**Supplement and supporting data (SSD)**

Supplementary table 1 – Table of circular RNAs with increased expression correlated to associated hallmarks, involved mechanism of action (target microRNA, target gene, and altered pathways), and code used in this work.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | | | |
| **CODE** | **CIRCULAR RNA** | **MECHANISM OF ACTION** | **ASSOCIATED HALLMARK** | **REFERENCE (Ref. code)** |
| C1 | circCAMSAP1 (hsa\_circ\_0001900) | ● Decreases miR-145- 5p ●Increases FLI1 expression | Invasion and metastasis; Proliferative signaling | Chen et al., 2021 (1) |
| C2 | hsa\_circDYNC1H1\_02 3 (hsa\_circ\_0002060) | ● Decreases miR-198 ● Increases ABCB1 expression | Resistance to cell death | Ji et al., 2020 (2) |
| C3 | Circ\_SIPA1L1 (hsa\_circ\_0032462) | ● Decreases miR-379- 5p ● Increases expression of MAP3K9 | Invasion and metastasis; Proliferative signaling | Jun et al., 2020 (3) |
| ● Increases KIF3B | Invasion and metastasis; Proliferative signaling | Gu et al., 2020 (4) |
| ● Decreases miR-411- 5p ● Increases RAB9A expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Xu et al., 2021 (5) |
| C4 | hsa\_circCNIH3\_012 (hsa\_circ\_0002137) | ● Decreases miR-433- 3p ● Increases IGF1R expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhang et al., 2022 (6) |
| C5 | circATRNL1 (hsa\_circ\_0092796) | ● Decreases miR-409- 3p ● Increases LDHA expression | Resistance to cell death; Cellular energy dysregulation | Zhang et al., 2021 (7) |
| C6 | circ\_0008932 | ● Decreases miR-145- 5p | Proliferative signaling; Invasion and metastasis; Resistance to cell death | Cao et al., 2021 (8) |
| C7 | circ-CNST (hsa\_circ\_0017311) | ● Decreases miR-578 ● Increases LDHA and PDK1 expression | Invasion and metastasis; Resistance to cell death; Cellular energy dysregulation | Hu et al., 2021 (9) |
| Circular RNA\_CNST (hsa\_circ\_0017311) | ● Decreases miR-421 ● Increases SLC25A3 | Proliferative signaling | Wang et al., 2020 (10) |
| C8 | circPRKAR1B (hsa\_circ\_0008039) | ● Decreases miR-361- 3P ●Increases FZD4 expression ● Stimulates Wnt/B-catenin axis | Invasion and metastasis; Proliferative signaling; Resistance to cell death; Induction of angiogenesis | Feng et al., 2021 (11) |
| C9 | hsa\_circCHD7\_003 (hsa\_Circ\_0084582) | ● Decreases miR-485- 3p ● Increases JAG1 expression | Invasion and metastasis; Proliferative signaling; Induction of angiogenesis | Gao et al., 2021 (12) |
| C10 | hsa\_circADAM22\_002 (Hsa\_circ\_0004674) | ● Decreases miR- 342-3p ● Increases FBN1 expression ● Active via Wnt/β-catenin | Proliferative signaling; Resistance to cell death | Bai et al., 2021 (13) |
| circRNA\_0004674 | ● Decreases miR142-5p ● Increases MCL1 expression | Invasion and metastasis; Signage Proliferative; Resistance to cell death | Ma et al., 2021 (14) |
| C11 | Hsa\_circ\_0032463 | ● Decreases miR330-3p ● Increases PNN expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Qin and Wu, 2021 (15) |
| C12 | Hsa\_circ\_001422 | ● Decreases miR-195-5p ● Increases FGF2 expression ● Active via PI3K/Akt | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Yang et al., 2021 (16) |
| C13 | CircRAB3IP | ● Decreases miR-580- 3p ● Increases TWIST1 expression | Invasion and metastasis; Proliferative signaling | Tang et al., 2021 (17) |
| C14 | Circ\_0056285 | ● Decreases miR-1244 ● Increases TRIM 44 expression | Proliferative signaling; Resistance to cell death; Cellular energy dysregulation | Huo and Dou, 2021 (18) |
| C15 | CircUBAP2 | ● Decreases miR-204- 3p ● Increases HGMA2 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Ma et al., 2021 (19) |
| circUBAP2 | ● Decreases miR 641 ● Increases expression of YAP1 | Invasion and metastasis; Proliferative signaling | Wu et al., 2020 (20) |
| CircUBAP2 | ● Decreases miR-506-3p ● Activates the WNT/β-catenin pathway | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Dong and Qu, 2020 (21) |
| circular RNA UBAP2 | ● Decreases miR-143 | Proliferative signaling; Resistance to cell death | Zhang et al., 2017 (22) |
| C16 | Circ\_0000527 | ● Decreases miR-646 ● Increases ARL2 expression | Invasion and metastasis; Proliferative signaling; Promotion of inflammation | Wu et al., 2021 (23) |
| C17 | hsa\_circ\_0000073 | ● Decreases miR - 1252-5p ● Increases expression of CCNE2 and MDM2 | Invasion and metastasis; Proliferative signaling | Ren et al., 2021 (24) |
| ● Decreases miR 145-5p and miR-151-3p ● IncreaseNRAS expression | Invasion and metastasis; Signage Proliferative; Resistance to cell death | Li et al., 2020 (25) |
| C18 | circPDSS1 | ● Decreases miR-502- 3p and miR-4436a | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Tang et al., 2022 (26) |
| C19 | circFOXP1 | ● Decreases miR-127- 5p ● Increases CDKN2AIP expression | Proliferative signaling; Induction of angiogenesis | Zhang et al., 2021 (27) |
| C20 | CircNRIP1 (hsa\_circ\_0004771) | ● Decreases miR-532- 3p ● Increases AKT3 expression ● Active via PI3K/AKT | Invasion and metastasis; Proliferative signaling | Shi et al., 2021 (28) |
| Circular RNA  circNRIP1 | ● Decreases miR-199a ● Increases FOXC2 expression | Invasion and metastasis; Signage Proliferative; Resistance to cell death | Meng et al., 2021 (29) |
| C21 | CircPVT1 (hsa\_circ\_0001821) | ● Decreases miR-423- 5p ● Active via Wnt5a/ROR2 | Invasion and metastasis; Proliferative signaling; Cellular energy dysregulation | Wan et al., 2021 (30) |
| circPVT1 | ● Decreases miR-137 ● Increases TRIAP1 expression | Invasion and metastasis; Signage Proliferative; Resistance to cell death | Li et al., 2021 (31) |
| CircPVT1 | ● Decreases miR-205-5p ● Increases cFLIP expression | Invasion and metastasis; Proliferative signaling | Liu et al., 2020 (32) |
| circPVT1  (hsa\_circ\_0001821) | ● Increases ABCB1 expression | Proliferative signaling; Resistance to cell death | Kun et al., 2018 (33) |
| Circular RNA PVT1 | ●Decreases miR-256b ●Increases FOXC2 expression | Invasion and metastasis | Yan et al., 2020 (34) |
| C22 | circANKIB1 | ● Decreases miR-217 ● Increases PAX3 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhu et al., 2021 (35) |
| Circ\_ANKIB1 | ● Increases miR-19b ● Inhibits SOCS3 and activates STAT3 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Du et al., 2020 (36) |
| C23 | Circular RNA circ\_0081001 | ● Decreases miR-494- 3p ● Increases TGM2 expression | Invasion and metastasis; Resistance to cell death | Wei et al., 2021 (37) |
| hsa\_circ\_0081001 | ● Pathological clinical analysis | Pathological clinical analysis | Kun et al., 2018 (38) |
| C24 | Circ-XPR1 (hsa\_circ\_0005909) | ●Decreases miR-214- 5p ● Increases DDX5 expression | Proliferative signaling | Mao et al., 2021 (39) |
| hsa\_circ\_0005909 | ● Decreases mir-338-3p ● Increases hmga1 expression ● Active via MAPK-ERK and PI3K | Proliferative signaling; Resistance to cell death | Zhang et al., 2021 (40) |
| hsa\_circ\_0005909 | ● Decreases mir-936 ● Increases HMGB1 expression | Invasion and metastasis; Proliferative signaling | Ding et al., 2020 (41) |
| C25 | hsa\_circ\_0007534 | ● Decreases miR- 219a-5p ● Increases SOX5 expression | Invasion and metastasis; Proliferative signaling | Zhang and Li, 2021 (42) |
| ● Activated AKT/GSK-3B | Proliferative signaling; Resistance to cell death | Li and Li, 2018 (43) |
| C26 | Circular RNA 0102049 | ● Decreases miR-520g-3p ● Increases PLK2 axis | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhang et al., 2021 (44) |
| circ\_0102049 | ● Decreases miR 1304-5p ● Increases MDM2 mRNA expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Jin et al., 2019 (45) |
| C27 | Circ\_0000885 | ● Decreases miR-1294 ● Increases FGFR1 expression | Invasion and metastasis; Proliferative signaling | Chen et al., 2020 (46) |
| hsa\_circ\_0000885 | ● Pathological clinical analysis | Pathological clinical analysis | Zhu et al., 2019 (47) |
| C28 | CircECE1 | ● Increases c-Myc expression ● Inhibits SPOP degradation and increases TXNIP expression | Invasion and metastasis; Proliferative signaling; Cellular energy dysregulation | Shen et al., 2020 (48) |
| C29 | circ\_ARF3 | ● Decreases miR-1299 ● Increases CDK6 expression | Proliferative signaling | Gao et al., 2020 (49) |
| C30 | Hsa circ 0003732 | ● Decreases miR-545 ● Increases CCNA2 expression | Proliferative signaling | Li et al., 2020 (50) |
| C31 | cir-ITCH | ● Increased cir-ITCH ● Increases miR-7 ● Increases EGFR expression | Invasion and metastasis; Proliferative signaling | Li et al., 2020 (51) |
| C32 | circHIPK3 | ● Decreases miR-637 ● Increases HDAC4 expression | Invasion and metastasis; Proliferative signaling | Wen et al., 2021 (52) |
