Supplementary Materials

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Materials and Methods

Collection and treatment of CHD blood and coronary artery samples

70 CHD patients and 30 controls were all selected based on the results of diagnostic coronary angiography. Patients with lung, liver, kidney, immune disease, other heart diseases and other underlying diseases were excluded. Blood samples were collected from patients with CHD who showed no less than 50% coronary stenosis before PCI treatment. The control samples were collected from patients with less than 50% coronary stenosis, based on coronary angiography. All participants were pretreated with conventional-dose Asprin and Clopidogrel before PCI. Age, gender, diabetes history, smoking history, alcohol intake, blood pressure, TG, cholesterol, LDL-C, and HDL-C data for the test subjects and controls were obtained from an electronic medical record system and analysed by t-test and Chi-square test. The detailed information were described in Supplementary material Table S3. We separated PBMCs using a PBMCs separation medium (Solarbio, China) and centrifuged twice for total 40 min according to the protocol. Then with the immediate addition of Trizol LS to the PBMCs, all Trizol LS-treated samples were stored at −80°C before sequencing.

Human coronary arteries were collected at the end of the transplant procedure, within 1–2 h of cessation of circulation, constantly under cold ischemic conditions. The coronary arteries with atherosclerotic plaques were matched with normal non-plaque arteries based on histopathological examination in the same individual. were collected at the end of the transplant procedure, within 1–2 h of cessation of circulation, constantly under cold ischemic conditions.

RNA isolation and circRNA sequencing

RNA was isolated according to standardized protocols, and total RNA concentration and quality
were assessed using a NanoDrop ND1000 spectrophotometer (NanoDrop, Wilmington, DE, USA). OD260/OD280 ratios between 1.8 and 2.1 were deemed acceptable. Five micrograms of RNA per sample was used as input material for RNA sample preparation. First, we used an Epicentre Ribo-zero™ rRNA Removal Kit (Epicentre, USA) to obtain rRNA-depleted ribosomal RNAs. rRNA-depleted RNAs were further treated with RNase R (Epicentre, USA). Subsequently, sequencing libraries were generated from the rRNA-depleted and RNase R digested RNAs using an NEBNext® Ultra™ Directional RNA Library Prep Kit for Illumina® (NEB, USA) following the manufacturer’s recommendations. Briefly, the RNA was fragmentated using divalent cations at an elevated temperature in NEBNext First Strand Synthesis Reaction Buffer. First-strand cDNA was synthesized using random hexamer primers and M-MuLV Reverse Transcriptase (RNaseH−). Second-strand cDNA synthesis was then completed using DNA Polymerase I and RNase H. In the reaction buffer, dNTPs with dTTP were replaced by dUTP. Remaining overhangs were converted into blunt ends via exonuclease/polymerase activity. After adenylation of the 3’ ends of DNA fragments, NEBNext Adaptors with hairpin loop structures were ligated to prepare for hybridization. To select cDNA fragments 150-200 bp in length, the library fragments were purified using an AMPure XP system (Beckman Coulter, Beverly, USA). Then 3 μl of USER Enzyme (NEB, USA) was allowed to react with size-selected, adaptor-ligated cDNA at 37°C for 15 min, followed by 5 min at 95°C before PCR. PCR was performed with Phusion High-Fidelity DNA polymerase, Universal PCR primers, and Index (X) Primers. Finally, the library was purified (AMPure XP system) and then qualified using an Agilent Bioanalyzer 2100 system. Clustering of the index-coded samples was performed on a cBot Cluster Generation System with a HiSeq PE Cluster Kit v4 cBot (Illumina) according to the manufacturer’s instructions. After cluster generation, the library
preparations were sequenced on an Illumina HiSeq 2500 platform, and 125-bp paired-end reads were generated. We defined a circRNA expressed or not by junction reads with software CIRI2 (version 2.0.5), CIRI AS (version 1.2) and find_circ (version 1.2). We defined the statistical criteria with software DESeq2 (version1.10.1) for significant differently expressed circRNA as having a p-value < 0.05 and a fold change ≥ 2.0 or ≤ 0.5.

