**Table S1. Primer pairs for real-time PCR analysis of expression of immunotherapy target genes**

|  |  |  |
| --- | --- | --- |
| Gene | 5’ primer | 3’ primer |
| *BIRC5* | GTTGCGCTTTCCTTTCTGTC | TCCGCAGTTTCCTCAAATTC |
| *CA9* | CCTTTGCCAGAGTTGACGA | CTCAGCGATTTCTTCCAAGC |
| *CCNB1* | TACCTATGCTGGTGCCAGTG | AGATGTTTCCATTGGGCTTG |
| *CD276* | GGAGAATGCAGGAGCTGAGG | AGCTGTAGGGAGGGGTAGC |
| *CEACAM5* | GCCAAAATCACGCCAAA | CCAGCTGAGAGACCAGGAGA |
| *CSPG4* | TTGGCTTTGACCCTGACTATG | CTGCAGGTCTATGTCGGTCA |
| *CYP1B1* | AACGTACCGGCCACTATCAC | CCACGACCTGATCCAATTCT |
| *EGFR* | AAACAACACCCTGGTCTGGAAG | TCTTAGGCCCATTCGTTGGA |
| *EPCAM* | TGGAATTGTTGTGCTGGTTATTTC | GTGTCCATTTGCTATTTCCCTTC |
| *EPHA2* | GTGCAGTGGATGGCGAGT | GGCTCTCAGATGCCTCAAAC |
| *ERBB2* | GCCTGCCACCCCTGTT | CACAGCCACCGGCACA |
| *FAP* | GCTGTGCTTGCCTTATTGGT | TCAGTGTGAGTGCTCTCATTGTAT |
| *FOSL1* | GGGCATGTTCCGAGACTTC | TGACTGCCACTCATGGTGTT |
| *KDR* | CTCCCGAGTTCTGGGCATT | AGCCTGGGCAGATCAAGAGA |
| *LCK* | GATCTCACAATCTCAGGGACCAT | GAGCCATTTCGGATGAGCA |
| *LGMN* | GAAGATTCGGACGTGGAAGA | GTTTCCATACTGCATGACGTG |
| *MGAT5* | ACCGGAACAAACTCAACCAA | AGTGAGGGTAGCCGTCCATA |
| *MSLN* | ATTTGAAGGCGCTCAGTCAG | CCAGAAGTTTCTGCACCTCAG |
| *MUC1* | GGTTCTGGTCATGCAAGCTCTAC | GAGACCCCAGTAGACAAAGCA |
| *MYCN* | CAGTCGGCGGGAGTGTT | TCCGCCCCGTTCGTT |
| *PDGFRB* | TGTCCAGAGCCTGGAACTGT | GCCCTGAGAGATCTGTGGTT |
| *RGS5* | GTGCAAAGGACTTGCAGCTT | GGTCTTGGCTGGTTTCTCTG |
| *RHOC* | CGGAAGCCTTGACTTCATCT | CACCAGCTTCTTTCGGATTG |
| *SART3* | CGAGTGGGAATATGACGAAGA | CATCCTCACCTTGGTAAGCTC |
| *TEK* | CTTGGCAACATATTCAAGTGACAAA | AAGCGTCTCACAGGTCCA |
| *TP53* | GCTTTCCACGACGGTGAC | GCTCGACGCTAGGATCTGAC |
| *WT1* | CGCTATTCGCAATCAGGGTTA | CCTCATGCTTGAATGAGTGGTT |
| *GAPDH* | CTCTGCTCCTCCTGTTCGAC | TTAAAAGCAGCCCTGGTGAC |