| ● Decreases miR-637 ● Increases STAT3 expression | Invasion and metastasis; Proliferative signaling | Huang et al., 2020 (53) |
| C33 | circSMARCA5 | ● Interacts with miR-17-3p, miR-432-5p, miR-561-3p, miR-10b-3p, and miR-181c-3p | Invasion and metastasis; Proliferative signaling | Zhang et al., 2020 (54) |
| C34 | hsa\_circ\_0002052 | ● Decreased miR- 382 ● Increased STX6 expression ● Active via Wnt/B-catenin | Invasion and metastasis; Proliferative signaling | Zhang et al., 2020 (55) |
| C35 | CircPRDM2 | ● Decreases miR-760 ● Increases EZH2 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Yuan et al., 2021 (56) |
| C36 | circ\_CDK14 (hsa\_circ\_0001721) | ● Decreases miR- 520a-3p ● Increases GAB1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wu et al., 2021 (57) |
| Circrna circ\_0001721 | ● Decreases miR-372-3p ● Increases MAPK7 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death; Cellular energy dysregulation | Gao et al., 2020 (58) |
| circ\_0001721 | ● Decreases miR-569 and miR-599 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Li et al., 2019 (59) |
| C37 | Hsa\_circ\_0008934 | ● Decreases miR- 145-5p ● Increases E2F3 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Li et al., 2020 (60) |
| C38 | hsa\_circRNA\_0008035 | ● Decreases miR-375 ● Increases NOTCH signaling pathway | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Gong et al., 2020 (61) |
| C39 | has-circ-0001146 | ● Decreases miR-26a-5p | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wang et al., 2020 (62) |
| C40 | hsa\_circ\_0136666 | ● Decreases miR 593-3p ● Increases ZEB2 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhang et al., 2020 (63) |
| C41 | Circular RNA circFAT1(e2) | ● Decreases miR-181b ● Increases HK2 expression | Invasion and metastasis; Proliferative signaling | Gu et al., 2020 (64) |
| C42 | CircUSP34 | ● Decreases miR-16-5p | Invasion and metastasis; Proliferative signaling | Lou et al., 2022 (65) |
| C43 | CircFAM120B (hsa\_circ\_0078767) | ● Decreases miR-1205 ● Increases PTBP1 expression | Invasion and metastasis; Proliferative signaling | Li et al., 2021 (66) |
| C44 | hsa-circ-0016347 | ● Decreases miR-214 ● Increases caspase 1 | Invasion and metastasis; Proliferative signaling | Jin et al., 2017 (67) |
| Circ\_0016347 | ● Decreases miR- 1225-3p ● Increases KCNH1 expression | Invasion and metastasis; Proliferative signaling; Cellular energy dysregulation | Li et al., 2021 (68) |
| C45 | Circ\_0010220 | ● Decreases miR-503-5P ● Increases CDCA4 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Li et al., 2020 (69) |
| Hsa\_circ\_0010220 | ● Decreases miR-198 ● Increases STX 6 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Lu et al., 2021 (70) |
| C46 | CircCRIM1 | ● Decreases miR-432-5p ● Increases HDAC4 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2020 (71) |
| C47 | circTUBGCP3 | ● Decreases miR-30b ● Increases Vimetin expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Xu et al., 2020 (72) |
| C48 | hsa\_circ\_0003496 | ● Decreases miR-370 ● Increases KLF12 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Xie et al., 2020 (73) |
| C49 | circCCDC66 | ● Decreases miR-338- 3p ● Increases PTBP1 expression | Invasion and metastasis; Proliferative signaling; | Xiang et al., 2020 (74) |
| C50 | circ\_001621 | ● Decreases miR- 578 ● Increases expression of VEGF, MMP9 and CDK4 | Invasion and metastasis; Proliferative signaling; | Ji et al., 2020 (75) |
| C51 | Circ100284 | ● Decreases PTEN and EMP1 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu and Liu, 2020 (76) |
| C52 | Circ0085539 | ● Decreases miR-526b-5p ● Increases PHLDA1 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2020 (77) |
| C53 | CircEIF4G2 | ● Decreases miR-218 | Invasion and metastasis; Proliferative signaling | Lin et al., 2020 (78) |
| C54 | circ\_001569 | ● Activates Wnt/β-catenin | Proliferative signaling; Resistance to cell death | Zhang et al., 2018 (79) |
| C55 | Circ-03955 | ● Decreases miR-3662 ● Increases MTDH expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wang et al., 2020 (80) |
| C56 | Circ\_0086996 | ● Decreases miR-125b-5p | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Luo et al., 2020 (81) |
| C57 | Circular RNA 0060428 | ● Decreases miR-375 ● Increases RPBJ expression | Proliferative signaling; Resistance to cell death | Cao and Liu, 2020 (82) |
| C58 | Circ\_0001658 | ● Decreases miR-382-5p ● Increases YB-1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wang et al., 2020 (83) |
| C59 | CircITGA7 | ● Decreases miR-370 ● Increases PIM1 expression | Invasion and metastasis; Proliferative signaling | Fang et al., 2020 (84) |
| C60 | hsa\_circ\_0000282 | ● Decreases miR-192 ● Increases XIAP expression | Proliferative signaling; Resistance to cell death | Li et al., 2020 (85) |
| C61 | circ\_0028171 | ● Increases miR-218-5p ● Decreases IKBKB expression | Invasion and metastasis; Proliferative signaling | Pan et al., 2020 (86) |
| C62 | Circ\_0000285 | ● Decreases miR-409-3p ● Increases IGFBP3 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Long et al., 2020 (87) |
| Hsa\_circ\_0000285 | ● Decreases miRNA 599 ● Increases TGFB2 | Proliferative signaling | Zhang et al., 2020 (88) |
| C63 | Circ-XPO1 | ● Decreases miR-23a-3p, miR-23b-3p, miR-23c, and miR-130a-5p ● Increases XPO1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death; Evasion of suppressive mechanisms | Jiang et al., 2020 (89) |
| C64 | CircSAMD4A | ● Decreases miR-218-5p ● Increases KLF8 expression | Proliferative signaling; Resistance to cell death | Wei et al., 2020 (90) |
| ● Decreases miR-342-3p ● Increases FZD7 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Xie et al., 2020 (91) |
| C65 | hsa\_circ\_0003074 | ● Pathological clinical analysis | Pathological clinical analysis | Lei and Xiang, 2020 (92) |
| C66 | Circular RNA 0001785 | ● Decreases miR-1200 ● Increases HOXB2 expression ● Active PI3K/Akt/Mtor | Proliferative signaling; Resistance to cell death | Li et al., 2019 (93) |
| C67 | CircMYO10 | ● Decreases miR-370-3p ● Increases RUVBL1 expression ● Active B-catenin/LEF1 complex | Invasion and metastasis; Proliferative signaling; Genome instability and mutation | Chen et al., 2020 (94) |
| C68 | Hsa\_circ\_0051079 | ● Decreases miR- 26a-5p ● Increases TGF-B1 expression | Invasion and metastasis; Proliferative signaling | Zhang et al., 2019 (95) |
| C69 | Circ-0003998 | ● Decreases miR-197-3p ● Increases KLF10 expression | Invasion and metastasis | Wang et al., 2019 (96) |
| C70 | circTADA2A (hsa\_circ\_0043278) | ● Decreases miR-203a-3p ● Increases CREB3 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wu et al., 2019 (97) |
| C71 | circRNA\_100876 | ● Decreases miR-136 | Proliferative signaling; Resistance to cell death | Jin et al., 2019 (98) |
| C72 | CircRNA LRP6 | ● Inhibits expression of KLF2 and APC | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zheng et al., 2019 (99) |
| C73 | circMMP9 | ● Decreases miR-1265 ● Increases CHI3L1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Pan et al., 2019 (100) |
| C74 | circ\_0000502 | ● Decreases miR-1238 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Qi et al., 2019 (101) |
| C75 | circRNA-0008717 | ● Decreases miR-203 ● Increases Bm1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhou et al., 2018 (102) |
| C76 | CircFAT1 | ● Decreases miR-375 ● Increases Yes-associated protein 1 (YAP1) | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2018 (103) |
| C77 | Hsa\_circ\_0009910 | ● Decreases miR-449a ● Increases IL6R expression ● Active JAK1/STAT3 | Proliferative signaling; Resistance to cell death | Deng et al., 2018 (104) |
| C78 | hsa\_circ\_0001564 | ● Decreases miR-29c-3p | Proliferative signaling; Resistance to cell death | Song and Li, 2018 (105) |
| C79 | circNASP | ● Decreases miR-1253 ● Increases FOXF1 expression | Invasion and metastasis; Proliferative signaling | Huang et al., 2018 (106) |
| C80 | Circular RNA GLI2 | ● Decreases miR-125-5b | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Li and Song, 2017 (107) |
| C81 | circ-NT5C2 (hsa\_circ\_0092509) | ● Decreases miR-448 | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2017 (108) |
| C82 | circ-CHI3L1.2 | ● Decreases miR-340-5p ● Increases LPAATB expression | Proliferative signaling; Resistance to cell death | Zhang et al., 2021 (109) |
| C83 | Circ\_ORC2 | ● Increases miR-19a ● Decreases PTEN expression ● Activates the AKT pathway | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Li et al., 2019 (110) |
| C84 | circ\_0000006 | ● Decreases miR-646 ● Increases BDNF expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Amuti et al., 2021 (111) |