**HUVECs culture and treatment**

HUVECs were acquired from ScienCell Research Laboratories (Carlsbad, CA, USA) and cultured in endothelial cell medium (ECM) (ScienCell, Carlsbad, CA) with 5% fetal bovine serum (FBS), 1% endothelial cell growth supplement and 1% penicillin/streptomycin at 37 °C in 5% CO2. Passage 4-8 were used for experiment. 100ug/ml human ox-LDL (Yiyuan Biotechnologies, Guangzhou, China) was added into cell culture according to experimental requirements.

**Transfection of stubRFP-sensGFP-LC3 adenovirus**

To observe the autophagy of HUVECs, stubRFP-sensGFP-LC3 adenovirus (Genechem, Shanghai, China) were transfected into cells according to the manufacturer’s instructions. Following transfection for 72 h, HUVECs were stimulated with 100ng/ml ox-LDL for 0 h, 3 h and 24 h. After fixed with 4% formaldehyde, the autophagosomes were photographed using confocal laser scanning microscopy.

**Northern blot**

Northern blot was performed as others described. In brief, the samples were run on a 1% formaldehyde-polyacrylamide-urea gel, transferred to positively charged Hybond N+ membranes (Amersham) followed by cross-linking through UV irradiation. The membranes were subjected to hybridization with 100 pmol 3’-digoxigenin (DIG)-labeled probe for hsa_circ_0030042 overnight.
at 50°C. hsa_circ_0030042 probe was synthesized with PCR DIG Probe Synthesis Kit (Roche). The detection was performed using a DIG High Prime DNA Labeling and Detection Starter Kit II (Roche) according to the protocol. The forward primer for hsa_circ_0030042 probe sequence was 5'-agtgactttggatggcatgtt-3'; the reverse primer was 5'-tctggattgagcatccaccaaga-3'. DIG-labeled GAPDH probe was used as control, and its forward primer was 5'-aatcccatcaceatctcc-3'; the reverse primer was 5'-catcaegccacagttcc-3'.

**Western blot**

HUVECs and aortic tissue samples were lysed using RIPA buffer (Solarbio, Beijing, China) for 20 min and collected by centrifugation at 12000 rpm for 10 min at 4°C. Nuclear and cytoplasmic proteins were extracted (Extraction Reagents, Thermo, USA) as needed according to the attached protocol. Equal amounts of proteins and pre-stained protein ladder (Thermo Fisher Scientific) were separated through 12% SDS-PAGE gels (TGX FastCast Acrylamide Kit, Bio-Rad, USA) Then, proteins were transferred to methanol-activated polyvinylidene fluoride membranes with a 0.2 μm pore size (Millipore, Billerica, MA, USA), and incubated with primary antibodies overnight at 4 °C. The membranes were incubated with secondary antibodies (ProteinTech, Rosemont, Penn., USA) the next day for 1 h at room temperature. Bands with antigen-antibody complexes were visualized using Immobilon ECL substrate (Millipore, Billerica, MA, USA), and blots were imaged with a LAS-4000 luminescent image analyser (Fujifilm USA, Valhalla, NY, USA). Protein expression was quantified using Adobe Photoshop CS6 (Adobe Systems, San Jose, CA, USA), normalized to GAPDH expression in each sample, and expressed as a percentage of the control. The anti-FOXO1 antibody (1:1000, 2880, CST), anti-beclin1 antibody (1:1000, ab207612), anti-LC3B antibody (1:2000, ab192890), anti-eIF4A3 antibody (1:1000, ab180573) and anti-GAPDH antibody (1:1000,
5174, CST) were used in this study.

**RNA and gDNA extraction and quantitative real-time PCR**

Total RNA was extracted from HUVECs or tissues using TRIzol reagent (Ambion, Life Technologies, Waltham, MA, USA). The RNA was treated with rRNA depletion (GeneRead, QIAGEN, Germany) or linear RNA depletion (Epicentre, Illumina, Germany) as required. The product was reverse-transcribed into cDNA using a PrimeScript RT Reagent Kit (TakaRa Biotechnology, Dalian, China). The cDNA (1 ng) was subjected to qPCR using SYBR Green (TakaRa) for the relative quantification of mRNA expression. Quantification was accomplished using the 2-ΔΔCt method. GAPDH was used to normalize mRNA levels. The hsa_circ_0030042 divergent primer 1: 5'- cttgacaatgttggtcaca-3' (forward); 5'-aggagattcctgccttg-3' (reverse). The hsa_circ_0030042 divergent primer 2: 5'-tggatggatactggatt-3' (forward); 5'-attgagcatccaagaag-3' (reverse). The beclin1 forward primer: 5'-aatggtggtttctgtggact-3'; the reverse primer: 5'-cctcctctgtgacatgga-3'; the reverse primer: 5'-aatgtagcctgtcactaactc-3'.