**Table S2. Characteristics of patients from whom CRC xenografts were established**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Subject | Site | Age | Sex | Pathology | Grade | Genetics | Location | Stage | LVI | Tx | # cells implanted | Doubling time (days) | Xenograft generations |
| *D49708* | VU | 63 | F | Adenocarcinoma | Poor | - | R colon | T3N2b | Yes | No | 1x104-1x106 | - | 1\* |
| D52955 | VU | 72 | M | Adenocarcinoma | Mod. | - | R colon | T3N0 | No | No | 1x106 | 35.9 | 1\* |
| *D55949* | VU | 49 | M | Adenocarcinoma with mucinous features | Mod. | K-ras mut†, BRAF WT† | R Colon | T3N2b | No | No | 1x104-1x105 | 7.3 | 10+ |
| D51638 | VU | 69 | F | Adenocarcinoma with mucinous features | Poor | - | R colon | T3N0 | No | No | 1x106 | 10.1 | 1⊗ |
| D52751 | VU | 47 | M | Adenocarcinoma with mucinous features | Mod. | - | R colon | T3N1bM1a | Yes | No | 1x106 | 16.2 | 1⊗ |
| D60739 | VU | 46 | F | Adenocarcinoma | Mod. | - | Sigmoid | T3N1bM1a | Yes | No | 1x106-2x106 | 7.0 | 3+ |
| P9625 | UW | 36 | F | Adenocarcinoma | Mod. | MSS | R colon | T3N1b | Yes | No | 1x106 | Non-exp. | 1\* |
| D61211 | VU | 80 | M | Adenocarcinoma | Mod. | - | Sigmoid | T3N0 | No | No | 6x105 | 5.3 | 3+ |
| D61540 | VU | 83 | M | Adenocarcinoma with minor neuroendocrine component | Poor | K-ras mut†, BRAF WT† | R Colon | T3N1b | Yes | No | 1x106 | 12.1 | 7+ |
| P2726 | UW | 41 | F | Metastatic adenocarcinoma | - | MSS, K-ras WT, BRAF WT† | Ovary,  Omentum,  Ascites | M1b | - | Yes | 1x106-2x106 | 5.7,  5.9,  Non-exp. | Ovary-10+, Omentum-1+, Ascites-1⊗ |
| P2750 | UW | 26 | M | Mucinous adenocarcinoma | - | MMRP, K-ras WT, BRAF WT† | R colon-peritoneal | M1b | - | Yes | 1x106 | Non-exp. | 2⊗ |
| P2762 | UW | 55 | M | Metastatic adenocarcinoma | - | - | Liver | M1a | - | Yes | 1x106 | 9.4 | 4+ |
| P2792 | UW | 49 | F | Metastatic adenocarcinoma | - | MMRP, K-ras mut | Liver | T4aN2aM1a | - | Yes | 1x106 | 7.8 | 6+ |
| P2773 | UW | 51 | F | Metastatic adenocarcinoma | - | K-ras mut | Retro-peritoneal | M1b | - | Yes | 2x105 | 8.6 | 5+ |
| WD2112 | VU | 50 | F | Adenocarcinoma | Mod. | MSS, K-ras WT | L colon | T3N2a | No | No | 1x106-2x106 | 11.3 | 2+ |
| WD2713 | VU | 78 | F | Adenocarcinoma | Poor | MSI | R colon | T3N0 | No | No | 1x106-2x106 | Non.exp. | 2⊗ |
| P2797 | UW | 66 | F | Adenocarcinoma | Well | MSS | Recto-sigmoid | T3N0 | No | No | 1x106 | Non-exp. | 1⊗ |
| P2796 | UW | 45 | M | Neuroendocrine | Well | - | Rectum | T3N1bM1b | Ind. | No | 6x105-1x106 | Non-exp. | 1⊗ |
| P2807 | UW | 63 | M | Metastatic adenocarcinoma | - | K-ras WT, BRAF WT | Liver | M1a | - | Yes | 3x105 | Non-exp. | 1\* |
| P2808 | UW | 66 | F | Metastatic adenocarcinoma | - | K-ras mut, BRAF WT | Lung | M1a | - | Yes | 1x106 | 9.4 | 5+ |
| P2816 | UW | 52 | M | Metastatic adenocarcinoma | - | K-ras WT, BRAF WT | Liver | M1a | - | No | 1x106 | 9.4 | 4+ |
| P2818 | UW | 61 | M | Metastatic adenocarcinoma | - | K-ras mut | Liver | M1a | - | Yes | 1x106 | 20.6 | 3+ |
| P2822 | UW | 64 | M | Adenocarcinoma | Mod. | - | Sigmoid | T3N2a | Yes | No | 2x106 | 34.0 | 2+ |
| P2824 | UW | 66 | M | Adenocarcinoma | Mod. | - | Sigmoid,  Liver | T3N0M1a | Ind. | Yes | 1x106 | 47.2,  138.6 | Sigmoid-1⊗, Liver-2⊗ |
| P2825 | UW | 64 | M | Metastatic adenocarcinoma | - | K-ras mut, BRAF WT | Omentum, Abdominal wall | M1b | - | Yes | 5x105-2x106 | 24.7,  Non-exp. | Omentum-1⊗, Abd. wall-1⊗ |
| P2827 | UW | 78 | M | Adenocarcinoma with mucinous features | Well | - | R colon,  Liver | T3N2aM1a | Ind. | Yes | 1x106-2x106 | 9.3,  19.1 | Colon-2+, Liver-2+ |
| P2842 | UW | 54 | F | Adenocarcinoma | Well | MMRP, K-ras mut | Rectum,  Liver | T1N0M1a | No | Yes | 2x106 | 7.3,  8.9 | Rectum-1+, Liver-1+ |