Ref. code: the corresponding number of the reference in the reference section. FLI1, Friend leukemia virus integration 1; ABCB1, ATP-binding cassette subfamily B member 1; MAP3K9, Mitogen-activated protein kinase kinase kinase 9; IGF1R, Insulin like growth factor1 receptor; LDHA, Lactate dehydrogenase A; PDK1, Pyruvate dehydrogenase kinase 1; FZD4, Frizzled class receptor 4; JAG1, Jagged canonical notch ligand 1; LEF1, Lymphoid enhancer binding Factor 1; FGF2, Fibroblast growth factor 2; TWIST1, Twist family BHLH transcription factor 1; TRIM44, Tripartite motif containing 44; HGMA2, High mobility group AT-hook 2; ARL2, ADP ribosylation factor like GTPase 2; MCL1, myeloid cell leukemia-1; CCNE2, Cyclin E2; MDM2, Murine doble minute 2 (regulador negativo da P53); CDKN2AIP, Cyclin-dependent kinase inhibitor 2a-interacting protein; AKT3, Serine/Threonine Kinase 3; PI3K, Phosphoinositide 3-kinase; AKT, Protein Kinase B; WNT5A, Wnt family member 5ª; ROR2, Receptor tyrosine kinase like orphan receptor 2; RAB9A, Ras-related protein Rab-9ª; PAX3, Paired box 3; TGM2, Transglutaminase 2; DDX5, DEAD box protein 5; SOX5, SRY-Box Transcription Factor 5; HMGA1, High mobility group AT-Hook; MAPK, Mitogen‑activated protein kinase; ERK, Extracellular signal-regulated kinase; PLK2, Polo like kinase 2; SOCS3, Suppressor Of Cytokine Signaling 3; STAT3, Signal transducer and activator Of transcription 3; FGFR1, Fibroblast growth factor receptor 1; TXNIP, Thioredoxin interacting protein; CDK6, Cyclin dependent kinase 6; CCNA2, Cyclin A2; EGFR, epidermal growth factor receptor; SLC25A3, Solute carrier family 25 member 3; HDAC4, Histone deacetylase 4; TRIAP1, TP53 Regulated Inhibitor Of Apoptosis 1; STX6, Syntaxin 6; EZH2, Enhancer of zeste 2 polycomb repressive complex 2 subunit; GAB1, GRB2-associated binder 1; E2F3, E2F Transcription Factor 3; ZEB2, Zinc finger E-Box binding homeobox 2; HK2, Hexokinase 2; PTBP1, Polypyrimidine tract binding protein; KCNH1, Potassium voltage-gated channel subfamily H member 1; KLF, Krueppel-like factor; KLF12, KLF Transcription Factor 12; MAPK7, Mitogen-activated protein kinase 7; VEGF, Vascular endothelial growth fator; MMP-9, Matrix metalloproteinase 9; CDK4, Cyclin dependent kinase 4; c-FLIP, Cellular FLICE (FADD-like IL-1β-converting enzyme) inhibitory protein; HMGB1, High mobility group box 1; PTEN, phosphatase and tensin homologue; EMP1, Epithelial membrane protein 1; KIF3B, Kinesin family member 3B; YAP1, Yes-associated protein 1; CDCA4, Cell Division Cycle Associated 4; PHLDA, Pleckstrin Homology Like Domain Family A Member 1; MTDH, Metadherin; YB-1, Y-box binding protein 1; PIM1, Proto-Oncogene, Serine/Threonine Kinase; XIAP, X-Linked Inhibitor Of Apoptosis; IKBKB, Inhibitor of nuclear factor kappa b kinase subunit beta; IGFBP3, Insulin-like growth factor-binding protein 3; XPO1, Exportin 1; KLF8, Kruppel Like Factor 8; TGFB2, transforming growth factor beta 2; FZD7, Frizzled class receptor 7; HOXB2, Homeobox B2; RUVBL1, RuvB Like AAA ATPase 1; KLF10, KLF Transcription factor 10; KLF2, KLF Transcription fator 2; APC, APC Regulator of wnt signaling pathway; CHI3L1, Chitinase 3 Like 1; GSK3B, Glycogen synthase kinase-3β; BM1, Proto-oncogene, polycomb ring finger; IL6R, Interleukin 6 Receptor; FOXF1, Forkhead Box F1; FOXC2, Forkhead Box C2; LPAATB, Lysophosphatidic acid acyltransferase b; BDNF, Brain Derived Neurotrophic Factor; PVT1, plasmacytoma variant translocation 1.