Total gDNA was extracted from HUVECs using Genomic DNA Extraction Kit (TAKARA) according to the procedure. The hsa_circ_0030042 convergent forward primer: 5'-ggcaggcagagcatcata-3', the convergent reverse primer: 5'-ttggtcagccagtctgcat-3'. The homo-GAPDH convergent forward primer: 5'-aagaagtttgtgaagcgc-3'; the convergent reverse primer: 5'-gtcaacaggtgaggggt-3'. The homo-GAPDH divergent forward primer: 5'-agaaggtgaggtcatttt-3'; the divergent reverse primer: 5'-tcgccccacttgattttgga-3'.

**Electron Microscopy**

Stable hsa_circ_0030042 overexpression HUVECs (c0030042) and empty vector transfected
HUVECs (circ-N.C) were transiently transfected with eIF4A3 siRNA for 48 h and 100ug/ml ox-LDL treated 24h. Then the cells were collected, 1,000 rpm centrifuge 5 min, the supernatant was discarded, 1 mL PBS resuspended; centrifuged 10 min, the supernatant was discarded, fixed with 2.5% glutaraldehyde, and then the cells were embedded in spur resin after dehydration. Thin sections were cut on a Reichert Ultracut E microtome. Sectioned grids were stained with saturated solution of uranyl acetate and lead citrate. Sections were examined at 80 kV with a Hitachi transmission electron microscope.

**Indirect Immunofluorescence Assay and Confocal Microscopy**

circ-N.C and c0030042 group cells were grown on cover slips in 24-well plates. Upon reaching 70–80% confluence, cells were fixed in 4% paraformaldehyde for 30 min at room temperature and washed with PBS. Subsequently, permeabilized with PBS containing 0.5% Triton-X-100 for 15 min and blocked with PBS containing 5% bovine serum albumin for 1 h at room temperature. Then, samples were incubated with anti-eIF4A3 antibody (1:500, ab180573) for 4°C overnight, followed by incubation with anti-rabbit IgG Alexa Fluor 594-conjugated antibody for 1 h, and cells nuclei were visualized with 4′,6-diamidino-2-phenylindole (DAPI, Invitrogen). All fluorescence images were acquired on an Olympus confocal microscope.

**Flow Cytometry**

Phosphotidylserine (PS) exposure of ox-LDL treated cells were analyzed using an Annexin V PE/7-Amino-Actinomycin (7-AAD) Apoptosis Detection Kit (BD Pharmingen, CA, USA) according to the protocol. Unstained control cells, cells stained with PE Annexin V only, and cells stained with 7-AAD only were used to set up compensation and to define quadrants. Apoptotic cells were examined within 1 h, and the percentage of PS positive cells (right quadrant) was measured using
FlowJo software (Tree Star, Ashland, OR, USA).

**Actinomycin D treatment**

To block transcription, cell culture medium was added with 10 ug/ml Actinomycin D (Sigma-Aldrich, St. Louis, MO, USA) in 0h, 3h, 6h, 9h and 12h. After treatment with Actinomycin D for different time points, the remaining of mRNA was assessed using qRT-PCR.

**Enzyme-Linked Immunosorbent Assay (ELISA)**

The level of IL-1β in mice plasma was determined using a mouse IL-1β ELISA Kit (ab197742, abcam, UK). The level of IL-6 in mice plasma was assessed using a mouse IL-6 ELISA Kit (ab222503). The level of MCP-1 in mice plasma was tested using a mouse MCP-1 ELISA Kit (R&D system, Minneapolis, MN, USA). All kits were used according to the manufacturer’s instructions. The OD value was recorded at 450 nm (with reference of 570 nm) in an ELISA plate reader.
## Table S1: Significant altered circRNA profile in CHD PBMCs

