

Supplementary Materials

Determinants of plasma branched-chain amino acids and associations with cardiometabolic biomarkers and proteomic signatures

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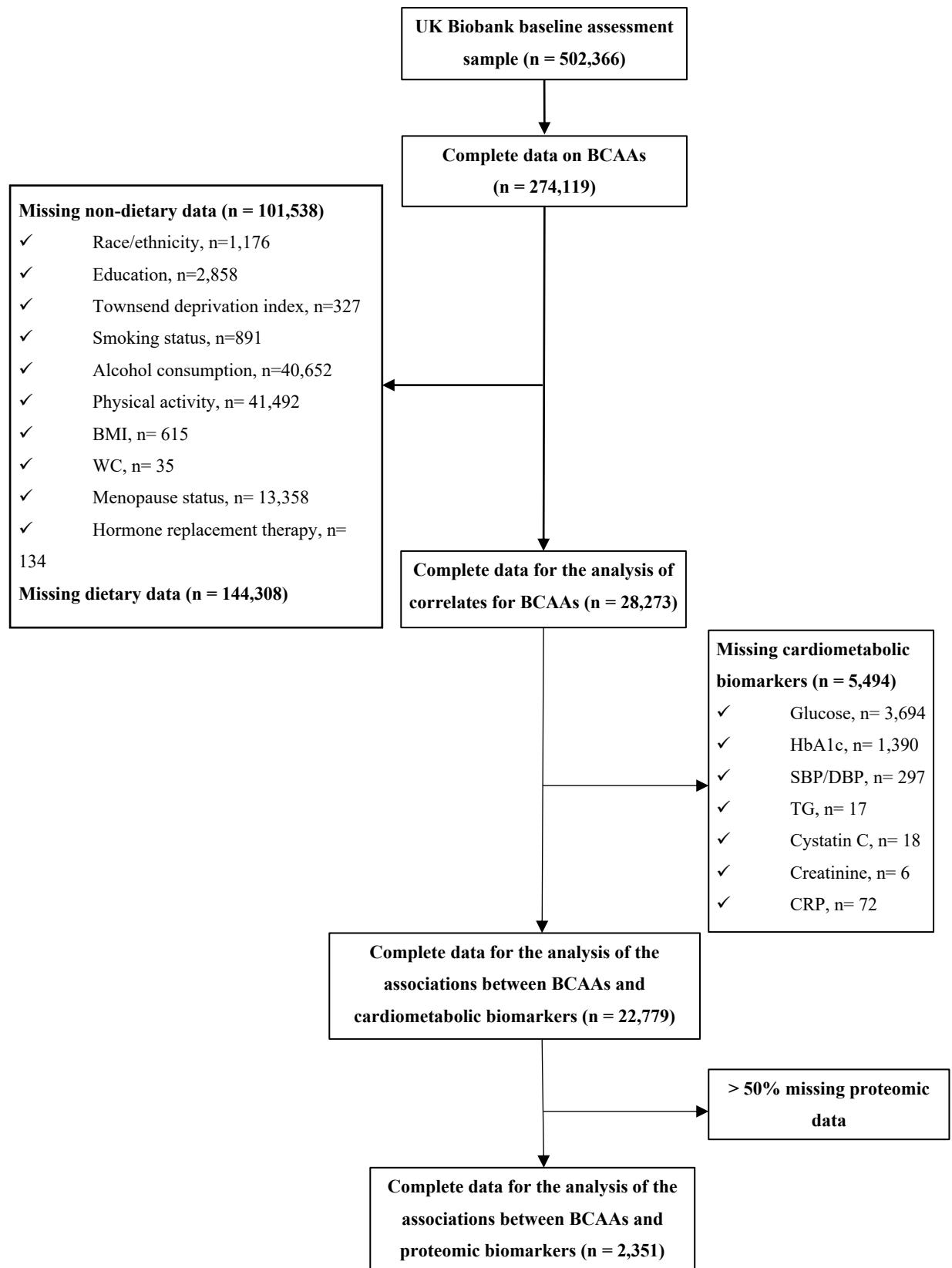