**References Supplementary table 1**

1. Chen Z, Xu W, Zhang D, et al (2021). circCAMSAP1 promotes osteosarcoma progression and metastasis by sponging miR-145-5p and regulating FLI1 expression. Mol Ther Nucleic Acids, 23, 1120-35.
2. Ji Y, Liu J, Zhu W, et al (2020). circ\_0002060 Enhances Doxorubicin Resistance in Osteosarcoma by Regulating the miR-198/ABCB1 Axis. Cancer Biother Radiopharm.
3. Jun L, Xuhong L, Hui L (2020). Circ\_SIPA1L1 Promotes Osteosarcoma Progression Via miR-379-5p/MAP3K9 Axis. Cancer Biother Radiopharm.
4. Gu R, Li X, Yan X, et al (2020). Circular RNA circ\_0032462 Enhances Osteosarcoma Cell Progression by Promoting KIF3B Expression. Technol Cancer Res Treat, 19, 1533033820943217.
5. Xu Y, Yao T, Ni H, et al (2021). Circular RNA circSIPA1L1 Contributes to Osteosarcoma Progression Through the miR-411-5p/RAB9A Signaling Pathway. Front Cell Dev Biol, 9, 642605.
6. Zhang M, Yu GY, Liu G, et al (2022). Circular RNA circ\_0002137 regulated the progression of osteosarcoma through regulating miR-433-3p/ IGF1R axis. J Cell Mol Med, 26, 1806-16.
7. Zhang Q, Wang L, Cao L, et al (2021). Novel circular RNA circATRNL1 accelerates the osteosarcoma aerobic glycolysis through targeting miR-409-3p/LDHA. Bioengineered, 12, 9965-75.
8. Cao C, Shu X (2021). Suppression of circ\_0008932 inhibits tumor growth and metastasis in osteosarcoma by targeting miR-145-5p. Exp Ther Med, 22, 1106.
9. Hu R, Chen S, Yan J (2021). Blocking circ-CNST suppresses malignant behaviors of osteosarcoma cells and inhibits glycolysis through circ-CNST-miR-578-LDHA/PDK1 ceRNA networks. J Orthop Surg Res, 16, 300.
10. Wang JH, Wu XJ, Duan YZ, et al (2020). Circular RNA\_CNST Promotes the Tumorigenesis of Osteosarcoma Cells by Sponging miR-421. Cell Transplant, 29, 963689720926147.
11. Feng ZH, Zheng L, Yao T, et al (2021). EIF4A3-induced circular RNA PRKAR1B promotes osteosarcoma progression by miR-361-3p-mediated induction of FZD4 expression. Cell Death Dis, 12, 1025.
12. Gao P, Zhao X, Yu K, et al (2021). Circ\_0084582 Facilitates Cell Growth, Migration, Invasion, and Angiopoiesis in Osteosarcoma via Mediating the miR-485-3p/JAG1 Axis. Front Genet, 12, 690956.
13. Bai Y, Li Y, Bai J, et al (2021). Hsa\_circ\_0004674 promotes osteosarcoma doxorubicin resistance by regulating the miR-342-3p/FBN1 axis. J Orthop Surg Res, 16, 510.
14. Ma XL, Zhan TC, Hu JP, et al (2021). Doxorubicin-induced novel circRNA\_0004674 facilitates osteosarcoma progression and chemoresistance by upregulating MCL1 through miR-142-5p. Cell Death Discov, 7, 309.
15. Qin G, Wu X (2021). Hsa\_circ\_0032463 acts as the tumor promoter in osteosarcoma by regulating the miR‑330‑3p/PNN axis. Int J Mol Med, 47.
16. Yang B, Li L, Tong G, et al (2021). Circular RNA circ\_001422 promotes the progression and metastasis of osteosarcoma via the miR-195-5p/FGF2/PI3K/Akt axis. J Exp Clin Cancer Res, 40, 235.
17. Tang G, Liu L, Xiao Z, et al (2021). CircRAB3IP upregulates twist family BHLH transcription factor (TWIST1) to promote osteosarcoma progression by sponging miR-580-3p. Bioengineered, 12, 3385-97.
18. Huo S, Dou D (2021). Circ\_0056285 Regulates Proliferation, Apoptosis and Glycolysis of Osteosarcoma Cells via miR-1244/TRIM44 Axis. Cancer Manag Res, 13, 1257-70.
19. Ma W, Xue N, Zhang J, et al (2021). circUBAP2 regulates osteosarcoma progression via the miR‑204‑3p/HMGA2 axis. Int J Oncol, 58, 298-311.
20. Wu H, Li W, Zhu S, et al (2020). Circular RNA circUBAP2 regulates proliferation and invasion of osteosarcoma cells through miR-641/YAP1 axis. Cancer Cell Int, 20, 223.
21. Dong L, Qu F (2020). CircUBAP2 promotes SEMA6D expression to enhance the cisplatin resistance in osteosarcoma through sponging miR-506-3p by activating Wnt/beta-catenin signaling pathway. J Mol Histol, 51, 329-40.
22. Zhang H, Wang G, Ding C, et al (2017). Increased circular RNA UBAP2 acts as a sponge of miR-143 to promote osteosarcoma progression. Oncotarget, 8, 61687-97.
23. Wu X, Yan L, Liu Y, et al (2021). Circ\_0000527 promotes osteosarcoma cell progression through modulating miR-646/ARL2 axis. Aging (Albany NY), 13, 6091-102.
24. Ren Z, Yang Q, Guo J, et al (2021). Circular RNA hsa\_circ\_0000073 Enhances Osteosarcoma Cells Malignant Behavior by Sponging miR-1252-5p and Modulating CCNE2 and MDM2. Front Cell Dev Biol, 9, 714601.
25. Li X, Liu Y, Zhang X, et al (2020). Circular RNA hsa\_circ\_0000073 contributes to osteosarcoma cell proliferation, migration, invasion and methotrexate resistance by sponging miR-145-5p and miR-151-3p and upregulating NRAS. Aging (Albany NY), 12, 14157-73.
26. Tang S, Tang X, Jin Z, et al (2022). Circular RNA circPDSS1 promotes osteosarcoma progression by sponging miR-502-3p and miR-4436a. Anticancer Drugs, 33, 257-67.
27. Zhang H, Yu Z, Wu B, et al (2021). Circular RNA circFOXP1 promotes angiogenesis by regulating microRNA -127-5p/CDKN2AIP signaling pathway in osteosarcoma. Bioengineered, 12, 9991-9.
28. Shi Z, Wang K, Xing Y, et al (2021). CircNRIP1 Encapsulated by Bone Marrow Mesenchymal Stem Cell-Derived Extracellular Vesicles Aggravates Osteosarcoma by Modulating the miR-532-3p/AKT3/PI3K/AKT Axis. Front Oncol, 11, 658139.
29. Meng Y, Hao D, Huang Y, et al (2021). Circular RNA circNRIP1 plays oncogenic roles in the progression of osteosarcoma. Mamm Genome, 32, 448-56.
30. Wan J, Liu Y, Long F, et al (2021). circPVT1 promotes osteosarcoma glycolysis and metastasis by sponging miR-423-5p to activate Wnt5a/Ror2 signaling. Cancer Sci, 112, 1707-22.
31. Li D, Huang Y, Wang G (2021). Circular RNA circPVT1 Contributes to Doxorubicin (DXR) Resistance of Osteosarcoma Cells by Regulating TRIAP1 via miR-137. Biomed Res Int, 2021, 7463867.
32. Liu YP, Wan J, Long F, et al (2020). circPVT1 Facilitates Invasion and Metastasis by Regulating miR-205-5p/c-FLIP Axis in Osteosarcoma. Cancer Manag Res, 12, 1229-40.
33. Kun-Peng Z, Xiao-Long M, Chun-Lin Z (2018). Overexpressed circPVT1, a potential new circular RNA biomarker, contributes to doxorubicin and cisplatin resistance of osteosarcoma cells by regulating ABCB1. Int J Biol Sci, 14, 321-30.
34. Yan M, Gao H, Lv Z, et al (2020). Circular RNA PVT1 promotes metastasis via regulating of miR-526b/FOXC2 signals in OS cells. J Cell Mol Med, 24, 5593-604.
35. Zhu X, Liu C, Shi J, et al (2021). Circular RNA circANKIB1 promotes the progression of osteosarcoma by regulating miR-217/PAX3 axis. J Bone Oncol, 27, 100347.
36. Du YX, Guo LX, Pan HS, et al (2020). Circ\_ANKIB1 stabilizes the regulation of miR-19b on SOCS3/STAT3 pathway to promote osteosarcoma cell growth and invasion. Hum Cell, 33, 252-60.
37. Wei W, Ji L, Duan W, et al (2021). Circular RNA circ\_0081001 knockdown enhances methotrexate sensitivity in osteosarcoma cells by regulating miR-494-3p/TGM2 axis. J Orthop Surg Res, 16, 50.