| Sequencing ID | circBase ID | log2Fold Change | pval   | padj    | significant | trend | chrom | txStart | txEnd | length | GeneName     | Catalog     |
|---------------|-------------|-----------------|--------|---------|-------------|-------|-------|---------|-------|--------|--------------|-------------|
| hg38_circ_0052138 | hg38_circ_0052138 | 3.1318          | 3.06E-12 | 1.43E-09 | TRUE        | up    | chr19 | 39883304 | 39896143 | 1000    | FCGBP        | exonic      |
| hg38_circ_0081334 | hsa_circ_0119359 | 3.0972          | 9.32E-10 | 1.51E-07 | TRUE        | up    | chr2  | 232851276 | 232851449 | 173     | GIGYF2       | antisense   |
| hg38_circ_0114298 |              | 2.9897          | 4.01E-07 | 2.08E-05 | TRUE        | up    | chr6  | 32661966 | 32757883 | 100     | HLA-DQB1     | sense overlapping |
| hg38_circ_0050204 |              | 2.919           | 1.03E-09 | 1.62E-07 | TRUE        | up    | chr19 | 12792306 | 12792484 | 500     | HOOK2       | intronic    |
| hg38_circ_0052139 |              | 2.8563          | 9.14E-06 | 0.000257 | TRUE        | up    | chr19 | 39885672 | 39899697 | 1000    | FCGBP        | exonic      |
| hg38_circ_0085746 | hsa_circ_0006251 | 2.719           | 1.40E-13 | 1.15E-10 | TRUE        | up    | chr2  | 74046277 | 74048411 | 2134    | TET3        | exonic      |
| hg38_circ_0074649 | hsa_circ_0110941 | 2.6958          | 4.57E-06 | 0.000147 | TRUE        | up    | chr1  | 1637761  | 1704655  | 66894   | CDK11B      | sense overlapping |
| hg38_circ_0057643 |              | 2.6231          | 4.73E-10 | 8.77E-08 | TRUE        | up    | chr1  | 1636332 | 1703269  | 100     | CDK11B      | sense overlapping |
| hg38_circ_0074503 | hsa_circ_0001232 | 2.5501          | 6.67E-09 | 7.67E-07 | TRUE        | up    | chr22 | 39015594 | 39021536 | 5942    | AL022318.4  | intronic    |
| hg38_circ_0052140 |              | 2.4768          | 4.28E-05 | 0.000864 | TRUE        | up    | chr19 | 39885990 | 39902124 | 1000    | FCGBP       | exonic      |
| hg38_circ_0006441 |              | 2.4594          | 4.30E-06 | 0.00014   | TRUE        | up    | chr11 | 105030329 | 105066245 | 100     | CASP1       | sense overlapping |
| hg38_circ_0036776 |              | 2.3949          | 5.30E-23 | 1.09E-18 | TRUE        | up    | chr16 | 31362610 | 31410524 | 100     | ITGAX       | sense overlapping |
| hg38_circ_0113938 |              | 2.3868          | 5.18E-15 | 8.89E-12 | TRUE        | up    | chr6  | 29945450 | 30009367 | 100     | HCG9        | sense overlapping |
| hg38_circ_0073043 | hsa_circ_0062287 | 2.3855          | 0.00023315 | 0.003293 | TRUE        | up    | chr22 | 20052464 | 20056013 | 3549    | TANGO2      | exonic      |
| hg38_circ_0057646 | hsa_circ_0110940 | 2.363           | 1.36E-05 | 0.000349 | TRUE        | up    | chr1  | 1637407 | 1704344 | 66937   | CDK11B      | sense overlapping |
| hg38_circ_0057551 |              | 2.3542          | 6.04E-07 | 2.94E-05 | TRUE        | up    | chr1  | 161548420 | 161626402 | 100     | FCGR3B      | sense overlapping |
| hg38_circ_0009842 |              | 2.3409          | 0.0002752 | 0.003761 | TRUE        | up    | chr11 | 48027270 | 48027508 | 500     | PTPRJ       | intronic    |
| hg38_circ_0013083 |              | 2.2578          | 0.00019466 | 0.002845 | TRUE        | up    | chr11 | 9248409  | 9248643  | 100     | DENND5A     | antisense   |
| hg38_circ_0056414 | hsa_circ_0004482 | 2.0927          | 0.0013975 | 0.012973 | TRUE        | up    | chr1  | 151262160 | 151264028 | 1868    | PSMD4       | exonic      |
| hg38_circ_0035431 |              | 2.0904          | 0.0014127 | 0.013061 | TRUE        | up    | chr16 | 1744583  | 1744762  | 100     | MAPK8IP3    | antisense   |