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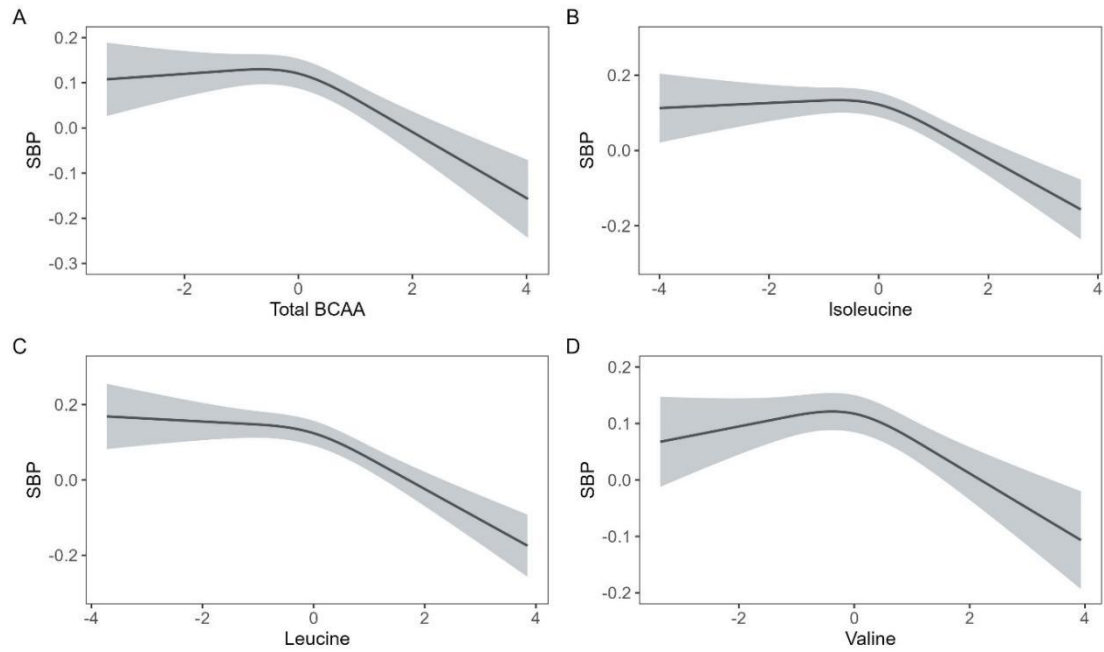
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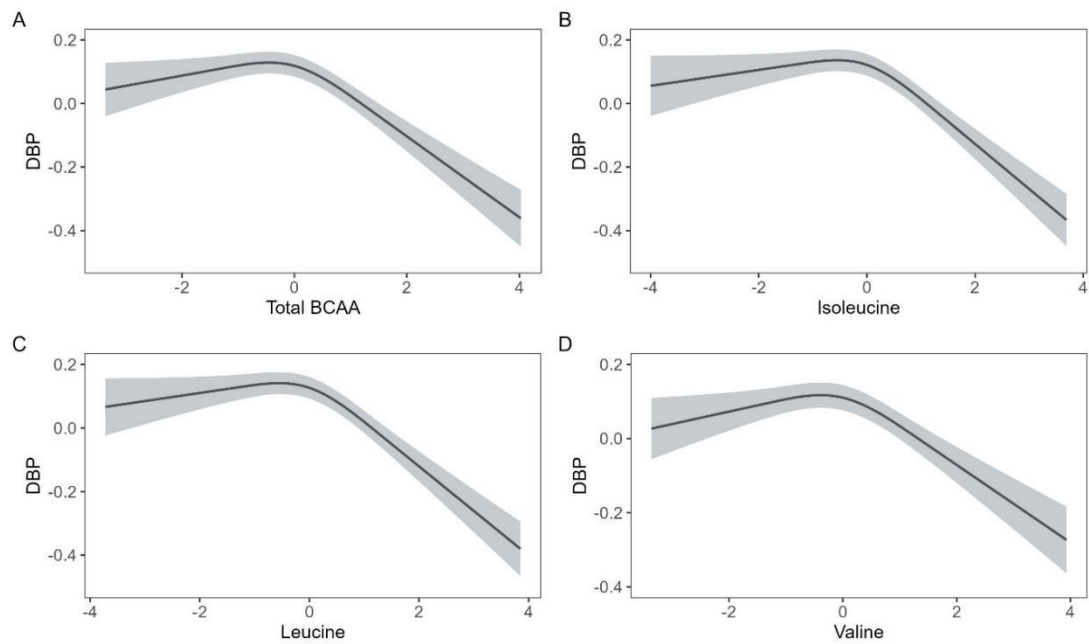