38. Kun-Peng Z, Chun-Lin Z, Jian-Ping H, et al (2018). A novel circulating hsa\_circ\_0081001 act as a potential biomarker for diagnosis and prognosis of osteosarcoma. Int J Biol Sci, 14, 1513-20.
39. Mao X, Guo S, Gao L, et al (2021). Circ-XPR1 promotes osteosarcoma proliferation through regulating the miR-214-5p/DDX5 axis. Hum Cell, 34, 122-31.
40. Zhang C, Na N, Liu L, et al (2021). CircRNA hsa\_circ\_0005909 Promotes Cell Proliferation of Osteosarcoma Cells by Targeting miR-338-3p/HMGA1 Axis. Cancer Manag Res, 13, 795-803.
41. Ding S, Zhang G, Gao Y, et al (2020). Circular RNA hsa\_circ\_0005909 modulates osteosarcoma progression via the miR-936/HMGB1 axis. Cancer Cell Int, 20, 305.
42. Zhang P, Li J (2021). Down-regulation of circular RNA hsa\_circ\_0007534 suppresses cell growth by regulating miR-219a-5p/SOX5 axis in osteosarcoma. J Bone Oncol, 27, 100349.
43. Li B, Li X (2018). Overexpression of hsa\_circ\_0007534 predicts unfavorable prognosis for osteosarcoma and regulates cell growth and apoptosis by affecting AKT/GSK-3beta signaling pathway. Biomed Pharmacother, 107, 860-6.
44. Zhang X, Hu Z, Li W, et al (2021). Circular RNA 0102049 suppresses the progression of osteosarcoma through modulating miR-520g-3p/PLK2 axis. Bioengineered, 12, 2022-32.
45. Jin Y, Li L, Zhu T, et al (2019). Circular RNA circ\_0102049 promotes cell progression as ceRNA to target MDM2 via sponging miR-1304-5p in osteosarcoma. Pathol Res Pract, 215, 152688.
46. Chen Y, Zhang S, Bai C, et al (2020). Circ\_0000885 Enhances Osteosarcoma Progression by Increasing FGFR1 Expression via Sponging MiR-1294. Cancer Manag Res, 12, 6441-52.
47. Zhu K, Niu L, Wang J, et al (2019). Circular RNA hsa\_circ\_0000885 Levels are Increased in Tissue and Serum Samples from Patients with Osteosarcoma. Med Sci Monit, 25, 1499-505.
48. Shen S, Yao T, Xu Y, et al (2020). CircECE1 activates energy metabolism in osteosarcoma by stabilizing c-Myc. Mol Cancer, 19, 151.
49. Gao AM, Yuan C, Hu AX, et al (2020). circ\_ARF3 regulates the pathogenesis of osteosarcoma by sponging miR-1299 to maintain CDK6 expression. Cell Signal, 72, 109622.
50. Li L, Kong XA, Zang M, et al (2020). Hsa\_circ\_0003732 promotes osteosarcoma cells proliferation via miR-545/CCNA2 axis. Biosci Rep, 40.
51. Li H, Lan M, Liao X, et al (2020). Circular RNA cir-ITCH Promotes Osteosarcoma Migration and Invasion through cir-ITCH/miR-7/EGFR Pathway. Technol Cancer Res Treat, 19, 1533033819898728.
52. Wen Y, Li B, He M, et al (2021). circHIPK3 promotes proliferation and migration and invasion via regulation of miR‑637/HDAC4 signaling in osteosarcoma cells. Oncol Rep, 45, 169-79.
53. Huang Z, Yuan C, Gu H, et al (2020). Circular RNA circHIPK3 Promotes Cell Metastasis through miR-637/STAT3 Axis in Osteosarcoma. Biomed Res Int, 2020, 2727060.
54. Zhang H, Meng F, Dong S (2020). circSMARCA5 Promoted Osteosarcoma Cell Proliferation, Adhesion, Migration, and Invasion through a Competing Endogenous RNA Network. Biomed Res Int, 2020, 2539150.
55. Zhang PR, Ren J, Wan JS, et al (2020). Circular RNA hsa\_circ\_0002052 promotes osteosarcoma via modulating miR-382/STX6 axis. Hum Cell, 33, 810-8.
56. Yuan J, Liu Y, Zhang Q, et al (2021). CircPRDM2 Contributes to Doxorubicin Resistance of Osteosarcoma by Elevating EZH2 via Sponging miR-760. Cancer Manag Res, 13, 4433-45.
57. Wu PF, Tang XM, Sun HL, et al (2021). Depletion of circRNA circ\_CDK14 inhibits osteosarcoma progression by regulating the miR-520a-3p/GAB1 axis. Neoplasma, 68, 798-809.
58. Gao Y, Ma H, Gao Y, et al (2020). CircRNA Circ\_0001721 Promotes the Progression of Osteosarcoma Through miR-372-3p/MAPK7 Axis. Cancer Manag Res, 12, 8287-302.
59. Li L, Guo L, Yin G, et al (2019). Upregulation of circular RNA circ\_0001721 predicts unfavorable prognosis in osteosarcoma and facilitates cell progression via sponging miR-569 and miR-599. Biomed Pharmacother, 109, 226-32.
60. Li S, Zeng M, Yang L, et al (2020). Hsa\_circ\_0008934 promotes the proliferation and migration of osteosarcoma cells by targeting miR-145-5p to enhance E2F3 expression. Int J Biochem Cell Biol, 127, 105826.
61. Gong G, Han Z, Wang W, et al (2020). Silencing hsa\_circRNA\_0008035 exerted repressive function on osteosarcoma cell growth and migration by upregulating microRNA-375. Cell Cycle, 19, 2139-47.
62. Wang J, Ni J, Song D, et al (2020). The regulatory effect of has-circ-0001146/miR-26a-5p/MNAT1 network on the proliferation and invasion of osteosarcoma. Biosci Rep, 40.
63. Zhang C, Zhou H, Yuan K, et al (2020). Overexpression of hsa\_circ\_0136666 predicts poor prognosis and initiates osteosarcoma tumorigenesis through miR-593-3p/ZEB2 pathway. Aging (Albany NY), 12, 10488-96.
64. Gu H, Cheng X, Xu J, et al (2020). Circular RNA circFAT1(e2) Promotes Osteosarcoma Progression and Metastasis by Sponging miR-181b and Regulating HK2 Expression. Biomed Res Int, 2020, 3589871.
65. Lou J, Zhang H, Xu J, et al (2022). circUSP34 accelerates osteosarcoma malignant progression by sponging miR-16-5p. Cancer Sci, 113, 120-31.
66. Li JJ, Xiong MY, Sun TY, et al (2021). CircFAM120B knockdown inhibits osteosarcoma tumorigenesis via the miR-1205/PTBP1 axis. Aging (Albany NY), 13, 23831-41.
67. Jin H, Jin X, Zhang H, et al (2017). Circular RNA hsa-circ-0016347 promotes proliferation, invasion and metastasis of osteosarcoma cells. Oncotarget, 8, 25571-81.
68. Li Z, Fu Y, Ouyang W, et al (2021). Circ\_0016347 Promotes Osteosarcoma Progression by Regulating miR-1225-3p/KCNH1 Axis. Cancer Biother Radiopharm.
69. Li J, Zhang F, Li H, et al (2020). Circ\_0010220-mediated miR-503-5p/CDCA4 axis contributes to osteosarcoma progression tumorigenesis. Gene, 763, 145068.
70. Lu Z, Wang C, Lv X, et al (2021). Hsa\_circ\_0010220 regulates miR-198/Syntaxin 6 axis to promote osteosarcoma progression. J Bone Oncol, 28, 100360.
71. Liu J, Feng G, Li Z, et al (2020). Knockdown of CircCRIM1 Inhibits HDAC4 to Impede Osteosarcoma Proliferation, Migration, and Invasion and Facilitate Autophagy by Targeting miR-432-5p. Cancer Manag Res, 12, 10199-210.
72. Xu Y, Yao T, Huang K, et al (2020). Circular RNA circTUBGCP3 Is Up-Regulated and Promotes Cell Proliferation, Migration and Survivability via Sponge ﻿mir-30b in Osteosarcoma. Onco Targets Ther, 13, 3729-37.
73. Xie C, Liang G, Xu Y, et al (2020). Circular RNA hsa\_circ\_0003496 Contributes to Tumorigenesis and Chemoresistance in Osteosarcoma Through Targeting (microRNA) miR-370/Kruppel-Like Factor 12 Axis. Cancer Manag Res, 12, 8229-40.
74. Xiang D, Li Y, Lin Y (2020). Circular RNA circCCDC66 Contributes to Malignant Phenotype of Osteosarcoma by Sponging miR-338-3p to Upregulate the Expression of PTP1B. Biomed Res Int, 2020, 4637109.
