, lipid lowering medication, anti-hypertensive medication, and body mass index.

²Diets with a statistically significant association.

³ β estimates represent the change in metabolite concentration per standardized unit increase in the respective dietary pattern indices.

⁴False discovery rate p value. Statistically significant (FDR $q \leq 0.05$) values are in bold.

Abbreviations: AHEI, Alternative Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension; MDS, Mediterranean Diet-style Score.

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al

Online Supplementary Material

Supplementary Table 3. Pathway over representation analysis of protein markers associated with the AHEI and DASH dietary pattern indices¹

AHEI	Pathway	Enrichment Ratio	p value²	FDR q value³	Matched Molecules
	Central carbon metabolism in cancer	15.12	1.7E-05	5.6E-03	EGFR, FGFR1, KIT, MET, NTRK3
	Complement and coagulation cascades	9.95	6.5E-04	8.0E-02	SERPINC1, C3, C3AR1, CPB2
	MicroRNAs in cancer	6.55	8.9E-04	8.0E-02	EGFR, MET, NOTCH1, BCL2L2, UBE2I
	Pathways in cancer	3.38	9.8E-04	8.0E-02	EGFR, FGFR1, HSP90AB1, IL5RA, KIT, MET, MMP2, NOTCH1, STAT6
	Endocrine resistance	8.02	1.5E-03	9.5E-02	EGFR, MMP2, NOTCH1, MED1
	Phenylalanine metabolism	23.12	3.3E-03	1.8E-01	MIF, DDC
	Estrogen signaling pathway	5.74	4.9E-03	2.1E-01	EGFR, CTSD, HSP90AB1, MMP2
	Adherens junction	8.19	5.7E-03	2.1E-01	EGFR, MET, FGFR1
	Melanoma	8.19	5.7E-03	2.1E-01	EGFR, MET, FGFR1
	Breast cancer	5.35	6.3E-03	2.1E-01	EGFR, KIT FGFR1, NOTCH1
DASH					
	Endocrine resistance	7.57	4.8E-04	8.4E-02	JAG1, EGFR, MMP2, NOTCH1, MED1
	HIF-1 signaling pathway	7.42	5.3E-04	8.4E-02	EGFR, GAPDH, SERPINE1, TEK, TF
	Central carbon metabolism in cancer	9.13	9.1E-04	8.4E-02	EGFR, FGFR1, MET, NTRK3
	Carbon metabolism	6.39	1.0E-03	8.4E-02	ESD, GAPDH, MDH1, TKT, TPI1
	Complement and coagulation cascades	7.51	1.9E-03	1.1E-01	PLAT, SERPINC1, CFH, C1S
	Fluid shear stress and atherosclerosis	5.38	2.2E-03	1.1E-01	HSP90AB1, MMP2, PLAT, SELE, BMPR1A
	PI3K-Akt signaling pathway	3.35	2.3E-03	1.1E-01	CDC37, EGFR, FGFR1, HSP90AB1, MET, NTRK2, TEK, THBS2
	Prostate cancer	6.12	4.0E-03	1.5E-01	EGFR, PLAT, HSP90AB1, FGFR1
	Malaria	9.09	4.3E-03	1.5E-01	MET, SELE, THBS2

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al

Online Supplementary Material

Proteoglycans in cancer	3.75	1.0E-02	3.0E-01	EGFR, FGFR1, GPC3, MET, MMP2
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¹All proteins analyzed were significantly ($FDR\ p \leq 0.05$) related to the respective dietary pattern scores in multivariable models adjusting for age, sex, total caloric intake, current smoking, physical activity index, lipid lowering medication, anti-hypertensive medication, and body mass index. Analyzed proteins were annotated to KEGG pathways with > 5 and < 2000 proteins.

²Unadjusted p value

³False discovery rate q value.

Abbreviations: AHEI, Alternative Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension; KEGG, Kyoto Encyclopedia of Genes and Genomes; MDS, Mediterranean-style Diet Score

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al

Online Supplementary Material

Supplementary Table 4. KEGG pathway mapping of metabolites associated with dietary pattern indices¹

AHEI	Pathway	Total Molecules	Matched Molecules
	Metabolic pathways	11	ADP, Choline, Phosphatidylcholine, Uridine, Isocitrate, cis-Aconitate , Triacylglycerol, Sphingomyelin, D-Lysine, Hiipurate, Glycocholate
	Bile secretion	4	Choline, Glycocholate, Cholesterol ester, Deoxycholic acid
	Glycerophospholipid metabolism	3	Choline, Phosphatidylcholine, 1-Acyl-sn-glycero-3-phosphocholine
	Cholesterol metabolism	3	Choline, Phosphatidylcholine, 1-Acyl-sn-glycero-3-phosphocholine
	Choline metabolism in cancer	3	Triacylglycerol, Glycocholate, Cholesterol ester
DASH			
	Metabolic pathways	16	L-Serine, L-Ornithine, Choline, Phosphatidylcholine, L-Threonine, Uridine, Isocitrate, Thiamine, cis-Aconitate, Sphingomyelin, 3-Hydroxyanthranilate, Betaine, D-Proline, Pantothenate, Hippurate, Glycocholate
	ABC transporters	7	L-Serine, L-Ornithine, Choline, L-Threonine, Uridine, Thiamine, Betaine
	Biosynthesis of amino acids	4	L-Serine, L-Ornithine, L-Threonine, Isocitrate
	Bile secretion	4	Choline, Glycocholate, Cholesterol ester, Deoxycholic acid
	Glycine, serine and threonine metabolism	4	L-Serine, L-Ornithine, L-Threonine, Betaine
	Glyoxylate and dicarboxylate metabolism	3	L-Serine, Isocitrate, cis-Aconitate
	Vitamin digestion and absorption	3	Thiamine, Pantothenate, Cholesterol ester
	Choline metabolism in cancer	3	Choline, Phosphatidylcholine, 1-Acyl-sn-glycero-3-phosphocholine
	2-Oxocarboxylic acid metabolism	3	L-Ornithine, Isocitrate, cis-Aconitate,
	Glycerophospholipid metabolism	3	Choline, Phosphatidylcholine, 1-Acyl-sn-glycero-3-phosphocholine

Proteomic and Metabolomic Correlates of Healthy Dietary Patterns: The Framingham Heart Study
Walker et al
Online Supplementary Material

MDS		
Metabolic pathways	13	AMP, L-Ornithine, Phosphatidylcholine, Uridine, Isocitrate, Thiamine, cis-Aconitate, Triacylglycerol, Sphingomyelin, Betaine, Pantothenate, Hippurate, Glycocholate
Vitamin digestion and absorption	4	Thiamine, Triacylglycerol, Pantothenate, Cholesterol ester
Oxocarboxylic acid metabolism	3	L-Ornithine, Isocitrate, cis-Aconitate
ABC transporters	4	L-Ornithine, Uridine, Thiamine, Betaine
Cholesterol metabolism	3	Triacylglycerol, Glycocholate, Cholesterol ester

¹Pathways with ≥ 3 mapped metabolites are displayed. All metabolites assessed were significantly (FDR $p < 0.05$) associated with the respective dietary pattern scores in multivariable models adjusting for age, sex, total caloric intake, current smoking, physical activity index, lipid lowering medication, anti-hypertensive medication, and body mass index. Abbreviations: AHEI, Alternative Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension; FDR, false discovery rate; KEGG, Kyoto Encyclopedia of Genes and Genomes; MDS, Mediterranean Diet Score.