Figure S1. Immunofluorescence and hematoxylin and eosin staining of EpCAM$^{-/-}$ and WT murine livers. (A) Immunofluorescence staining of EpCAM in the livers of EpCAM$^{-/-}$ mice and WT mice at embryonic day (E)18.5. (B) The expression of EpCAM was significantly decreased in the livers of EpCAM$^{-/-}$ mice at post-natal day (P)0. (C) Immunofluorescence staining of EpCAM in the livers of EpCAM$^{-/-}$ mice and WT mice at P0. (D) H&E staining at post-natal day (P)0 (upper panels) and P4 (lower panels). The livers of EpCAM$^{-/-}$ mice at P4 exhibited marked vacuolation compared with WT mice livers at P4. EpCAM, epithelial cell adhesion molecule; WT, wild-type.

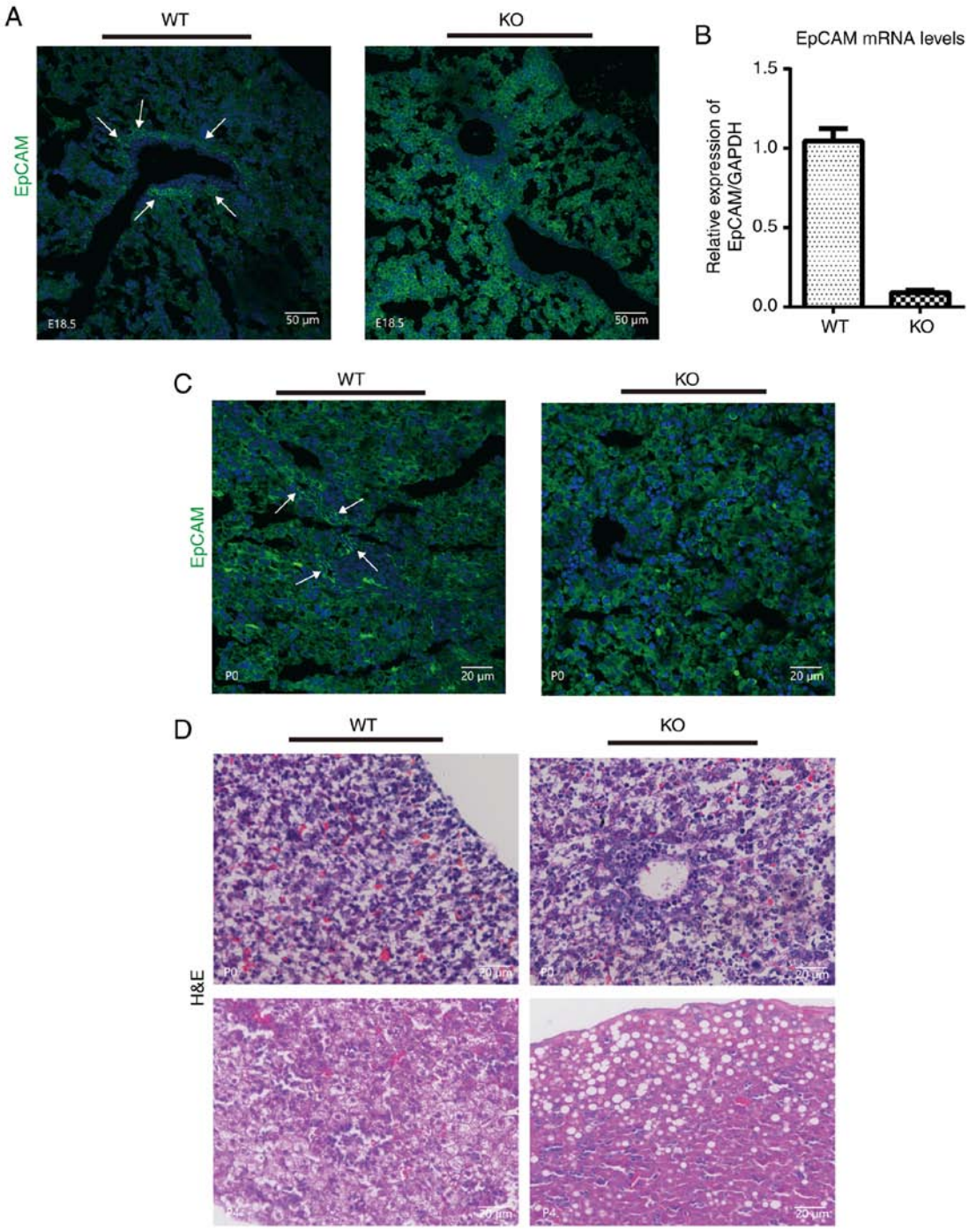

Figure S2. Overview of the known and novel circRNAs in the liver of EpCAM$^{-/-}$ mice. The length distribution of the (A) known circRNAs and (B) novel circRNAs were determined. The types of (C) known circRNAs and (D) novel circRNAs are presented. The chromosome distribution of (E) known circRNAs and (F) novel circRNAs were identified. circRNA, circular RNA; EpCAM, epithelial cell adhesion molecule.