75. Ji X, Shan L, Shen P, et al (2020). Circular RNA circ\_001621 promotes osteosarcoma cells proliferation and migration by sponging miR-578 and regulating VEGF expression. Cell Death Dis, 11, 18.
76. Liu YD, Liu LP (2020). Circ100284 promotes invasion and migration of osteosarcoma cells by down-regulating PTEN and EMP1. Eur Rev Med Pharmacol Sci, 24, 6540-50.
77. Liu P, Liu W, Gao H, et al (2020). Circ0085539 Promotes Osteosarcoma Progression by Suppressing miR-526b-5p and PHLDA1 Axis. Front Oncol, 10, 1250.
78. Lin E, Liu S, Xiang W, et al (2020). CircEIF4G2 Promotes Tumorigenesis and Progression of Osteosarcoma by Sponging miR-218. Biomed Res Int, 2020, 8386936.
79. Zhang H, Yan J, Lang X, et al (2018). Expression of circ\_001569 is upregulated in osteosarcoma and promotes cell proliferation and cisplatin resistance by activating the Wnt/beta-catenin signaling pathway. Oncol Lett, 16, 5856-62.
80. Wang Z, Deng M, Chen L, et al (2020). Circular RNA Circ-03955 Promotes Epithelial-Mesenchymal Transition in Osteosarcoma by Regulating miR-3662/Metadherin Pathway. Front Oncol, 10, 545460.
81. Luo Z, Yang Y, Li D, et al (2020). Circular RNA 0086996 regulates growth and migration of osteosarcoma cells via miR-125b-5p. Pathol Res Pract, 216, 153230.
82. Cao J, Liu XS (2020). Circular RNA 0060428 sponges miR-375 to promote osteosarcoma cell proliferation by upregulating the expression of RPBJ. Gene, 740, 144520.
83. Wang L, Wang P, Su X, et al (2020). Circ\_0001658 promotes the proliferation and metastasis of osteosarcoma cells via regulating miR-382-5p/YB-1 axis. Cell Biochem Funct, 38, 77-86.
84. Fang C, Wang X, Guo D, et al (2020). Circular RNA CircITGA7 Promotes Tumorigenesis of Osteosarcoma via miR-370/PIM1 Axis. Comput Math Methods Med, 2020, 1367576.
85. Li H, He L, Tuo Y, et al (2020). Circular RNA hsa\_circ\_0000282 contributes to osteosarcoma cell proliferation by regulating miR-192/XIAP axis. BMC Cancer, 20, 1026.
86. Pan F, Zhang J, Tang B, et al (2020). The novel circ\_0028171/miR-218-5p/IKBKB axis promotes osteosarcoma cancer progression. Cancer Cell Int, 20, 484.
87. Long Z, Gong F, Li Y, et al (2020). Circ\_0000285 regulates proliferation, migration, invasion and apoptosis of osteosarcoma by miR-409-3p/IGFBP3 axis. Cancer Cell Int, 20, 481.
88. Zhang Z, Pu F, Wang B, et al (2020). Hsa\_circ\_0000285 functions as a competitive endogenous RNA to promote osteosarcoma progression by sponging hsa-miRNA-599. Gene Ther, 27, 186-95.
89. Jiang Y, Hou J, Zhang X, et al (2020). Circ-XPO1 upregulates XPO1 expression by sponging multiple miRNAs to facilitate osteosarcoma cell progression. Exp Mol Pathol, 117, 104553.
90. Wei W, Ji L, Duan W, et al (2020). CircSAMD4A contributes to cell doxorubicin resistance in osteosarcoma by regulating the miR-218-5p/KLF8 axis. Open Life Sci, 15, 848-59.
91. Xie C, Chen B, Wu B, et al (2020). CircSAMD4A regulates cell progression and epithelial‑mesenchymal transition by sponging miR‑342‑3p via the regulation of FZD7 expression in osteosarcoma. Int J Mol Med, 46, 107-18.
92. Lei S, Xiang L (2020). Up-Regulation of circRNA hsa\_circ\_0003074 Expression is a Reliable Diagnostic and Prognostic Biomarker in Patients with Osteosarcoma. Cancer Manag Res, 12, 9315-25.
93. Li S, Pei Y, Wang W, et al (2019). Circular RNA 0001785 regulates the pathogenesis of osteosarcoma as a ceRNA by sponging miR-1200 to upregulate HOXB2. Cell Cycle, 18, 1281-91.
94. Chen J, Liu G, Wu Y, et al (2020). Correction to: CircMYO10 promotes osteosarcoma progression by regulating miR-370-3p/RUVBL1 axis to enhance the transcriptional activity of beta-catenin/LEF1 complex via effects on chromatin remodeling. Mol Cancer, 19, 75.
95. Zhang Z, Zhao M, Wang G (2019). Hsa\_circ\_0051079 functions as an oncogene by regulating miR-26a-5p/TGF-beta1 in osteosarcoma. Cell Biosci, 9, 94.
96. Wang L, Du ZG, Huang H, et al (2019). Circ-0003998 promotes cell proliferative ability and invasiveness by binding to miR-197-3p in osteosarcoma. Eur Rev Med Pharmacol Sci, 23, 10638-46.
97. Wu Y, Xie Z, Chen J, et al (2019). Circular RNA circTADA2A promotes osteosarcoma progression and metastasis by sponging miR-203a-3p and regulating CREB3 expression. Mol Cancer, 18, 73.
98. Jin J, Chen A, Qiu W, et al (2019). Dysregulated circRNA\_100876 suppresses proliferation of osteosarcoma cancer cells by targeting microRNA-136. J Cell Biochem, 120, 15678-87.
99. Zheng S, Qian Z, Jiang F, et al (2019). CircRNA LRP6 promotes the development of osteosarcoma via negatively regulating KLF2 and APC levels. Am J Transl Res, 11, 4126-38.
100. Pan G, Hu T, Chen X, et al (2019). Upregulation Of circMMP9 Promotes Osteosarcoma Progression Via Targeting miR-1265/CHI3L1 Axis. Cancer Manag Res, 11, 9225-31.
101. Qi H, Sun Y, Jiang Y, et al (2019). Upregulation of circular RNA circ\_0000502 predicts unfavorable prognosis in osteosarcoma and facilitates cell progression via sponging miR-1238. J Cell Biochem, 120, 8475-82.
102. Zhou X, Natino D, Qin Z, et al (2018). Identification and functional characterization of circRNA-0008717 as an oncogene in osteosarcoma through sponging miR-203. Oncotarget, 9, 22288-300.
103. Liu G, Huang K, Jie Z, et al (2018). CircFAT1 sponges miR-375 to promote the expression of Yes-associated protein 1 in osteosarcoma cells. Mol Cancer, 17, 170.
104. Deng N, Li L, Gao J, et al (2018). Hsa\_circ\_0009910 promotes carcinogenesis by promoting the expression of miR-449a target IL6R in osteosarcoma. Biochem Biophys Res Commun, 495, 189-96.
105. Song YZ, Li JF (2018). Circular RNA hsa\_circ\_0001564 regulates osteosarcoma proliferation and apoptosis by acting miRNA sponge. Biochem Biophys Res Commun, 495, 2369-75.
106. Huang L, Chen M, Pan J, et al (2018). Circular RNA circNASP modulates the malignant behaviors in osteosarcoma via miR-1253/FOXF1 pathway. Biochem Biophys Res Commun, 500, 511-7.
107. Li JF, Song YZ (2017). Circular RNA GLI2 promotes osteosarcoma cell proliferation, migration, and invasion by targeting miR-125b-5p. Tumour Biol, 39, 1010428317709991.
108. Liu X, Zhong Y, Li J, et al (2017). Circular RNA circ-NT5C2 acts as an oncogene in osteosarcoma proliferation and metastasis through targeting miR-448. Oncotarget, 8, 114829-38.
109. Zhang Z, Zhou Q, Luo F, et al (2021). Circular RNA circ-CHI3L1.2 modulates cisplatin resistance of osteosarcoma cells via the miR-340-5p/LPAATbeta axis. Hum Cell, 34, 1558-68.
110. Li X, Sun XH, Xu HY, et al (2019). Circ\_ORC2 enhances the regulatory effect of miR-19a on its target gene PTEN to affect osteosarcoma cell growth. Biochem Biophys Res Commun, 514, 1172-8.
111. Amuti A, Liu D, Maimaiti A, et al (2021). Doxorubicin inhibits osteosarcoma progression by regulating circ\_0000006/miR-646/ BDNF axis. J Orthop Surg Res, 16, 645.

