**Supplementary Table 1**. Baseline characteristics of study participants according to tertiles of the regional DNA methylation at *ABCG1*.

| | Tertiles of regional DNAm | | | |
|---|---|---|---|---|
| | T1 (N=224) | T2 (N=225) | T3 (N=224) | p |
| Age, years | 50.1 (9.3) | 51.3 (9.2) | 51.4 (9.4) | 0.38 |
| White | 171 (76.3) | 177 (78.7) | 190 (84.8) | 0.19 |
| Female | 149 (66.5) | 136 (60.4) | 127 (56.7) | 0.10 |
| BMI, kg/m$^2$ | 32.6 (3.9) | 32.7 (3.8) | 32.8 (3.9) | 0.86 |
| Body weight, kg | 92.5 (15.1) | 94.3 (15.7) | 93.7 (15.8) | 0.52 |
| Waist circumference, cm | 103 (12.5) | 104.4 (13.3) | 103.9 (13.4) | 0.58 |
| Body fat distribution | | | | |
| VAT, kg | 5.3 (2.7) | 5.7 (2.5) | 5.4 (2.4) | 0.81 |
| SAT, kg | 10.5 (2.4) | 11.2 (2.7) | 11.6 (2.7) | 0.15 |
| dSAT, kg | 5.7 (1.8) | 5.6 (1.4) | 5.9 (1.7) | 0.50 |
| TAT, kg | 15.8 (3.9) | 17.1 (4.0) | 16.9 (3.8) | 0.29 |
| SBP, mmHg | 119.9 (13.8) | 119 (14.2) | 120.1 (12.5) | 0.70 |
| DBP, mmHg | 75.7 (9.9) | 75.1 (9.5) | 75.8 (9.1) | 0.46 |
| LDL-c, mg/dL | 127.7 (33.1) | 124.4 (31.6) | 126.4 (33.0) | 0.70 |
| HDL-c, mg/dL | 49.6 (13.8) | 48.9 (14.1) | 48 (14.5) | 0.87 |
| Cholesterol, mg/dL | 204.6 (38.7) | 201.2 (37.5) | 203 (35.8) | 0.70 |
| Triglycerides, mg/dL | 117.0 [78.0, 164.5] | 118.0 [85.0, 192.0] | 128.0 [88.5, 182.5] | 0.95 |
| Glucose, mg/dL | 91.0 (10.8) | 92.5 (12.4) | 92.5 (12.2) | 0.68 |
| HbA1c, % | 5.4 (0.4) | 5.4 (0.4) | 5.4 (0.4) | 0.51 |
| Insulin, μU/mL | 10.3 [6.8, 14.8] | 10.3 [7.1, 15.7] | 10.5 [7.0, 15.5] | 0.59 |
| HOMA-IR | 2.2 [1.5, 3.4] | 2.4 [1.5, 3.7] | 2.4 [1.5, 3.6] | 0.56 |
| Lipid-lowering medication | 43 (19.2) | 41 (18.22) | 38 (16.96) | 0.83 |
| High-fat group | 111 (49.6) | 108 (48.0) | 126 (56.3) | 0.18 |
| High-protein group | 116 (51.8) | 100 (44.4) | 116 (51.8) | 0.20 |

Data are mean (SD), median [IQR], or N (%).
P values were calculated by Chi-square test for categorical variables and F test for continuous variables.
BMI: body mass index; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; dSAT: deep subcutaneous adipose tissue; TAT: total adipose tissue. SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL-c: low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; HOMA-IR: homeostatic model assessment of insulin resistance.