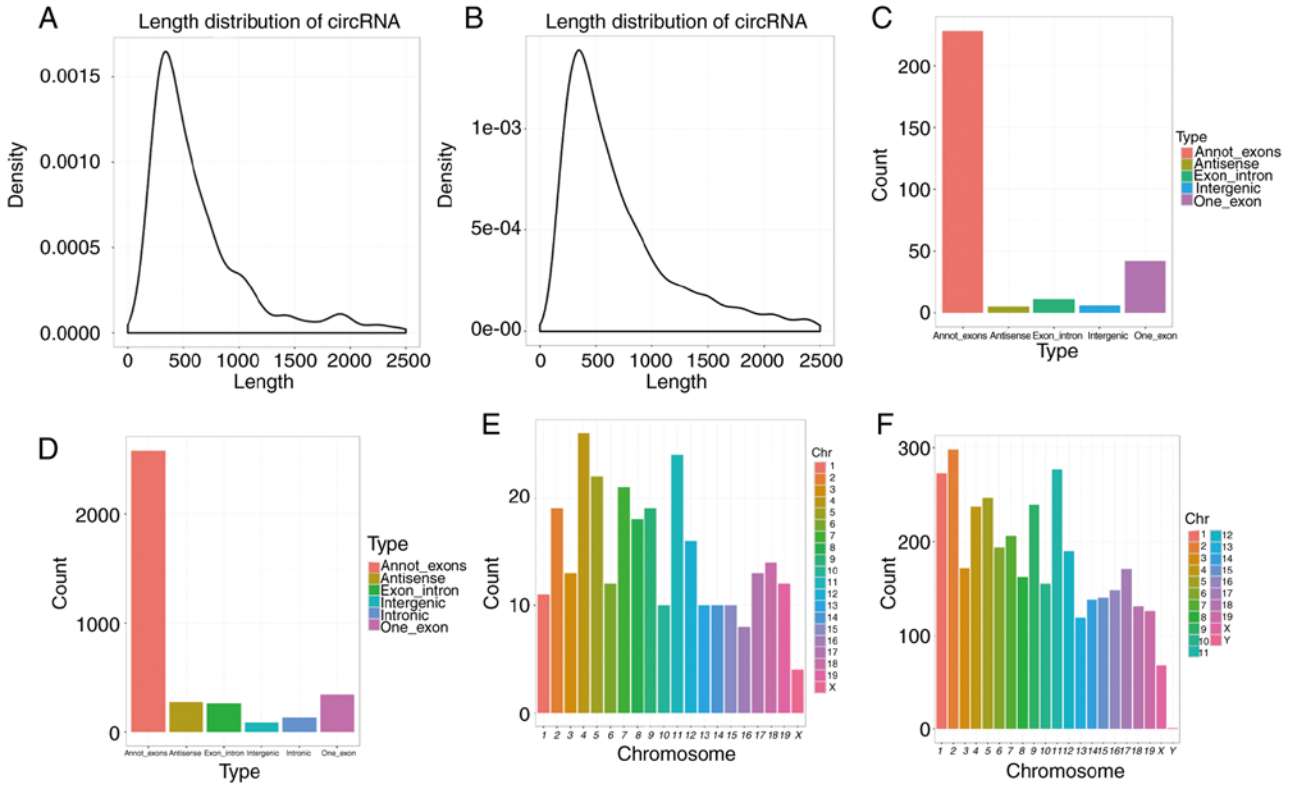

Figure S3. miRNA target sites of novel_circ_000189. Red represents the complementary sequence of circRNA with miRNAs, green represents the binding of guanine and uracil (GU), and blue demonstrates the section of miRNA that cannot bind to circRNA. circRNA direction: 5'-3', miRNA direction 3'-5'. miRNA, microRNA; circRNA, circular RNA.