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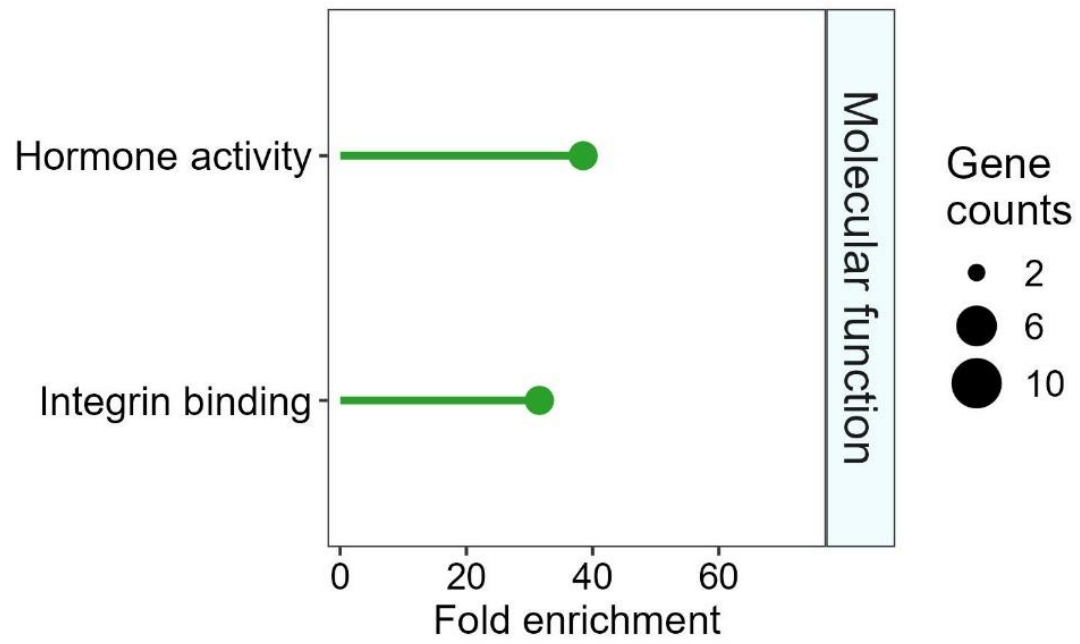
Supplementary Figure 1. Eligibility of study participants. BCAAs, branched-chain amino acids; BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.