| hg38_circ_0030223 | hsa_circ_0103395 | 2.0502          | 0.00014066 | 0.002234 | TRUE        | up    | chr15 | 39582470 | 39582680 | 210     | THBS1       | sense overlapping |
| hg38_circ_0056093 | hsa_circ_0000004 | 2.0306          | 1.31E-07 | 8.32E-06 | TRUE        | up    | chr1  | 1495484 | 1529331 | 33847   | ATAD3B      | sense overlapping |
| hg38_circ_0114300 |              | 2.0061          | 0.0014718 | 0.013445 | TRUE        | up    | chr6  | 32664797 | 32759131 | 100     | HLA-DQB1    | sense overlapping |
| hg38_circ_0056967 | hsa_circ_0014624 | 1.9942 | 0.0023522 | 0.019066 | TRUE | up | chr1 | 155764999 | 155766709 | 1710 | GON4L | exonic |
|------------------|-----------------|--------|------------|----------|-------|----|------|----------|----------|------|--------|--------|
| hg38_circ_0060201 |                 | 1.9798 | 0.0012041 | 0.01164  | TRUE | up | chr1 | 207563863 | 207578203 | 1000 | CR1    | exonic |
| hg38_circ_0113778 |                 | 1.9489 | 6.85E-06  | 0.000203 | TRUE | up | chr6 | 26407670  | 26444304  | 100  | BTN3A1 | sense overlapping |
| hg38_circ_0010305 | hsa_circ_0022392 | 1.9392 | 0.0014126 | 0.013061 | TRUE | up | chr11| 61862971  | 61863786  | 815  | FADS2  | exonic |
| hg38_circ_0124959 | hsa_circ_0083377 | 1.8628 | 6.89E-06  | 0.000204 | TRUE | up | chr8 | 13088486  | 13088704  | 218  | DLC1   | exonic |
| hg38_circ_0119325 |                 | 1.8091 | 0.0053904 | 0.034593 | TRUE | up | chr7 | 142791693 | 142796610 | 100  | TRBJ2-1| sense overlapping |
| hg38_circ_0010405 |                 | 1.8003 | 0.0080722 | 0.009096 | TRUE | up | chr11| 62539659  | 62539872  | 500  | AHNK   | intronic |
| hg38_circ_0119326 |                 | 1.7969 | 3.46E-11  | 1.11E-08 | TRUE | up | chr7 | 142791693 | 142796895 | 100  | TRBJ2-1| sense overlapping |
| hg38_circ_0052137 | hsa_circ_0109623 | 1.7821 | 0.00019458| 0.002845 | TRUE | up | chr19| 39877662  | 39893527  | 15865| FCGBP  | exonic |
| hg38_circ_0051386 |                 | 1.7679 | 0.0050955 | 0.033166 | TRUE | up | chr19| 3197909   | 3198222   | 100  | NCLN   | antisense |
| hg38_circ_0052591 |                 | 1.7416 | 2.97E-06  | 0.000106 | TRUE | up | chr19| 45227661  | 45228266  | 100  | AIFM2  | exonic |
| hg38_circ_0004576 |                 | 1.6917 | 0.0097274 | 0.053075 | FALSE| up | chr10| 70123404  | 70124097  | 1000 | ATP2A3 | exonic |
| hg38_circ_0042152 |                 | 1.6878 | 5.13E-06  | 0.000161 | TRUE | up | chr17| 3935191   | 3936469   | 1000 | HK3    | sense overlapping |
| hg38_circ_0054091 |                 | 1.6846 | 0.0052026 | 0.033692 | TRUE | up | chr19| 7643749   | 7643988   | 500  | STXB2  | intronic |
| hg38_circ_0054092 |                 | 1.6846 | 0.0052026 | 0.033692 | TRUE | up | chr19| 7643756   | 7643995   | 100  | STXB2  | antisense |
| hg38_circ_0054093 |                 | 1.6846 | 0.0052026 | 0.033692 | TRUE | up | chr19| 7643774   | 7644013   | 100  | STXB2  | antisense |
| hg38_circ_0105998 |                 | 1.6818 | 6.01E-05  | 0.001128 | TRUE | up | chr5 | 176891036 | 176893088 | 100  | HK3    | sense overlapping |
| hg38_circ_0057873 |                 | 1.6691 | 0.005902  | 0.037215 | TRUE | up | chr1 | 1676063   | 1738448   | 1000 | SLC35E2| sense overlapping |
| hg38_circ_0000077 |                 | 1.6684 | 0.003533  | 0.02474  | TRUE | up | chr10| 100529532 | 100529768 | 500  | HIF1AN | intronic |
| hg38_circ_0018333 | hsa_circ_0000400 | 1.6669 | 1.17E-10  | 2.83E-08 | TRUE | up | chr12| 49131297  | 49186833  | 55536| TUBA1A | sense overlapping |
| hg38_circ_0099741 |                 | 1.6607 | 0.00035954| 0.004608 | TRUE | up | chr4 | 3518033   | 3525051   | 1000 | LRPAP1 | exonic |
| hg38_circ_0004146 |                 | 1.6563 | 0.006082  | 0.037665 | TRUE | up | chr10| 67894973  | 67895137  | 500  | SIRT1   | intronic |