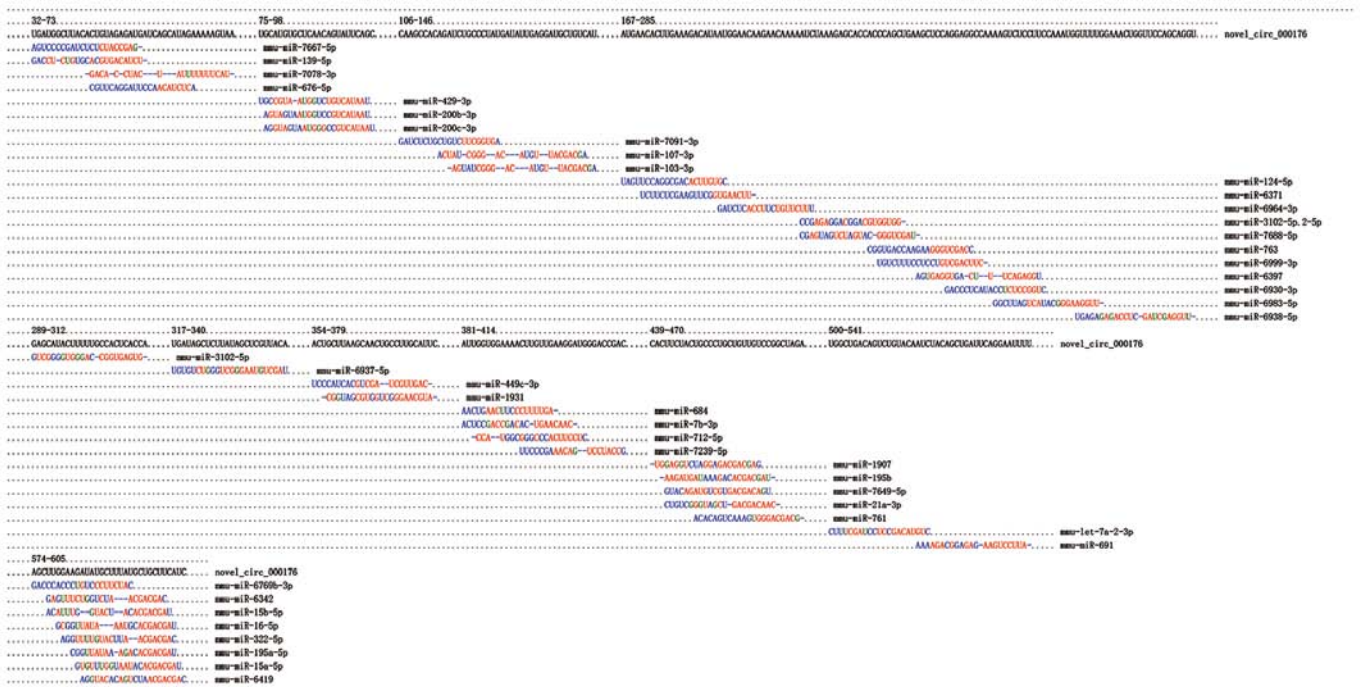

Figure S4. miRNA target sites of novel_circ_000176. Red represents the complementary sequence of circRNA with miRNAs, green represents the binding of guanine and uracil (GU), and blue demonstrates the section of miRNA that cannot bind to circRNA. CircRNA direction: 5'-3', miRNA direction 3'-5'. miRNA, microRNA; circRNA, circular RNA.