Supplementary table 2 – Table of circular RNAs with decreased expression correlated to associated hallmarks, involved mechanism of action (target microRNA, target gene, and altered pathways), and code used in this work.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **CODE** | **CIRCULAR RNA** | **MECHANISM OF ACTION** | **ASSOCIATED HALLMARK** | **REFERENCE (Ref. code)** |
| C84 | hsa\_circ\_SLC35E2B\_00 1 (hsa\_circ\_0000006) | ● Increases miR 361-3p ● Decreases LRIG1 expression | Invasion and metastasis; Proliferative signaling | Gao et al., 2021 (1) |
| C85 | Circular RNA circ\_0046264 | ● Increases miR-940 ● Decreases SFRP1 expression | Invasion and metastasis; Proliferative signaling | Du et al., 2021 (2) |
| C86 | circVRK1 | ● Increases miR-337-3p ● Decreases ZNF652 expression | Invasion and metastasis; Proliferative signaling | Cheng et al., 2021 (3) |
| C87 | Circular RNA MTO1 | ● Pathological clinical analysis | Pathological clinical analysis | Shi et al., 2021 (4) |
| ● Increases miR-630 ● Decreases KLF6 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2021 (5) |
| C88 | hsa\_circ\_0000658 | ● Increases miR-1227 ● Decreases IRF2 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Jiang and Chen, 2021 (6) |
| C89 | hsa\_circ\_0001649 | ● Increases miR-338-5p, miR-647 and miR-942 ● Active STAT3 signaling pathway | Proliferative signaling; Resistance to cell death | Sun and Zhu, 2020 (7) |
| C90 | Circ\_WWC3 | ● Increases miR-421 ● Decreases PDE7B | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Liu et al., 2021 (8) |
| C91 | Hsa\_circ\_0088212 | ● Increases miR-520h ●Decreases APOA1 expression | Proliferative signaling; Resistance to cell death | Liu et al., 2021 (9) |
| C92 | circ\_0001105 | ● Increases miR-766 ● Decreases YTHDF2 expression | Invasion and metastasis; Proliferative signaling; Genome instability and mutation | Yang et al., 2020 (10) |
| C93 | Hsa\_circ\_0008792 | ● Increases miR-711 ● Decreases ZFP1 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Chen et al., 2020 (11) |
| C94 | hsa\_circ0021347 | ● B7-H3 decreases hsa\_circ0021347 | Not cited | Wang et al., 2019 (12) |
| C31 | CircITCH | ● Increases miR-524 ● Decreases RASSF6 expression | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Zhou et al., 2021 (13) |
| C32 | circ\_HIPK3 | ● Not cited | Invasion and metastasis; Proliferative signaling | Xiao-long et al., 2018 (14) |
| C34 | hsa\_circ\_0002052 | ● Increases miR-1205 ● Decreases APC2 expression ● Active Wnt/B-catenin | Invasion and metastasis; Proliferative signaling; Resistance to cell death | Wu et al., 2018 (15) |