| hg38_circ_0050770 | hsa_circ_0050001 | 1.6466 | 0.0013571 | 0.012649 | TRUE | up | chr19| 17530754  | 17532388  | 1634 | FAM129C| exonic |
| hg38_circ_0053488 |                 | 1.6266 | 0.0081784 | 0.047082 | TRUE | up | chr19| 54221827  | 54241127  | 100  | LILRB3 | sense overlapping |
| hg38_circ_0056768 | hsa_circ_000135 | 1.6158 | 0.013197  | 0.066006 | FALSE| up | chr1 | 155212384 | 155232845 | 20461| MTX1    | sense overlapping |
| hg38_circ_0031586 | hsa_circ_0035271 | 1.6113 | 0.013751  | 0.067835 | FALSE| up | chr15| 50958491  | 50958794  | 303  | AP4E1  | exonic |
| hg38_circ_0057816 | hsa_circ_0000006 | 1.6017 | 4.62E-09  | 5.57E-07 | TRUE | up | chr1 | 1669663   | 1734835   | 65172| SLC35E2| sense overlapping |
| Gene         | CircId         | Log2Fold | SeqType  | AffectedChr | AffectedPosition       | pvalue   |
|--------------|----------------|----------|----------|-------------|------------------------|----------|
| ARFGEF1      | hsa_circ_00001978 | -1.21E-15 | 1.28E-06 | TRUE        | 148666278              | 861      |
| STAG1        | hsa_circ_0001707 | 9.17E-13  | 4.96E-10 | TRUE        | 48502125               | 427      |
| FOXP1        | hsa_circ_00001669 | 1.56E-11  | 5.62E-09 | TRUE        | 148651998              | 10770    |
| MIS18BP1     | hsa_circ_0003915 | -2.9407   | 2.69E-08 | TRUE        | 199368604              | 64910    |
| TRPM7        | hsa_circ_0001640 | 2.45E-13  | 1.72E-10 | TRUE        | 177353307              | 7370     |
| TPT1         | hsa_circ_00126249 | -3.3155   | 9.43E-09 | TRUE        | 38790069               | 1162     |
| MYBL1        | hsa_circ_0004176 | 2.61E-08  | 2.19E-06 | TRUE        | 67966682               | 47504    |
| DNM2         | hsa_circ_00135105 | -3.1455   | 7.53E-06 | TRUE        | 92517275               | 980      |
| THEMIS       | hsa_circ_0012983 | 1.09E-07  | 7.21E-06 | TRUE        | 33351218               | 36926    |
| AC005154.1   | hsa_circ_0005893 | -3.1646   | 9.04E-06 | TRUE        | 5396632               | 34540    |
| FARS2        | hsa_circ_0004176 | 2.61E-08  | 2.19E-06 | TRUE        | 67966682               | 47504    |
| HERC4        | hsa_circ_00135105 | -3.1455   | 7.53E-06 | TRUE        | 92517275               | 980      |
| PEX1         | hsa_circ_0012983 | 1.09E-07  | 7.21E-06 | TRUE        | 33351218               | 36926    |
| CACNA1D      | hsa_circ_0012983 | 1.09E-07  | 7.21E-06 | TRUE        | 33351218               | 36926    |
| FBNW7       | hsa_circ_0006247 | 3.92E-06  | 0.00013 | TRUE        | 243637610              | 58106    |
| AKT3         | hsa_circ_0013752 | -2.9883   | 2.09E-07 | TRUE        | 65051461               | 24451    |
| intergenic   | hsa_circ_0013752 | -2.9883   | 2.09E-07 | TRUE        | 65051461               | 24451    |
| exonic       | hsa_circ_0022874 | -2.8693   | 1.45E-05 | TRUE        | 45336535               | 853      |
| overpeaking  | hsa_circ_0022874 | -2.8693   | 1.45E-05 | TRUE        | 45336535               | 853      |
| TRPM7        | hsa_circ_0031188 | 1.48E-08  | 1.42E-06 | TRUE        | 50586391               | 6235     |
| exonic       | hsa_circ_0031188 | 1.48E-08  | 1.42E-06 | TRUE        | 50586391               | 6235     |
| exonic       | hsa_circ_0025991 | -2.8371   | 3.43E-06 | TRUE        | 45246742               | 635      |
| exonic       | hsa_circ_0025991 | -2.8371   | 3.43E-06 | TRUE        | 45246742               | 635      |
| exonic       | hsa_circ_0025991 | -2.8371   | 3.43E-06 | TRUE        | 45246742               | 635      |
| exonic       | hsa_circ_0025991 | -2.8371   | 3.43E-06 | TRUE        | 45246742               | 635      |
| exonic       | hsa_circ_0025991 | -2.8371   | 3.43E-06 | TRUE        | 45246742               | 635      |
circRNAs with a padj ≤0.05 and a fold change ≥2.0 or ≤0.5 were considered differentially expressed.