**Supplementary Table 2**. Changes in adiposity and abdominal fat distribution at 6 months and 2 years according to average-/high-protein group.

| **6 months** | **average-protein group** | **high-protein group** | **p-difference between groups** |
|---|---|---|---|
| Body weight, kg | -6.4 (-7.1, -5.7) | -6.9 (-7.5, -6.3) | 0.29 |
| Waist circumference, cm | -6.6 (-7.3, -5.9) | -7.1 (-7.8, -6.4) | 0.30 |
| VAT, kg | -1.1 (-1.5, -0.7) | -1.1 (-1.4, -0.8) | 0.96 |
| SAT, kg | -2.2 (-2.7, -1.7) | -1.8 (-2.2, -1.4) | 0.17 |
| dSAT, kg | -1.2 (-1.5, -1.0) | -1.0 (-1.2, -0.7) | 0.12 |
| TAT, kg | -3.3 (-4.0, -2.5) | -3.0 (-3.7, -2.4) | 0.60 |
| **2 years** | | | |
| Body weight, kg | -3.6 (-4.5, -2.6) | -4.6 (-5.4, -3.8) | 0.10 |
| Waist circumference, cm | -5.3 (-6.3, -4.3) | -6.2 (-7.1, -5.4) | 0.17 |
| VAT, kg | -1.0 (-1.5, -0.5) | -0.7 (-1.1, -0.4) | 0.42 |
| SAT, kg | -1.5 (-2.4, -0.7) | -0.9 (-1.3, -0.5) | 0.19 |
| dSAT, kg | -1.0 (-1.4, -0.5) | -0.6 (-0.8, -0.3) | 0.12 |
| TAT, kg | -2.5 (-3.8, -1.1) | -1.6 (-2.4, -0.9) | 0.25 |

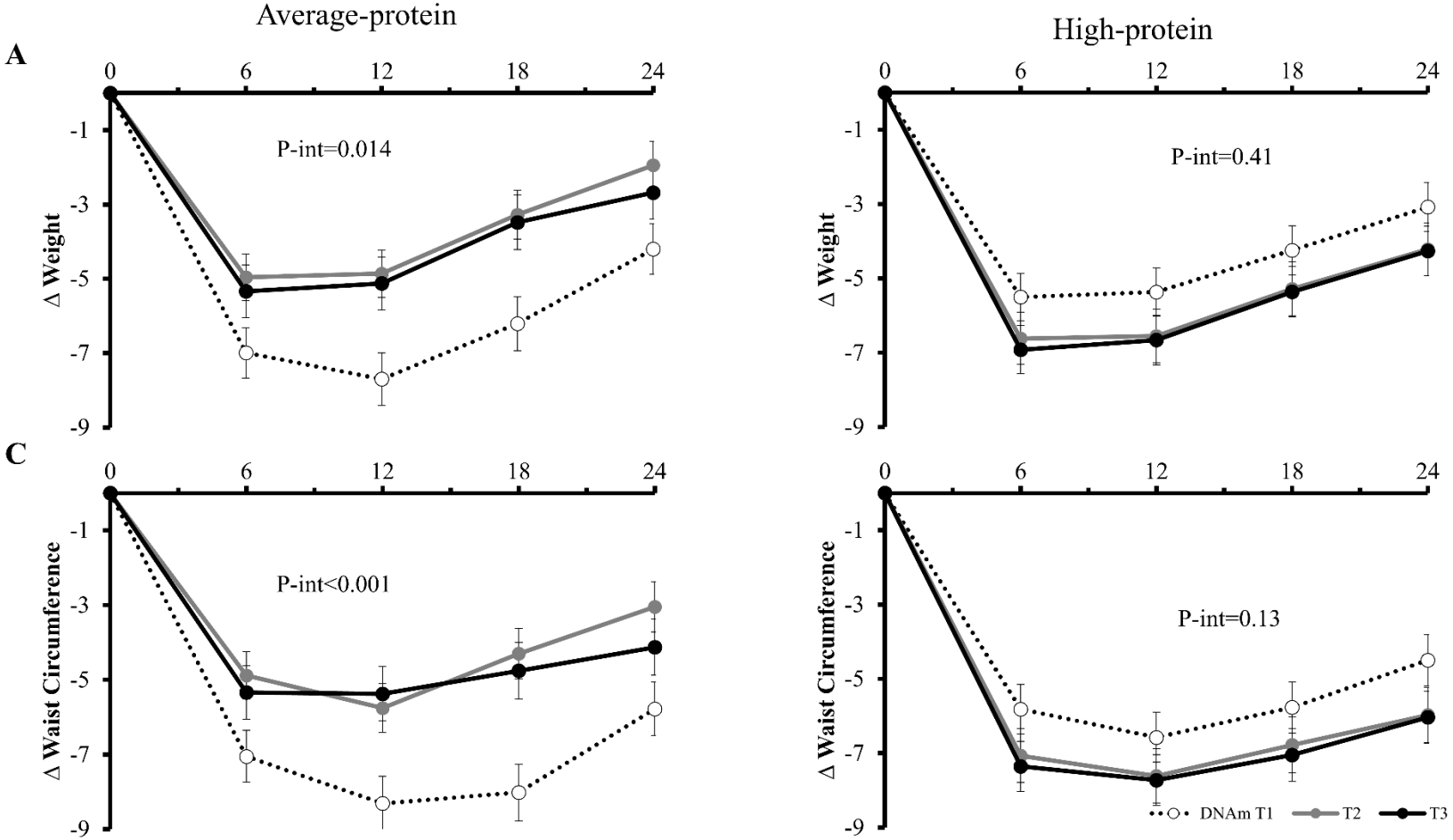
VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; dSAT: deep subcutaneous adipose tissue; TAT: total adipose tissue.