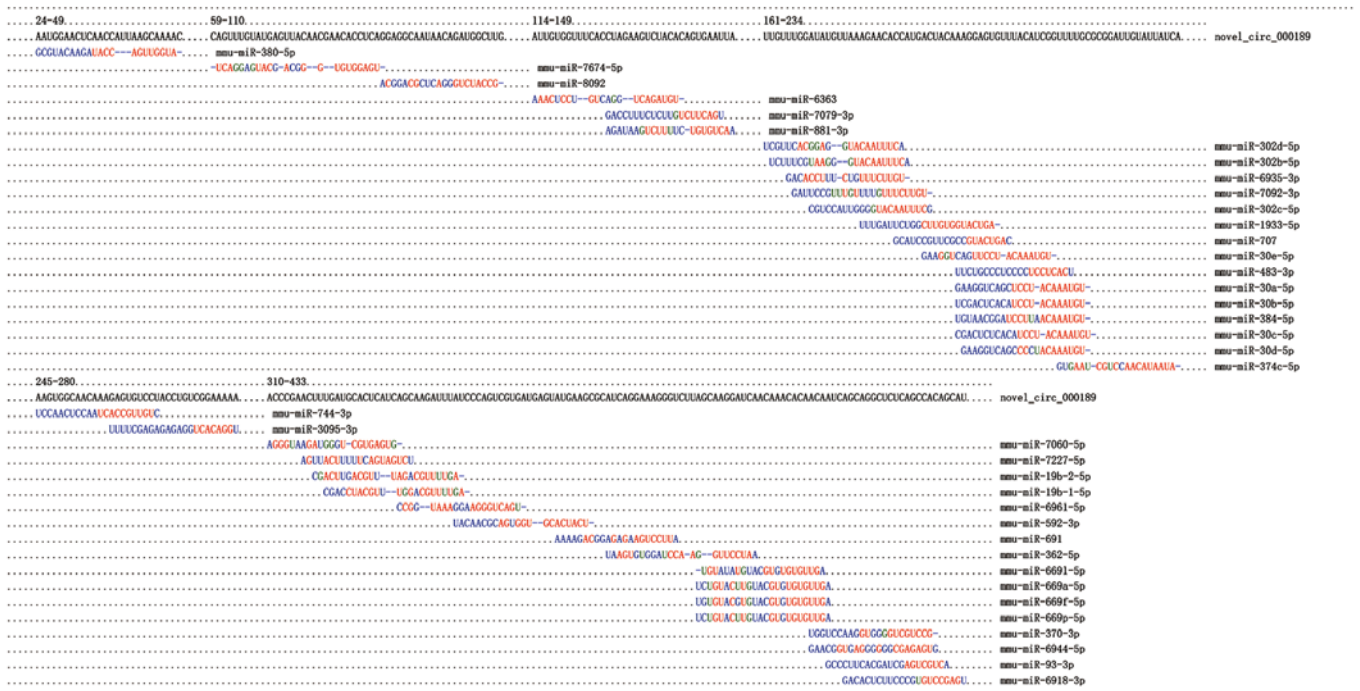

Figure S5. miRNA target sites of novel_circ_002561. Red represents the complementary sequence of circRNA with miRNAs, green represents the binding of guanine and uracil (GU), and blue demonstrates the section of miRNA that cannot bind to circRNA. CircRNA direction: 5'-3', miRNA direction 3'-5'. miRNA, microRNA; circRNA, circular RNA.