**Table S1** Top 50 significantly upregulated and 50 down regulated in CHD PBMCs were shown in details. The red color represented the up-regulated circRNAs. The green color represented the down-regulated circRNAs in CHD. The blue color showed the selected exonic CHD related circRNA, hsa_circ_0030042. Differential expression analysis between the two groups was performed using DESeq2. The adjusted p-value (padj) is the p-value adjusted for multiple testing using Benjamini-Hochberg to estimate the false discovery rate (FDR). circRNAs with a padj < 0.05 and a fold change ≥2.0 or ≤0.5 were considered differentially expressed.
Table S2: Interaction probabilities of three RBPs to hsa_circ_0030042

| RBP   | Tags of RBPs matching flanking regions on hsa_circ_0030042 | RF classifier | SVM classifier |
|-------|-------------------------------------------------------------|---------------|---------------|
| AGO2  | 8                                                           | 0.75          | 0.9           |
| eIF4A3 | 6                                                           | 0.75          | 0.83          |
| HuR   | 3                                                           | 0.8           | 0.75          |

Table S2: Detailed information of RPISeq (version 1.0) predicting the probabilities of three RBPs combine with hsa_circ_0030042.

Table S3: Basic information of selected coronary heart disease patients and controls.

| Variables                          | ctrl n = 30 | CHD n = 70 | P       |
|------------------------------------|-------------|------------|---------|
| Mean ± SD or n (percentage)        |             |            |         |
| Stenosis of the left main coronary trunk or maximum stenosis in a major epicardial artery (%) | 16.67±17.29 | 79.21±17.40 | < 0.0001 |
| TC (mmol/l)                        | 4.148±0.17  | 4.040±0.13 | ns      |
| LDL-C (mmol/l)                     | 2.456±0.12  | 2.597±0.12 | ns      |
| HDL-C (mmol/l)                     | 1.303±0.06  | 1.198±0.03 | ns      |
| Age (years)                        | 57.57±1.39  | 60.99±1.18 | ns      |
| Gender (M/FM)                      | 16(53)/14(47) | 49(70)/21(30) | ns      |
| Diabetes (yes/no)                  | 4(13)/26(87) | 16(23)/54(77) | ns      |
| Smoking history (yes/no)           | 10(33)/20(67) | 37(53)/33(47) | ns      |
| Family history of CHD (yes/no)     | 4(13)/26(87) | 19(27)/51(73) | ns      |
| Alcohol intake history (yes/no)    | 9(30)/21(70) | 26(37)/44(63) | ns      |
| Other underlying diseases          | no          | no         | ns      |
| Pharmacological therapy            | Aspirin and Clopidogrel | Aspirin and Clopidogrel | ns      |