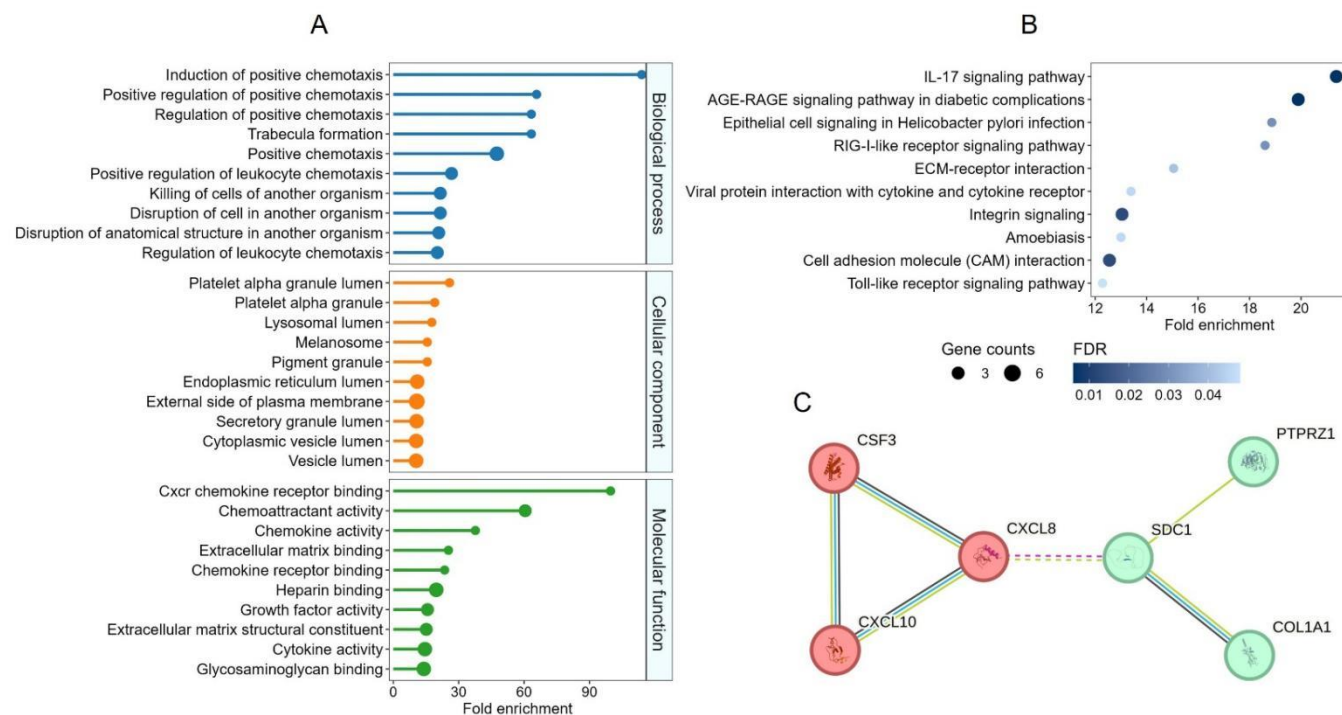
Supplementary Figure 2. Associations between plasma BCAAs and SBP using restricted cubic splines-based regression. All FDR for overall and nonlinear < 0.05 . BCAAs, branched-chain amino acids; FDR, false discovery rate; SBP, systolic blood pressure.



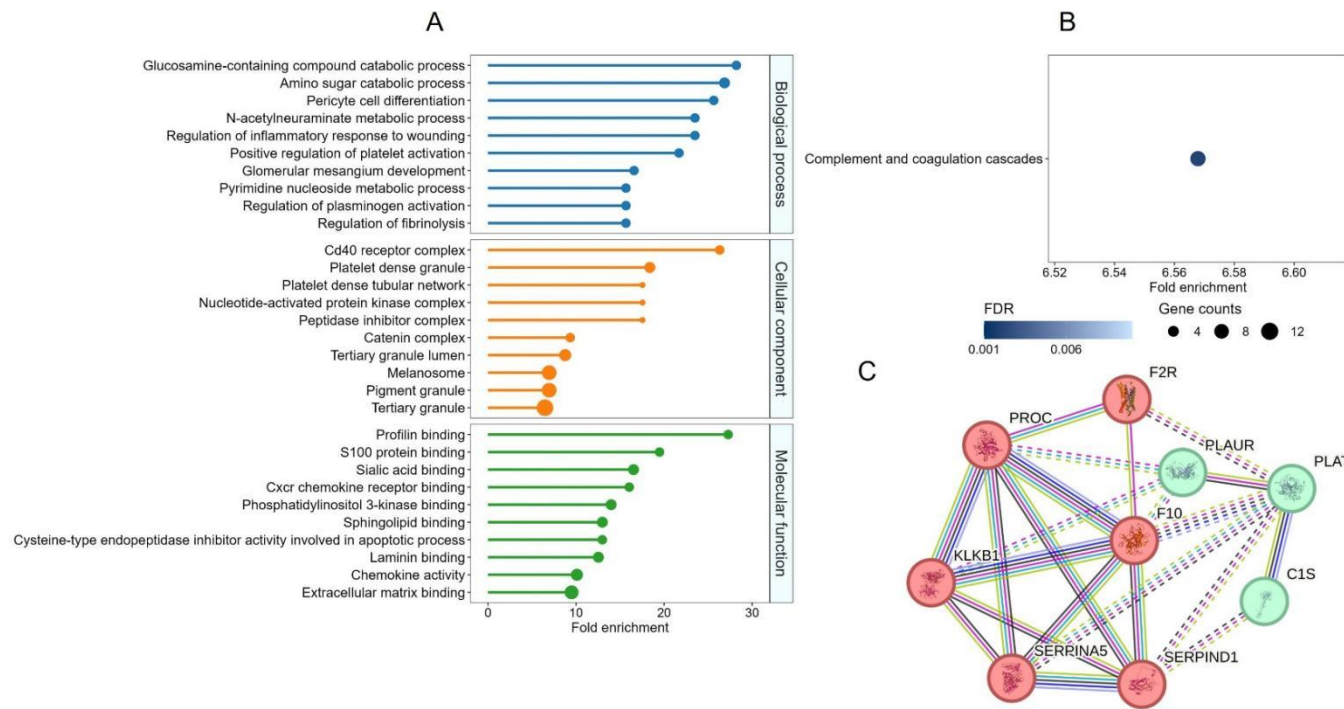
Supplementary Figure 3. Associations between plasma BCAAs and DBP using restricted cubic splines-based regression. All FDR for overall and nonlinear < 0.05 . BCAAs, branched-chain amino acids; DBP, diastolic blood pressure; FDR, false discovery rate.



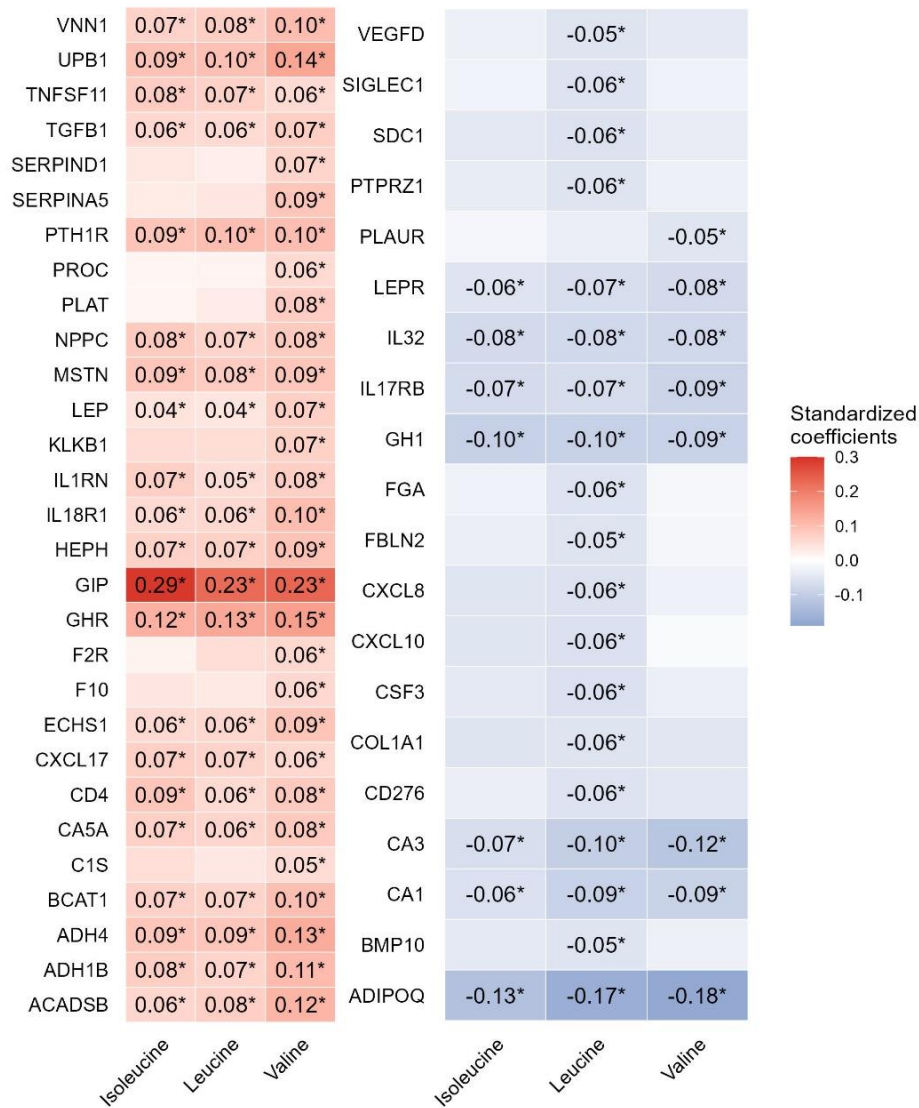
Supplementary Figure 4. GO enrichment analyses of isoleucine-specific proteins. KEGG enrichment analysis of isoleucine-specific proteins did not identify any significant pathways. GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.



Supplementary Figure 5. Functional enrichment and PPI network analyses of leucine-specific proteins. (A) GO enrichment analysis of the specific proteins. For visualization purposes, only the top 10 significantly