**Table S1. Key reagents and resources.**

|  |  |  |
| --- | --- | --- |
| **REAGENT or RESOURCE** | **SOURCE** | **IDENTIFIER or SEQUENCE** |
| **Antibodies** |
| Anti-CDK8 | SantaCruz | Cat#sc-1521 |
| Anti-CDK19 | Sigma | Cat#HPA007053 |
| Anti-SMAD4 | Cell Signaling | Cat#9515s |
| Anti-β-Catenin | Cell Signaling | Cat#9587s |
| Anti-TIMP3 | Abcam | Cat#ab39184 |
| Anti-MMP3 | ThermoFisher Scientific | Cat#MA5-17123 |
| Anti-β-Actin | Cell Signaling | Cat#3700 |
| HRP-anti-goat IgG  | SantaCruz | Cat#sc-2020 |
| HRP-anti-rabbit IgG | ThermoFisher Scientific | Cat#31460 |
| HRP-anti-mouse IgG | ThermoFisher Scientific | Cat#31430 |
| Alexa Fluor® 488-anti-rabbit IgG | ThermoFisher Scientific | Cat#A-21206 |
| Alexa Fluor® 594-anti-rabbit IgG | ThermoFisher Scientific | Cat#A-21203 |
| **Bacterial and Virus Strains**  |
| One Shot® Stbl3™ Competent E. coli | ThermoFisher Scientific | Cat#C737303 |
| **Chemicals, Peptides, and Recombinant Proteins** |
| Senexin B | Senex Biotechnology  |  |
| **Critical Commercial Assays** |
| MycoAlert™ Mycoplasma Detection Kit | Lonza | Cat#LT07 |
| RNeasy Mini Kit | Qiagen | Cat#74106 |
| iScript cDNA synthesis kit | Bio-Rad Laboratories  | Cat#1708891 |
| iTaqTM Universal SYBR® Green Supermix | Bio-Rad Laboratories | Cat#172-5124 |
| QiaQuick Gel Extraction Kit  | Qiagen | Cat#28706 |
| CloneDirect™ Rapid Ligation Kit | Lucigen | Cat#40020 |
| Lipofectamine™ 3000 | ThermoFisher Scientific | Cat#L3000015 |
| SureBeads Protein G Mag beads | Bio-Rad Laboratories | Cat#1614023 |
| DC Protein Assay Kit | Bio-Rad Laboratories | Cat#5000116 |
| E. *coli* Poly(A) Polymerase | New England BioLabs | Cat#M0276 |
| Tetro Reverse Transcriptase kit | Bioline | Cat#BIO-65050 |
| RNA picochip and reagents, Bioanalyzer 2100 |  |  |
| DNA 7500 chip and reagents, Bioanalyzer 2100 |  |  |
| **Experimental Models: Cell Lines** |
| CT26 | ATCC | CRL2638 |
| HCT-116 | ATCC | CRL-247 |
| LoVo | ATCC | CRL-229 |
| SW620 | ATCC | CRL-227 |
| SW480 | ATCC | CRL-228 |
| SW948 | ATCC | CRL-237 |
| SW48 | ATCC | CRL-231 |
| DLD-1 | ATCC | CCL-221 |
| HT-29 | ATCC | HTB-38 |
| SW116 | ATCC | CCL-233 |
| HCT-15 | ATCC | CCL-225 |
| 293FT | ThermoFisher Scientific | R70007 |
| **Experimental Models: Organisms/Strains** |
| Mouse: BALB/cJ | The Jackson Laboratory | Stock No: 000651 |
| Mouse: Athymic nude (nu/nu) | The Jackson Laboratory | Stock No: 002019 |
| **Recombinant DNA: Vectors and Oligonucleotides** |
| hTIMP3-TGA-XbaI | This paper | TCAGGTCTAGATCAGGGGTCTGTGGCATTGATGATG |
| hTIMP3-ATG-XbaI | This paper | TCAGGTCTAGAGCGGCAATGACCCCTTGGCTCGGGCTCA |
| pLenti6-TR | Thermo Fisher Scientific | Cat# V48020 |
| pRK5M-TIMP3 | Addgene | Plasmid #31715 |
| Tet-pLKO-puro | Addgene | Plasmid #21915 |
| shCDK8-1 | Sigma-Aldrich | TRCN0000322327 |
| shCDK8-2 | Sigma-Aldrich | TRCN0000322410 |
| shCDK19-1 | Sigma-Aldrich | TRCN0000023283 |
| shCDK19-2 | Sigma-Aldrich | TRCN0000360760 |
| shMMP3-1 | Sigma-Aldrich | TRCN0000031237 |
| shMMP3-2 | Sigma-Aldrich | TRCN0000348486 |
| shMMP3-3 | Sigma-Aldrich | TRCN000031234 |
| shSMAD4-1 | Sigma-Aldrich | TRCN0000025885 |
| shSMAD4-2 | Sigma-Aldrich | TRCN0000025900  |
| shSMAD4-3 | Sigma-Aldrich | TRCN0000362660 |
| shSTAT1-1 | Sigma-Aldrich | TRCN0000054924 |
| shSTAT1-2 | Sigma-Aldrich | TRCN0000054926  |
| shCTNNB1-1 | Sigma-Aldrich | TRCN0000012688 |
| shCTNNB1-2 | Sigma-Aldrich | TRCN0000012692 |
| human shCDK8  | This paper | GCTTCCAAGTTGTACCTATTT |
| Mmu-miR-181-5p-mimic | Dharmacon | C-310587-07-0002 |
| miRIDIAN microRNA mmu-miR-181b-5p hairpin inhibitor | Dharmacon | IH-310587-08-0002 |
| Mimic negative control #1 | Dharmacon | CN-001000-01-05 |
| **Software and Algorithms** |
| GraphPad Prism 5  | GraphPad Software | Prism 5 |
| SurvExpressFor the Kaplan-Meier study with clinical data | Aguirre-Gamboa et al., 2013 | http://bioinformatica.mty.itesm.mx:8080/Biomatec/SurvivaX.jsp |
| Microarray data analysis | Thermo Fisher Scientific | Expression Console |
| shRNA design | Broad Institute | <https://portals.broadinstitute.org/gpp/public/seq/search> |