Table S3: Detailed information of coronary heart disease patients and controls where PBMCs acquired. TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol.
Supplementary Figure 1: qRT-PCR validated mmu_circ_0010680 in 3-month-old C57BL/6 and ApoE/- mice. Data are presented as mean ± SD. Student’s t-test. *p < 0.05, **p < 0.01. n = 6 pairs.
Supplementary Figure 2 Western blot for quantifying protein levels in 12h shear stress-stimulated c0030042 and circ-N.C (HCAECs). Two-way ANOVA. Compared with circ-N.C + static, *p < 0.05, **p < 0.001; compared with circ-N.C+OSS, ^p < 0.05, ^^p < 0.01, ^^^p < 0.001; compared with circ-N.C+PSS, #p < 0.05, ###p < 0.001. n = 6. PSS, unidirectional pulsatile shear stress, 12 dyne/cm2, OSS, oscillatory shear stress, 0±4 dyne/cm2. Data are presented as mean ± SD.
Supplementary Figure 3:

A

100ug/ml ox-LDL

circ-N.C+N.C
circ-N.C+eIF4A3-siR
c0030042+N.C
c0030042+eIF4A3-siR

B

Double membrane vacuoles per cell

circ-N.C+N.C
circ-N.C+eIF4A3-siR
c0030042+N.C
c0030042+eIF4A3-siR

C

DAPI  eIF4A3  Merge

circ-N.C
c0030042
**Supplementary Figure 3** eIF4A3 depression could further decrease the autophagic vacuoles in both c0030042 and circ-N.C group. **A.** Autophagy by Electron Microscope (×15000). Stable hsa_circ_0030042 overexpression HUVECs (c0030042) and empty vector transfected HUVECs (circ-N.C) were transiently transfected with eIF4A3 siRNA or N.C for 48 h and 100ug/ml ox-LDL treated 24h. Autophagic vacuoles were indicated. Scale bar, 5µm. **B.** Each group counts six cells and showing the average number of double membrane vacuoles per cell. The data were expressed as mean ± SD. One-way ANOVA. Compared with circ-N.C+N.C, **p < 0.01; compared with c0030042+N.C, ###p < 0.001). n = 6. **C.** Immunofluorescence confocal results of eIF4A3 localization in circ-N.C and c0030042 group. Scale bar, 10µm.

**Supplementary Figure 4:**

**Supplementary Figure 4** Murine eIF4A3 could interact with mmu_circ_0010680 and hsa_circ_0030042. RNA immunoprecipitation of eIF4A3 from mice with 6-weeks c0030042-lentivirus transfection. hsa_circ_0030042, mmu_circ_0010680 and GAPDH qRT-PCR products were determined by agarose gel electrophoresis. n=5 mice of each sample.
Supplementary Figure 5:

A: Triglyceride level in plasma (mmol/L)
B: Total cholesterol level in plasma (mmol/L)
C: Glucose level in plasma (mmol/L)
D: LDL-C level in plasma (mmol/L)
E: HDL-C level in plasma (mmol/L)
F: Images of thoracic and abdominal aorta
G: Lipid area(% of thoracic aorta cross-section)
H: Lipid area(% of abdominal aorta cross-section)
Supplementary Figure 5 The lipid level and deposition in four groups. A - E ELISA tested plasma level of triglyceride, total cholesterol, LDL-C, HDL-C and glucose in four groups of mice (GFP-N.C, c0030042, h-eIF4A3-GFP and c0030042+h-eIF4A3-GFP group). Data are presented as mean ± SD. One-way ANOVA. n ≥ 7. F – H Oil Red O staining of cross section of thoracic and abdominal aortas and quantification in four groups of mice. Data are presented as mean ± SD. One-way ANOVA. Compared with GFP-N.C, **p < 0.01, ***p < 0.001; compared with h-eIF4A3-GFP, ###p < 0.001). n = 6.