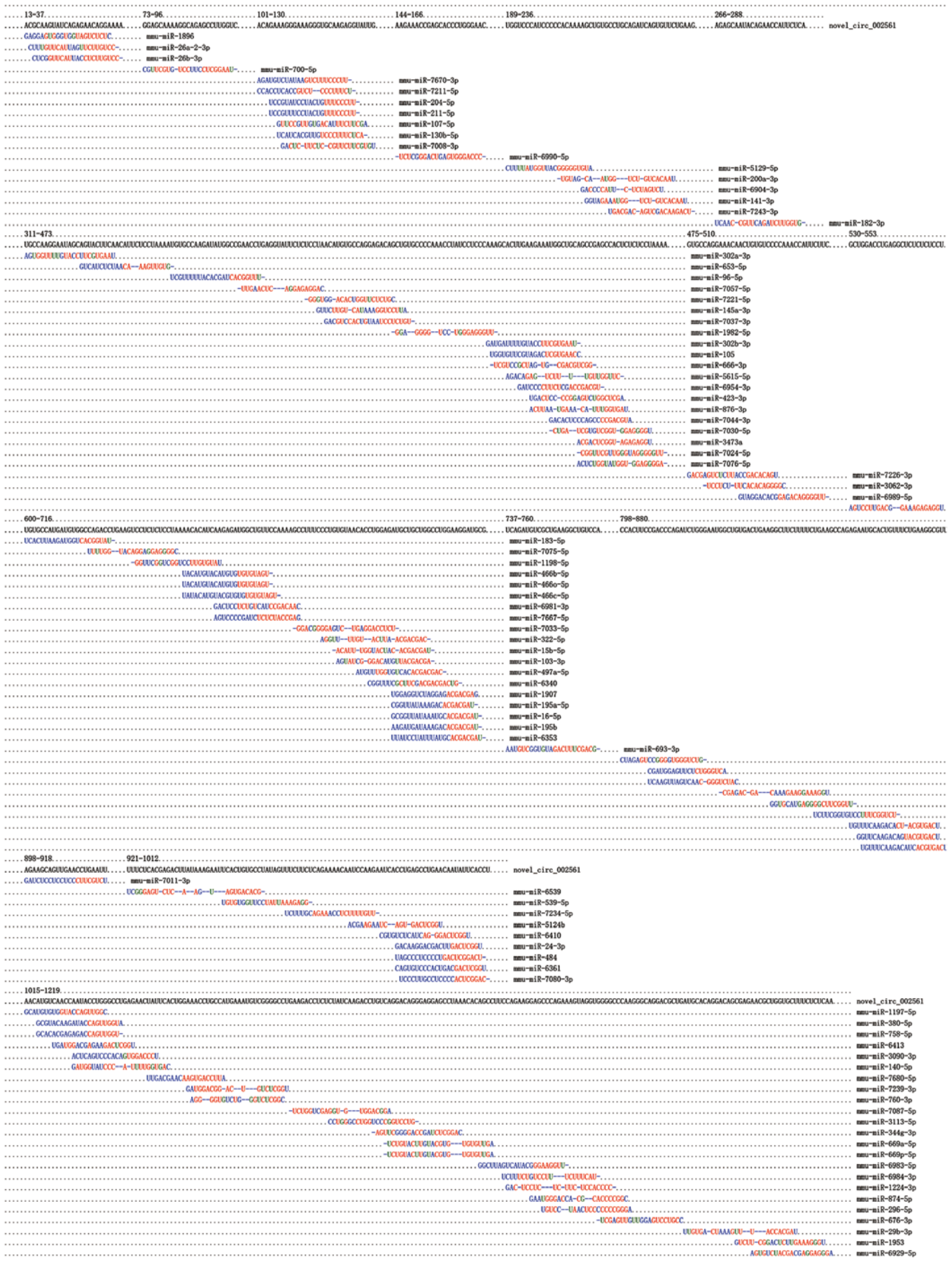

Figure S6. Prediction of target associations of the circRNA-microRNA-mRNA network. The circRNA-microRNA-mRNA association networks of (A) novel_circ_002561, (B) novel_circ_000176 and (C) novel_circ_000189 target genes. circRNA, circular RNA.

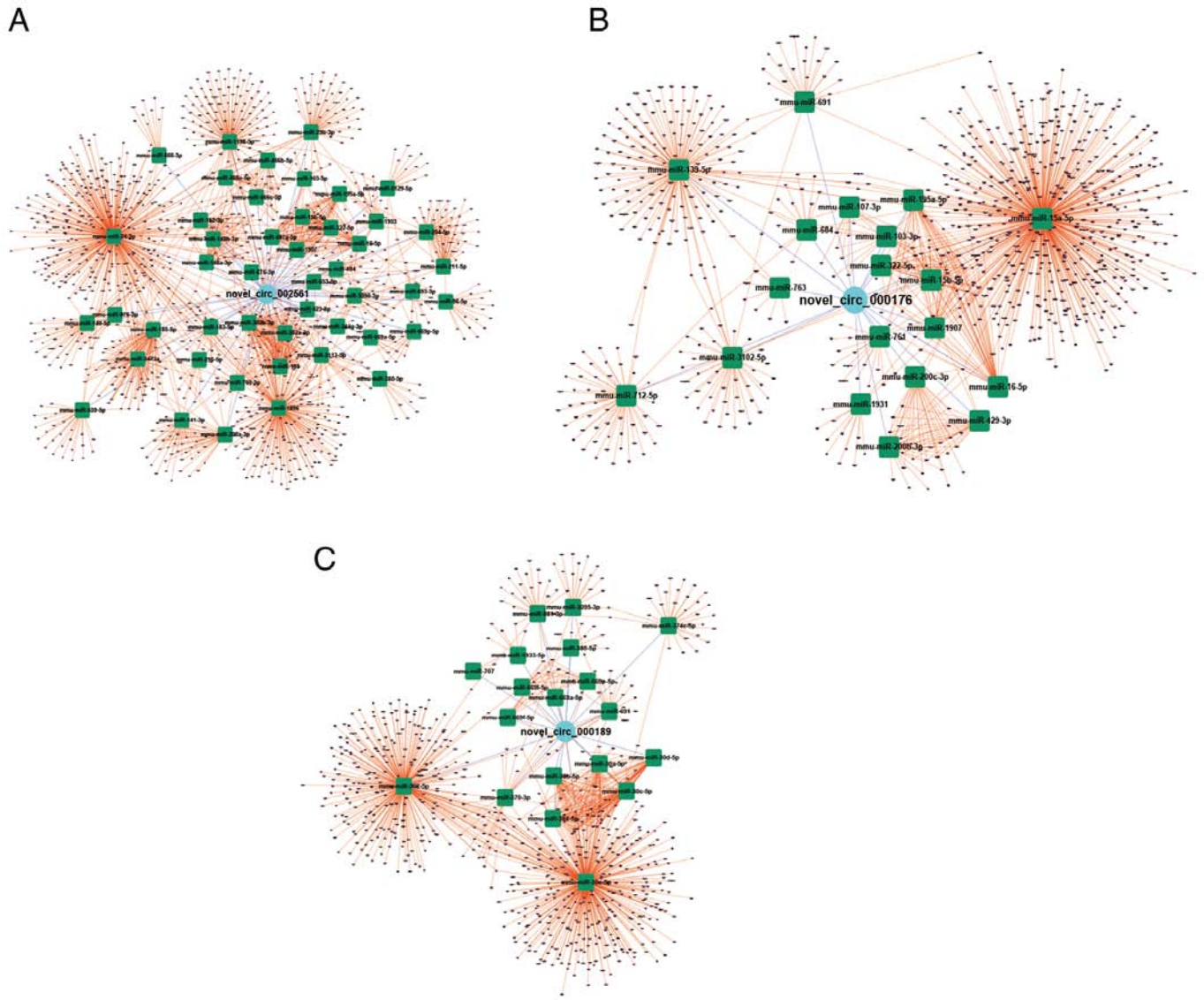

Figure S7. Prediction of target associations of circRNA-microRNA-mRNA network of known differentially expressed circRNAs. The circRNA-microRNA-mRNA associations networks of (A) novel_circ_000125, (B) novel_circ_000596, (C) novel_circ_000649, (D) novel_circ_002754, (E) novel_circ_002813 and (F) novel_circ_003291. circRNA, circular RNA.