enriched terms with the highest fold enrichment are displayed across biological process, cellular component, and molecular function categories; (B) KEGG pathway enrichment analysis of the specific proteins; (C) PPI network constructed from 12 proteins mapped to the significantly enriched KEGG pathway. Proteins are clustered (from left to right, top to bottom) into two functional modules: interleukin-10 signaling and other interleukin signaling. Unconnected nodes were excluded. AGE, advanced glycation end products; ECM, extracellular matrix; FDR, false discovery rate; GO, Gene Ontology; IL, interleukin; KEGG, Kyoto Encyclopedia of Genes and Genomes; PPI, protein-protein interaction; RAGE, receptor for advanced glycation end products; RIG, retinoic acid-inducible gene.



Supplementary Figure 6. Functional enrichment and PPI network analyses of valine-specific proteins. (A) GO enrichment analysis of the specific proteins. For visualization purposes, only the top 10 significantly enriched terms with the highest fold enrichment are displayed across biological process, cellular component, and molecular function categories; (B) KEGG pathway enrichment analysis of the specific proteins; (C) PPI network constructed from 9 proteins mapped to the significantly enriched KEGG pathway. Proteins are clustered (from left to right, top to bottom) into two functional modules: formation of fibrin clot (clotting cascade) and dissolution of fibrin clot. Unconnected nodes were excluded. CD, cluster of differentiation; FDR, false discovery rate; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; PPI, protein-protein interaction.



Supplementary Figure 7. Associations between plasma BCAAs and 49 proteins identified via KEGG enrichment analyses. The heatmap displays standardized regression coefficients derived from fully adjusted multivariable linear regression models. Plasma BCAAs were log-transformed and Z-score standardized prior to analysis. Proteins were Z-score standardized before analysis. Numerical labels indicate FDR < 0.05. BCAAs, branched-chain amino acids; FDR, false discovery rate; KEGG, Kyoto Encyclopedia of Genes and Genomes.