The last successful serial passage of a xenograft line is indicated for each parental human tumor. **Bold** = injected subcutaneously; Underline = injected under kidney capsule; *Italics* = CD133 sorted; VU = CHTN - Vanderbilt University; UW = University of Washington; M = male; F = female; Mod. = moderate; MSS = microsatellite stable; MSI = microsatellite instability; MMRD/P = mismatch repair deficient/proficient; WT = wild type; mut = mutant; † = determined from RNA-seq data; LVI = lymphovascular invasion; Ind. = indeterminate; Tx = received chemotherapy prior to resection; # cells implanted = number of cells implanted from parental human tumor; Non exp. = R2 < 0.5 when tumor growth data fitted to an exponential growth curve; + = successfully xenografted without failure; \* = did not attempt passage; ⊗ = could not continue serial xenografts

**Table S3. Characteristics of patients from whom CRC xenografts could not be established.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Subject | Site | Age | Sex | Pathology | Grade | Genetics | Location | Stage | LVI | Tx | # cells implanted | Alive > 1 wk |
| P3802 | UW | 55 | M | Metastatic adenocarcinoma | - | - | Liver | M1a | - | Yes | 1x105 | Yes |
| P4816 | UW | 66 | F | Metastatic adenocarcinoma | - | - | Liver | M1a | - | Yes | 1x104-2x106 | No |
| P8172 | UW | 56 | F | Metastatic adenocarcinoma | - | K-ras mut | Liver | M1a | - | Yes | 5x105 | Yes |
| D56241 | VU | 75 | M | Adenocarcinoma | Mod. | - | Cecum | T3N0 | No | No | 2x105 | Yes |
| *D46208* | VU | 50 | M | Adenocarcinoma | Mod. | - | L colon | T3N1 | No | No | < 104 | Yes |
| *D56242* | VU | 67 | M | Adenocarcinoma | Mod. | - | Rectum | T3N0 | No | No | 1x105-5x105 | Yes |
| *D49849* | VU | 73 | F | Adenocarcinoma with focal mucin production | Mod. | - | R colon | T3N0 | No | No | 1x104 | Yes |
| D50147 | VU | 47 | M | Medullary carcinoma | Poor | - | Cecum | T3N1 | Yes | No | 1x106 | No |
| D50473 | VU | 89 | F | Adenocarcinoma | Mod | - | R colon | T4bN0 | No | No | 1x106 | Yes |
| D51646 | VU | 79 | F | Mucinous adenocarcinoma | Mod. | - | Sigmoid | T4bN0 | No | No | 5x105 | Yes |
| P1892 | UW | 49 | F | Adenocarcinoma | Well | MMRD | Transverse colon | T3N0 | No | No | 5x105 | No |
| D57405 | VU | 62 | F | Adenocarcinoma | Mod. | - | Recto-sigmoid, liver | T3N2aM1a | Yes | No | 3mm piece | No |
| P8948 | UW | 49 | F | Metastatic adenocarcinoma | - | MSS | Liver | M1a | - | Yes | 1x106 | No |
| P7654 | UW | 37 | M | Metastatic adenocarcinoma | - | MSS, K-ras WT | Liver | M1a | - | Yes | 1x104 | Yes |
| P7028 | UW | 68 | F | Metastatic adenocarcinoma with mucinous features | - | K-ras mut | Omentum | M1b | - | Yes | 3x104 | Yes |
| P1854 | UW | 70 | F | Adenocarcinoma | Well | - | Rectum | T3N1 | No | Yes | 3x105 | Yes |
| D60877 | VU | 77 | M | Adenocarcinoma | Mod. | - | L colon | T3N2a | No | No | 1x106 | No |
| D61121 | VU | 52 | F | Adenocarcinoma | Mod. | MSS | L colon | T4aN2b | Yes | No | 1x106 | Yes |
| D61187 | VU | 84 | F | Adenocarcinoma | Mod. | MSS | Rectum | T3N2b | No | No | 1x106 | Yes |
| P1442 | UW | 59 | M | Adenocarcinoma | Well | K-ras WT | Sigmoid | T3N2bM1a | No | Yes | 3x105 | Yes |
| D61462 | VU | 64 | F | Adenocarcinoma | Mod. | - | Sigmoid | T3N1a | No | No | 1x106 | Yes |
| WD349 | VU | 70 | F | Adenocarcinoma with medullary features | Poor | MSI | R colon | T2N1c | No | No | 1x106 | Yes |
| P2820 | UW | 65 | F | Metastatic mucinous adenocarcinoma | - | - | Liver | M1a | - | Yes | 1x106 | Yes |

**Bold** = injected subcutaneously; Underline = injected under kidney capsule; *Italics* = CD133 sorted; VU = CHTN - Vanderbilt University; UW = University of Washington; M = male; F = female; Mod. = moderate; MSS = microsatellite stable; MSI = microsatellite instability; MMRD/I = mismatch repair deficient/intact; WT = wild type; mut = mutant; LVI = lymphovascular invasion; Tx = received chemotherapy prior to resection; Alive > 1 wk = mice injected with CRC survived longer than 1 week.