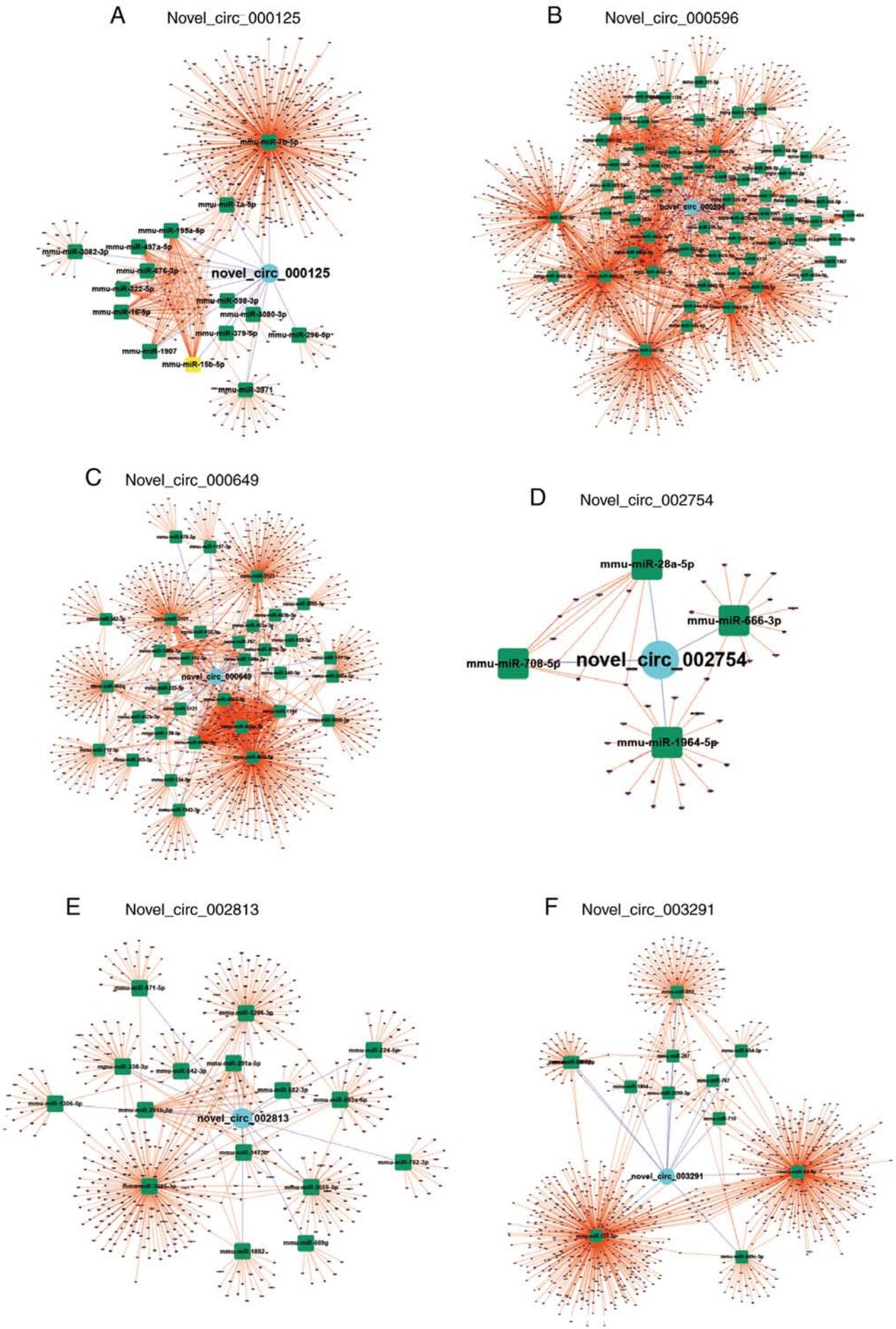

Figure S8. Prediction of target associations of circRNA-microRNA-mRNA network of novel differentially expressed circRNAs. The circRNA-microRNA-mRNA association networks of (A) novel_circ_000461, (B) novel_circ_000813, (C) novel_circ_002426, (D) novel_circ_001018, (E) novel_circ_003491 and (F) novel_circ_002569. circRNA, circular RNA.

