**Table S1. Targeting sequences of CRISPR system.**

|  |  |  |
| --- | --- | --- |
| **Gene** | **Protospacer (5’→3’)** | **PAM(5’→3’)** |
| KRAS-KO#1 | caattactacttgcttcctgt | aggaat |
| MEK1-KO#1 | catagaagcccacgatgtacg | gagagt |
| PIK3CA-KO#1 | tgatgcccccaagaatcctag | tagaat |
| MTOR-KO#1 | tagagactgtggaccgcctga | cggagt |
| KRAS-KO#2 | taattcagaatcattttgtgg | acgaat |
| MEK1-KO#2 | gcctcctccaaaactgcccag | tggagt |
| PIK3CA-KO#2 | agtagaatgtttactaccaaa | tggaat |
| MTOR-KO#2 | tggcaggggacacttttaccg | ctgagt |

**Table S2. PCR primers of molecular cloning, Sanger sequencing, T7E1 and RT-qPCR.**

|  |  |
| --- | --- |
| **Name** | **Primer (5’→3’)** |
| EXADR Forward | AGAGCGATCGCATGgcgctcctgctgtgc |
| EXADR Reverse | cgcGGATCCGTGATGATGATGATGATGtccagctttatttga |
| Fibritin Forward | cgcGGATCCcgcggattaaccaattca |
| Fibritin Reverse | cgtacgcgttgctggtgataaaaaggt |
| Anti-EpCAM scFv Forward | cgtACGCGTGGCGGAGGGGGATCAGGA |
| Anti-EpCAM scFv Reverse | ccgCTCGAGTTACCCTGAGGACACGGT |
| Anti-MUC1 scFv Forward | cgtACGCGTGGCGGAGGGGGATCAGGA |
| Anti-MUC1 scFv Reverse | ccgCTCGAGTTAcgctctcttgatctc |
| Anti-Hexon scFv Forward | AGAGCGATCGCATGGGCAGCAGCCATCA |
| Anti-Hexon scFv Reverse | cgtacgcgtGCTGCCTCCCCCTCCGCT |
| KRAS Exon2 Forward | CTTTGAGAGCCTTTAGCC |
| KRAS Exon2 Reverse | ACTTCCAATCAAAATGCACA |
| PIK3CA Exon10 Forward | TAACCAAATAAATTACTGGA |
| PIK3CA Exon10 Reverse | TAAATATACCCGTATCACC |
| PIK3CA Exon21 Forward | GTATTAACATCATTTGCTCC |
| PIK3CA Exon21 Reverse | ATTCCTATGCAATCGGTC |
| KRAS#1 T7E1 Forward | TATTTCCACATTTTGGGTA |
| KRAS#1 T7E1 Reverse | GATTTAGTATTATTTATGGCAA |
| MEK1#1 T7E1 Forward | CCTGCCTTAGTACAATGACAC |
| MEK1#1 T7E1 Reverse | CTCCTTCCACTAACGTGCAT |
| PIK3CA#1 T7E1 Forward | GAATTATTACTACTTAGCCTA |
| PIK3CA#1 T7E1 Reverse | ATCTTTTCTTCACGGTTG |
| MTOR#1 T7E1 Forward | TAAGTTGTTTGATGCCCCT |
| MTOR#1 T7E1 Reverse | AAATAAGGCAGAAGAGCACC |
| KRAS#2 T7E1 Forward | CTTTGAGAGCCTTTAGCC |
| KRAS#2 T7E1 Reverse | ACTTCCAATCAAAATGCACA |
| MEK1#2 T7E1 Forward | TAGTTCAAAATCACCCGACA |
| MEK1#2 T7E1 Reverse | CTGGGCTTGATTCATCCTC |
| PIK3CA#2 T7E1 Forward | AAATAAATTCTTTGTAGCCTA |
| PIK3CA#2 T7E1 Reverse | ATCTTTTCTTCACGGTTG |
| MTOR#2 T7E1 Forward | CTCCTCCCCTCCAATGACC |
| MTOR#2 T7E1 Reverse | GCTGATGCTTCTGATCCCC |
| EpCAM Forward | TTATGATCCTGACTGCGATG |
| EpCAM Reverse | GTAGGTTCTCACTCGCTCA |
| MUC1 Forward | CCTACCATCCTATGAGCGAGT |
| MUC1 Reverse | CTGCTGCCACCATTACCTG |
| SaCas9 Forward | GCAACAAACTGAACGCCCAT |
| SaCas9 Reverse | TCCAGATTCTTCACGGTCAC |
| -Actin Forward | TTAGTTGCGTTACACCCTTT |
| -Actin Reverse | ACCTTCACCGTTCCAGTTT |
| KRAS gRNA Forward | CACCGAATTACTACTTGCT |
| KRAS gRNA Reverse | TCTCGCCAACAAGTTGAC |
| MEK1 gRNA Forward | ATGTACGGTTTTAGTACTCT |
| MEK1 gRNA Reverse | TCTCGCCAACAAGTTGAC |
| PIK3CA gRNA Forward | CCCCAAGAATCCTAGGTT |
| PIK3CA gRNA Reverse | ACGAGATAAACACGGCAT |
| MTOR gRNA Forward | CACCGAGAGACTGTGGACC |
| MTOR gRNA Reverse | TCTCGCCAACAAGTTGAC |

**Table S3. Clinical and mutation information of primary and PDX tumors of CRC.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ID** | **Gender** | **Age** | **TNM stage** | **Mutation status** |
| Primary tumors | | | |  |
| CRC-P01 | M | 39 | T4aN2M0 | KRAS 38G>A (G13D);  PIK3CA 3140A>G (H1047R) |
| CRC-P02 | F | 62 | T2N0M0 | KRAS 35G>A (G12D);  PIK3CA 3140A>G (H1047R) |
| CRC-P03 | M | 52 | T3N0M0 | KRAS 35G>T (G12V);  PIK3CA 3140A>G (H1047R) |
| CRC-P04 | M | 67 | T3N0M0 | KRAS 35G>A (G12D) |
| PDX model | | | |  |
| CRC-PDX01 | F | 62 | T3N0M1 | KRAS 35G>T (G12V) |
| CRC-PDX02 | F | 62 | T3N2M1 | KRAS 37G>T (G13C) |
| CRC-PDX03 | M | 60 | T3N1M1 | KRAS 38G>A (G13D) |