**Table S4. Association of tumor characteristics with engraftment**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristic | Condition | Success | Fail | Percentage | P-value |
| Site | UW | 17 | 7 | 71% | 0.19 |
|  | VU | 8 | 9 | 47% |  |
| Age | >60 | 13 | 10 | 57% | 0.54 |
|  | <60 | 12 | 6 | 67% |  |
| Sex | M | 14 | 4 | 78% | 0.06 |
|  | F | 11 | 12 | 48% |  |
| Mucinous | Yes | 3 | 3 | 50% | 0.66 |
|  | No | 22 | 13 | 63% |  |
| Primary vs metastatic\* | Primary | 15 | 12 | 56% | 0.35 |
|  | Metastasis | 13 | 5 | 72% |  |
| LVI (primary only) | Yes | 5 | 3 | 63% | 0.67 |
|  | No | 7 | 9 | 44% |  |
| Location (primary only) | Colon | 9 | 9 | 50% | 1.00 |
|  | Rectum | 3 | 3 | 50% |  |
| Received chemotherapy | Yes | 12 | 6 | 67% | 0.54 |
|  | No | 13 | 10 | 57% |  |

The characteristics of human CRC tumors from which bulk tumor cells were subcutaneously implanted into NSG mice were evaluated to determine whether they were associated with successful engraftment or not. P-values were determined by two-tailed Fisher’s exact test. UW = University of Washington; VU = CHTN, Vanderbilt University; \* = primary versus metastatic site of tumor, which includes synchronously resected primary and metastatic tumors from 3 patients; LVI = lymphovascular invasion.

**Table S5. Distribution of differentially expressed gene sets between mouse and human transcriptomes.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Xenograft | Mouse only | Mouse > Human | Human only | Human > Mouse | Neither |
| PHT > CX | | | | | |
| D61540.T2.X1 | 243 (22%) | 665 (61%) | 85 (8%) | 12 (1%) | 81 (7%) |
| D61540.T2.X2 | 292 (27%) | 615 (56%) | 74 (7%) | 8 (1%) | 99 (9%) |
| P2726.Ov.X1 | 206 (19%) | 618 (57%) | 109 (10%) | 7 (1%) | 146 (13%) |
| P2726.Ov.X2 | 248 (23%) | 486 (45%) | 140 (13%) | 6 (1%) | 206 (19%) |
| D55949.X2 | 238 (22%) | 606 (56%) | 95 (9%) | 38 (3%) | 109 (10%) |
| D55949.X3F | 284 (26%) | 624 (57%) | 64 (6%) | 42 (4%) | 72 (7%) |
| D55949.X3M | 253 (23%) | 587 (54%) | 94 (9%) | 40 (4%) | 112 (10%) |
| D55949.X4 | 360 (33%) | 536 (49%) | 54 (5%) | 34 (3%) | 102 (9%) |
| D55949.X7 | 227 (21%) | 571 (53%) | 112 (10%) | 35 (3%) | 141 (13%) |
| SX > PHT | | | | | |
| D61540.T2.X1 | 87 (10%) | 581 (66%) | 78 (9%) | 87 (10%) | 41 (5%) |
| D61540.T2.X2 | 96 (11%) | 583 (67%) | 77 (9%) | 76 (9%) | 42 (5%) |
| P2726.Ov.X1 | 50 (6%) | 607 (69%) | 125 (14%) | 45 (5%) | 47 (5%) |
| P2726.Ov.X2 | 75 (9%) | 525 (60%) | 134 (15%) | 41 (5%) | 99 (11%) |
| D55949.X2 | 97 (11%) | 590 (68%) | 65 (7%) | 53 (6%) | 69 (8%) |
| D55949.X3F | 128 (15%) | 610 (70%) | 45 (5%) | 49 (6%) | 42 (5%) |
| D55949.X3M | 95 (11%) | 594 (68%) | 78 (9%) | 41 (5%) | 66 (8%) |
| D55949.X4 | 159 (18%) | 567 (65%) | 52 (6%) | 49 (6%) | 47 (5%) |
| D55949.X7 | 73 (8%) | 594 (68%) | 85 (10%) | 38 (4%) | 84 (10%) |

Genes preferentially expressed in parental human tumors over carcinoma xenografts (PHT > CX) or in stromal xenografts over parental human tumors (SX > PHT), indicated in Figure 3C, were evaluated for whether they were expressed predominantly as mouse or human orthologues in each xenograft. Only genes with mouse and human orthologues were evaluated.