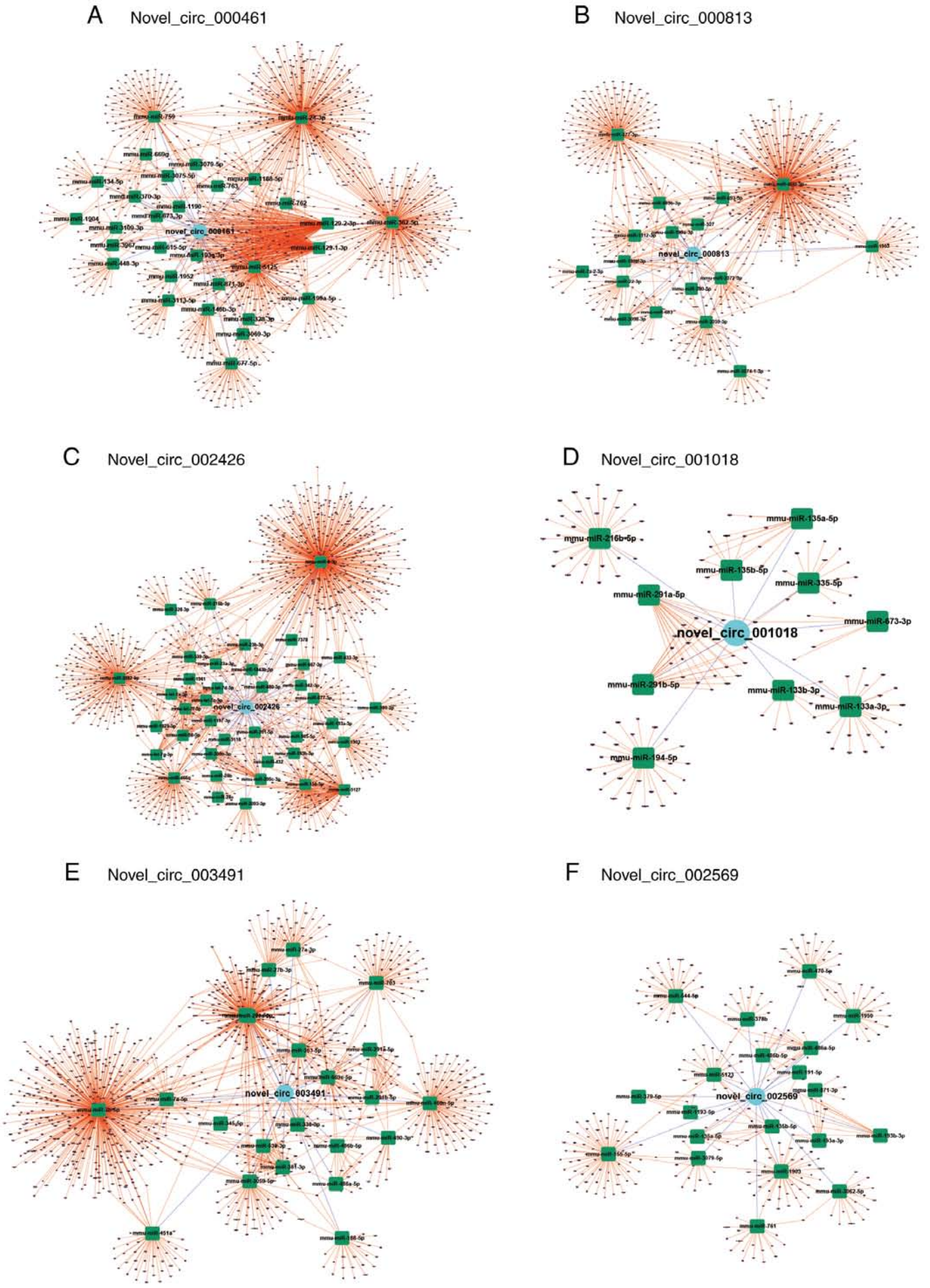

Table SI. Primer sequences of genes.

