**Supplementary information**

**Transcriptome-wide** **N6-methyladenosine methylation landscape of** **coronary artery disease**

**Supplementary Figure Legends:**

**Supplementary Figure 1. Flow chart of participants included in the study.** CAD, Coronary artery disease.

**Supplementary Figure 2. The mRNA expression level of the main m6A regulators (methyltransferase: METTL3 METTL14, demethylases: FTO, ALKBH5) in PBMCs of CAD patients and controls from microarray data. PBMCs, peripheral blood mononuclear cells. \*\*P<0.01, \*\*\*P<0.001; ns, not significant.**

**Supplementary Figure 3. Overview of m6A methylation within lncRNAs in CAD group and control group.** (A) Venn diagram showing the overlap of m6A peaks within lncRNAs in the two groups. (B) Proportion of genes harboring different numbers of m6A on lncRNA peaks in CAD cases and controls. (C) Pie charts showing the percentage of m6A peaks within lncRNAs in six groups, which were grouped according to positional relationship of lncRNA to near coding gene transcripts. n=5 in CAD/control group (A-C). CAD, Coronary artery disease; m6A, N6-methyladenosine.

**Supplementary Figure 4. Distribution of differentially methylated m6A sites within lncRNA in CAD group compared with control group**. (A) Distribution of differentially methylated m6A sites of lncRNA with significance in chromosomes of human beings. (B) Relative occupancy of differentially methylated m6A sites of lncRNAs in each chromosome normalized by length of respective chromosome. (C) Pie chart showing the percentage of DMM peaks of lncRNAs in six groups. (D) Motif analysis of all differentially methylated m6A peaks of lncRNAs between CAD and control group, containing RRACH sequences. n=5 in CAD/control group (A-D). CAD, Coronary artery disease; m6A, N6-methyladenosine.

**Supplementary Figure 5.** **GO and KEGG pathway analysis of mRNAs with differentially methylated m6A sites.**(A) The top 10 GO terms of biological processes were significantly enriched for genes with upregulated m6A peaks in CAD group compared with control group. (B) The top 10 GO terms of biological processes were significantly enriched for genes with downregulated m6A peaks in CAD group compared with control group. (C) The top 10 significantly enriched pathways of genes with upregulated m6A peaks in CAD group compared with control group. (D) The top 10 significantly enriched pathways of genes with downregulated m6A peaks in CAD group compared with control group. Statistical analysis was carried out by Fisher’s exact test. GO, Gene Ontology annotation; KEGG, the Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses.

**Supplementary Figure 6.** **GO and KEGG pathway analysis of** **lncRNAs with differentially methylated m6A sites.** (A) The top 10 gene ontology terms of biological processes were significantly enriched for lncRNAs with upregulated m6A peaks in CAD group compared with control group. (B) The top 10 gene ontology terms of biological processes were significantly enriched for lncRNAs with downregulated m6A peaks in CAD group compared with control group. (C) The top 10 significantly enriched pathways of lncRNAs with upregulated m6A peaks in CAD group compared with control group. (D) The top 10 significantly enriched pathways of lncRNAs with downregulated m6A peaks in CAD group compared with control group. Statistical analysis was carried out by Fisher’s exact test. GO, Gene Ontology annotation; KEGG, the Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses.

**Supplementary Figure 7. Hub DMGs identification and subsequent GO and KEGG pathway analysis.** (A) The PPI network and identification of hub genes. A node represents a gene. The undirected link between two nodes indicates an edge. Red nodes and green nodes represent hypermethylated and hypomethylated genes, respectively. The size of nodes indicates the degree connectivity of genes. Width of solid edge lines indicates combined scores between different genes. (B) The top 10 GO terms of biological processes were significantly enriched for 15 hub genes. (C) The top 10 KEGG pathways of 15 hub genes. The x-axis represents the ratio number of genes and the y-axis represents the GO and KEGG terms, the adjust *P* value of each term is colored on the basis of the legend. Statistical analysis was carried out by Fisher’s exact test. GO, Gene Ontology annotation; KEGG, the Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses.

**Supplementary Figure 8. GSEA analysis of DMGs with differential expression.** (A) The normalized enrichment score (NES) of pathways illustrating both differential m6A RNA methylation (NES of pathway methylation) and gene expression (NES of pathway expression). Pathways with hypermethylated and upregulated expression were marked in red; pathways with hypomethylated and downregulated expression were marked in blue. (B) Pathways showing hypermethylated and upregulated expression included some pathways associated with inflammation and immune responses (red); pathways showing hypomethylated and downregulated expression included some pathways associated with inflammation and immune responses or cell proliferation, metabolism and transcription (blue), Enriched pathways were selected based on statistical significance (Nominal *P* value < 0.05). Nominal *P* value was estimated by an empirical phenotype-based permutation test procedure using GSEA software. Specifically, nominal p-value is the probability under the null distribution of obtaining an ES value that is as strong or stronger than that observed for your experiment under the permutation-generated null distribution. (C) Representatives of pathways illustrating hypermethylated and upregulated expression. “Reactome Beta Catenin Independent WNT Signaling” and “Reactome Interferon GAMMA Signaling”. (D) Representatives of pathways illustrating hypomethylated and downregulated expression. “KEGG MAPK Signaling” and “Reactome RAF-independent MAPK1/3 Activation”. NES, normalized enrichment score; GSEA, gene set enrichment analyses.

**Supplementary Figure 9. Conjoint analysis of differentially methylated lncRNA peaks and differentially expressed lncRNA.** (A) Heatmap of lncRNAs showing the differentially expressed lncRNAs between CAD and control group. (B) Four-quadrant graph showing the distribution of lncRNA transcripts, which indicates the relationship of the m6A level of lncRNA and the lncRNA expression between CAD and control group. (C) m6A peak visualization of CTA-29F11.1, a representative “hypo-down” lncRNA in the CAD group relative to the control group. n=5 in CAD/control group (A-C).

**Supplementary Table Legends:**

**Supplementary Table 1.** Primes for MeRIP-qPCR validation.

**Supplementary Table 2.** Clinical characteristics of CAD patients and healthy controls.

**Supplementary Table 3.** Clinical characteristics of CAD patients and healthy controls for MeRIP-seq.

**Supplementary Table 4.** The top 10 differently methylated m6A peaks in lncRNAs.

**Supplementary Table 5.** The protein-protein interaction (PPI) network analysis of the corresponding DMGs through searching STRING database.

**Supplementary Table 6.** List of 15 hub DMGs retrieved from PPI network constructed through STRING database.

**Supplementary Table 7.** Differentially methylated genes (DMGs) in or near susceptibility loci identified by CAD or Lipid GWAS.

**Supplementary Table 8.** The list of genes with significant change in both m6A level and mRNA transcript abundance in CAD group.

**Supplementary Table 9.** The list of lncRNAs with significant change in both m6A level and lncRNA transcript abundance in CAD group.