**Supplementary Table 3.** Associations between baseline regional DNA methylation at *ABCG1* and changes in adiposity and abdominal fat distributions

| | 6 months | | 2 years | |
|---|---|---|---|---|
| | β (SE) | p | β (SE) | p |
| Body weight, kg | -1.2 (3.1) | 0.69 | 1.2 (4.1) | 0.77 |
| Waist circumference, cm | -1.1 (3.3) | 0.75 | 2.0 (4.3) | 0.64 |
| VAT, kg | 1.3 (1.5) | 0.38 | 3.5 (2.0) | 0.09 |
| SAT, kg | 1.2 (2.2) | 0.58 | 6.5 (3.3) | 0.06 |
| dSAT, kg | 1.6 (1.3) | 0.22 | 4.5 (1.7) | 0.01 |
| TAT, kg | 1.6 (3.5) | 0.64 | 9.0 (5.4) | 0.10 |

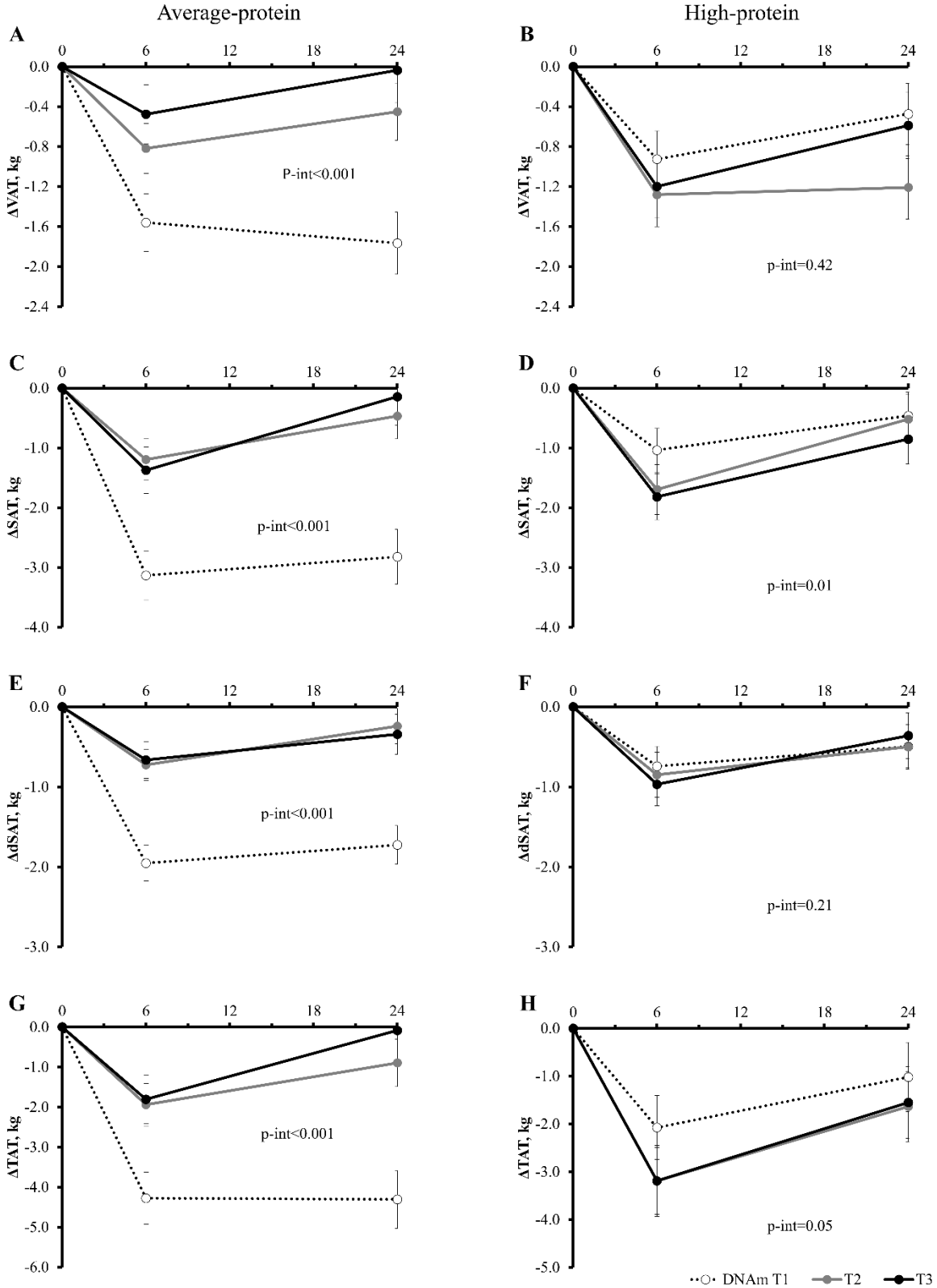
VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; dSAT: deep subcutaneous adipose tissue; TAT: total adipose tissue.

**Supplementary Figure 1**. Trajectory of changes in body weight (A & B) and waist circumference (C & D) according to regional DNA methylation at *ABCG1* in response to average-/high-protein weight-loss diets.




Data are mean ± SE after adjustment for age, race, sex, use of lipid-lowering medications, baseline values of respective outcomes, and blood cell composition. Linear mixed models were used to test the effect of DNA methylation on the trajectory of changes in the outcomes. Sample size: average-protein group: T1=88, T2=97, T3=85; high-protein group: T1=91, T2=86, T3=96.

**Supplementary Figure 2**. Trajectory of changes in VAT (A & B), SAT (C & D), dSAT (E & F), and TAT (G & H) according to regional DNA methylation at ABCG1 in response to average or high-protein weight-loss diet during 2 years.




Data are mean ± SE after adjustment for age, race, sex, BMI at baseline, use of lipid-lowering medications, baseline values of respective outcomes, and blood cell composition. Linear mixed models were used to test the effect of DNA methylation on the trajectory of changes in the outcomes. VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; dSAT: deep subcutaneous adipose tissue; TAT: total adipose tissue. Sample size: average-protein group T1=13, T2=14, T3=12; high-protein group T1=17, T2=16, T3=13.