Gene	Forward sequence	Reverse sequence
DLK1	GGCCATCTGCTTCACCATCCTG	GCTCCTCGCCGCTGTTATACTG
ALB	CAAAATGCCATTCTAGTTCGCT	ACAGATAGTCTTCCACACAAGG
CD26	CCAATTCCAGAAGACAACCTTG	CATCTGCCGTTCCATGAATAAG
H19	GAACAGAAGCATTCTAGGCTG	TTCTAAGTGAATTACGGTGGG
CD34	GTTATTTCCTGATGAACCGTCG	CTCCACCATTCTCCGTGTAATA
Thy1	ATAACTCCATCCAGCATGAGTT	GGTAAGGACCTTGATATAGGGC
Axin2	ATGTTAGAGAGTGAGCGGCAGA	CTTCAGCATCCTCCTGTATGGA
Lgr5	ACCCGCCAGTCTCCTACATC	GCATCTAGGCGCAGGGATTG
Hnf1β	GTCCGTGTCTACAACTGGTTCGC	TGGAGAGGAGCTTGGCTGATGG
CK19	CTCCCGAGATTACAACCACTAC	GTTCTGTCTCAAACTTGGTTCTG
CD133	ATGATCCTTGTGGTTCTTACGT	ATTGTTCCTTGAGCAGATAGGG
SOX9	GAGTTTGACCAATACTTGCCAC	GTAACTGCCAGTGTAGGTGAC
PYGL	CTTGCTGCCTGCTTCCTGGAC	TCTGCCTCTTCTACCTGCCATCC
G6PC	TCCGTGCCTATAATAAAGCAGT	TGGCTTTTTCTTTCCTCGAAAG
GCK	GCATCCTGCTCAACTGGACC	GCCACCGTGTCATTCACCAT
UGP2	GGTGCTTCTCAGTTCCAAGAGGTC	CTCATGTGAGGCTGCTGTGGTAAG
PPP1R3B	CGCAGCCTTCCGCAGATTACTTAG	CGATGGCCTTATCCTTCAGCACAC
PPP1CA	GGAACCATGAGTGTGCCAGCATC	GGCAGGCAGTTGAAGCAGTCAG
PHKB	CGAGCCAGGCATCACCATTACC	AGCCAGACAACCGCAGTCATTC
PHKG2	GGCCAAAGAGTTTTACCAGAAG	ATGATCTTCACTGCGAACTCAT
PASK	CTGCTGCTGGCTGGTGAAGG	GCTAGGCAGACTGGCAAGGAAC
SLC2A2	CTCAGCTTTATTCTGGGCAATC	TTTCTGGACAGAAGAGCAGTAG
GAPDH	GCATCCACTGGTGCTGCC	TCATCATACTTGGCAGGTTTC

DLK1, marker of hepatoblast delta-like 1 homologue; ALB, albumin; CD26, dipeptidyl peptidase-4; Thy1, thymus cell antigen 1; Axin2, axis inhibition protein 2; Lgr5, leucine rich repeat containing G-protein coupled receptor; Hnf1β, hepatocyte nuclear factor 1β; CK19, cytokeratin 19; Sox9, SRY box 9; PYGL, glycogen phosphorylase; G6PC, glucose-6-phosphatase; GCK, glucokinase; UPG2, UDP-glucose pyrophosphorylase 2; PPP1R3B, regulatory subunit of phosphoprotein phosphatase-1, PPC1CA, protein phosphatase 1 catalytic subunit α; PHKB, common β subunit of phosphorylase kinase; PHKG2, γ subunit hepatic phosphorylase kinase; PASK, PAS domain containing serine/threonine kinase; SLC2A2, solute carrier family 2 member 2; GAPDH, glyceraldehyde-3-phosphate dehydrogenase.

Table SII. Primer sequences of circRNAs.

circRNAs	Forward	Reverse
novel_circ_000176	GGCTGACAGTCTGTACAATC	CAAATGTGCACTCTTTATGG
novel_circ_002561	GTGCTTTCTCTCAAGAGAAC	GTGACCAAGGCTCTGCCTTT
novel_circ_000189	GAGTATGAAGCGCATCAGGA	CAGCCTGAGACATTTCTGTT
β-actin	GCTTCTAGGCGGACTGTTAC	CCATGCCAATGTTGTCTCTT

circRNAs, circular RNAs.

Table SIII. Overview of circRNA sequencing information.

Sample	Clean reads	HQ clean reads (%)	Mapped rRNA (%)	Unmapped rRNA (%)	Unmapped reads (%)	Unique mapped reads (%)
KO-A	78126736	76851674 (98.37)	1451532 (1.89)	75400142 (98.11)	4801042 (6.37)	68504568 (90.85)
KO-B	86518844	85414500 (98.72)	1662814 (1.95)	83751686 (98.05)	5672815 (6.77)	75930175 (90.66)
KO-C	90743396	89543232 (98.68)	2023882 (2.26)	87519350 (97.74)	9931079 (11.35)	75236041 (85.97)
WT-A	90234724	88967060 (98.6)	1724264 (1.94)	87242796 (98.06)	9432904 (10.81)	75197806 (86.19)
WT-B	71579338	70559246 (98.57)	1273894 (1.81)	69285352 (98.19)	3720702 (5.37)	63705678 (91.95)
WT-C	108796994	107281610 (98.61)	2095500 (1.95)	105186110 (98.05)	8715423 (8.29)	93883407 (89.25)

From left to right columns: The numbers of clean reads, high quality (HQ) clean reads, HQ clean reads mapped rRNA, HQ clean reads unmapped rRNA, the number of unmapped rRNA that could be unmapped (unmapped reads) or mapped (unique mapped reads) to known mouse genome, respectively. KO, EpCAM KO mice; WT, wild type mice.