Ref. code: the corresponding number of the reference in the reference section. STAT3, Signal transducer and activator Of transcription 3; LRIG1, Immunoglobulin-like domains protein 1; RASSF6, Ras association domain family member 6; SFRP1, Secreted Frizzled Related Protein 1; ZNF652, Zinc Finger Protein 652; IRF2, Interferon regulatory factor 2; KLF6, KLF Transcription fator 6; PDE7B, Phosphodiesterase 7B; APOA 1, Apolipoprotein A1; YTHDF2, YTH N6-methyladenosine rna binding protein 2; ZFP1, ZFP1 Zinc Finger Protein; APC2, APC Regulator Of WNT Signaling Pathway 2.

**References Supplementary table 2**

1. Gao Y, Liu C, Zhao X, et al (2021). hsa\_circ\_0000006 induces tumorigenesis through miR-361-3p targeting immunoglobulin-like domains protein 1 (LRIG1) in osteosarcoma. Ann Transl Med, 9, 1242.
2. Du R, Fu B, Sun G, et al (2021). Circular RNA circ\_0046264 Suppresses Osteosarcoma Progression via microRNA-940/Secreted Frizzled Related Protein 1 Axis. Tohoku J Exp Med, 254, 189-97.
3. Cheng C, Zhang H, Dai Z, et al (2021). Circular RNA circVRK1 suppresses the proliferation, migration and invasion of osteosarcoma cells by regulating zinc finger protein ZNF652 expression via microRNA miR-337-3p. Bioengineered, 12, 5411-27.
4. Shi Z, Wen Y, Zhang S, et al (2021). Circular RNA MTO1 intercorrelates with microRNA-630, both associate with Enneking stage and/or pathological fracture as well as prognosis in osteosarcoma patients. J Clin Lab Anal, 35, e23987.
5. Liu DY, Li Z, Zhang K, et al (2021). Circular RNA CircMTO1 suppressed proliferation and metastasis of osteosarcoma through miR-630/KLF6 axis. Eur Rev Med Pharmacol Sci, 25, 86-93.
6. Jiang X, Chen D (2021). Circular RNA hsa\_circ\_0000658 inhibits osteosarcoma cell proliferation and migration via the miR-1227/IRF2 axis. J Cell Mol Med, 25, 510-20.
7. Sun D, Zhu D (2020). Circular RNA hsa\_circ\_0001649 suppresses the growth of osteosarcoma cells via sponging multiple miRNAs. Cell Cycle, 19, 2631-43.
8. Liu S, Zhang J, Zheng T, et al (2021). Circ\_WWC3 overexpression decelerates the progression of osteosarcoma by regulating miR-421/PDE7B axis. Open Life Sci, 16, 229-41.
9. Liu F, Zhang X, Wu F, et al (2021). Hsa\_circ\_0088212-mediated miR-520 h/APOA1 axis inhibits osteosarcoma progression. Transl Oncol, 14, 101219.
10. Yang J, Han Q, Li C, et al (2020). Circular RNA circ\_0001105 Inhibits Progression and Metastasis of Osteosarcoma by Sponging miR-766 and Activating YTHDF2 Expression. Onco Targets Ther, 13, 1723-36.
11. Chen L, Shan Y, Zhang H, et al (2020). Up-Regulation of Hsa\_circ\_0008792 Inhibits Osteosarcoma Cell Invasion and Migration and Promotes Apoptosis by Regulating Hsa-miR-711/ZFP1. Onco Targets Ther, 13, 2173-81.
12. Wang L, Zhang GC, Kang FB, et al (2019). hsa\_circ0021347 as a Potential Target Regulated by B7-H3 in Modulating the Malignant Characteristics of Osteosarcoma. Biomed Res Int, 2019, 9301989.
13. Zhou W, Liu Y, Wu X (2021). Down-regulation of circITCH promotes osteosarcoma development and resistance to doxorubicin via the miR-524/RASSF6 axis. J Gene Med, 23, e3373.
14. Xiao-Long M, Kun-Peng Z, Chun-Lin Z (2018). Circular RNA circ\_HIPK3 is down-regulated and suppresses cell proliferation, migration and invasion in osteosarcoma. J Cancer, 9, 1856-62.
15. Wu Z, Shi W, Jiang C (2018). Overexpressing circular RNA hsa\_circ\_0002052 impairs osteosarcoma progression via inhibiting Wnt/beta-catenin pathway by regulating miR-1205/APC2 axis. Biochem Biophys Res Commun, 502, 465-71.

**Supplementary materials and methods**

*Research strategy in databases.*

PUBMED

#1 ((((((((((((((((RNA, Circular) OR (circRNAs)) OR (Closed Circular RNA)) OR (Circular RNA, Closed)) OR (RNA, Closed Circular)) OR (Circular RNA)) OR (Circular RNAs)) OR (RNAs, Circular)) OR (circRNA)) OR (Circular Intronic RNA)) OR (Intronic RNA, Circular)) OR (RNA, Circular Intronic)) OR (ciRNA)) OR (exonic circRNA)) OR (ecircRNA)) OR (EIciRNA)) OR (exon-intron circRNA)

AND

#2 (((((((((Osteosarcoma) OR (Osteosarcomas)) OR (Osteosarcoma Tumor)) OR (Osteosarcoma Tumors)) OR (Tumor, Osteosarcoma)) OR (Tumors, Osteosarcoma)) OR (Sarcoma, Osteogenic)) OR (Osteogenic Sarcomas)) OR (Sarcomas, Osteogenic)) OR (Osteogenic Sarcoma)

SCOPUS

((circular ribonucleic acid) OR (circular RNA) OR (RNA, circular) OR (circRNA) OR (Closed Circular RNA) OR (RNA, Closed Circular) OR (Circular Intronic RNA) OR (Intronic RNA, CircularOR (RNA, Circular Intronic) OR (ciRNA) OR (exonic circRNA) OR (ecircRNA) OR (EIciRNA) OR (exon-intron circRNA))

((osteosarcoma) OR (bone AND sarcoma) OR (intracortical AND sarcoma) OR (osteogenic AND sarcoma) OR (osteoide AND sarcoma) OR (osteolytic AND sarcoma) OR (osteosarcoma, AND uxtacortical) OR (primary AND osteogenic AND sarcoma) OR (sarcoma, AND bone) OR (sarcoma, AND osteogenic))

EMBASE

#1 'circular ribonucleic acid'/exp OR (circular RNA) OR (RNA, circular) OR (CircRNA) OR (Closed Circular RNA) OR (RNA, Closed Circular) OR (Circular Intronic RNA) OR (Intronic RNA, Circular) OR (RNA, Circular Intronic) OR (ciRNA) OR (exonic circRNA) OR (ecircRNA) OR (EIciRNA) OR (exon-intron circRNA)

#2 'osteosarcoma'/exp OR (Bone Sarcoma) OR (Intracortical Sarcoma) OR (Osteogenic Sarcoma) OR (Osteoid Sarcoma) Or (Osteolytic Sarcoma) OR (Osteosarcoma, Juxtacortical) OR (Primary Osteogenic Sarcoma) OR (Sarcoma, Bone) OR (Sarcoma, osteogenic)

OVID

#1 'osteosarcoma'/exp OR 'osteosarcoma' OR (('bone'/exp OR bone) AND ('sarcoma'/exp OR sarcoma)) OR (intracortical AND ('sarcoma'/exp OR sarcoma)) OR (osteogenic AND ('sarcoma'/exp OR sarcoma)) OR (('osteoid'/exp OR osteoid) AND ('sarcoma'/exp OR sarcoma)) OR (osteolytic AND ('sarcoma'/exp OR sarcoma)) OR (('osteosarcoma,'/exp OR osteosarcoma,) AND juxtacortical) OR (primary AND osteogenic AND ('sarcoma'/exp OR sarcoma)) OR (('sarcoma,'/exp OR sarcoma,) AND ('bone'/exp OR bone)) OR (('sarcoma,'/exp OR sarcoma,) AND osteogenic)

#2 'circular ribonucleic acid'/exp OR 'circular ribonucleic acid' OR (circular AND ('rna'/exp OR rna)) OR (('rna,'/exp OR rna,) AND circular) OR 'circrna'/exp OR circrna OR (closed AND circular AND ('rna'/exp OR rna)) OR (('rna,'/exp OR rna,) AND closed AND circular) OR (circular AND intronic AND ('rna'/exp OR rna)) OR (intronic AND ('rna,'/exp OR rna,) AND circular) OR (('rna,'/exp OR rna,) AND circular AND intronic) OR cirna OR (exonic AND ('circrna'/exp OR circrna)) OR ecircrna OR eicirna OR ('exon intron' AND ('circrna'/exp OR circrna))

WEB OF SCIENCE

((circular ribonucleic acid) OR (circular RNA) OR (RNA, circular) OR (circRNA) OR (Closed Circular RNA) OR (RNA, Closed Circular) OR (Circular Intronic RNA) OR (Intronic RNA, CircularOR (RNA, Circular Intronic) OR (ciRNA) OR (exonic circRNA) OR (ecircRNA) OR (EIciRNA) OR (exon-intron circRNA))

((osteosarcoma) OR (bone AND sarcoma) OR (intracortical AND sarcoma) OR (osteogenic AND sarcoma) OR (osteoide AND sarcoma) OR (osteolytic AND sarcoma) OR (osteosarcoma, AND juxtacortical) OR (primary AND osteogenic AND sarcoma) OR (sarcoma, AND bone) OR (sarcoma, AND osteogenic))