**Extended Data Tables**

| **Characteristics** | **Number** | **%** |
| --- | --- | --- |
| **Gender** |  |  |
|  Female | 427 | 42.4 |
|  Male | 579 | 57.6 |
| **Age at diagnosis (years)** |  |  |
|  Median | 67 |
|  Range | 58-76 |
| **BMI** |  |  |
|  Median | 23.5 |
|  Range | 21.2-26 |
| **Tumor size (cm)** |  |  |
|  Median | 4 |
|  Range | 4-6 |
| **Tumor location** |  |  |
|  Ascending colon | 241 | 24 |
|  Transverse colon | 50 | 5 |
|  Descending colon | 46 | 4.6 |
|  Sigmoid colon | 247 | 24.6 |
|  Rectum | 422 | 41.9 |
| **Gross morphology** |  |  |
|  Ulcer type | 720 | 71.6 |
|  Eminence type | 272 | 27 |
|  Infiltration type | 14 | 1.4 |
| **Histological type** |  |  |
|  Adenocarcinoma | 910 | 90.5 |
|  Other\* | 96 | 9.5 |
| **Tumor differentiation** |  |  |
|  Well and Moderate | 783 | 77.8 |
|  Poor | 223 | 22.2 |
| **Lymphovascular invasion** |  |  |
|  Positive | 728 | 72.4 |
|  Negative | 276 | 27.4 |
| **T (tumor stage)** |  |  |
|  T1 | 24 | 2.4 |
|  T2 | 121 | 12 |
|  T3 | 368 | 36.6 |
|  T4 | 493 | 49 |
| **N (regional lymph node)** |  |  |
|  N0 | 538 | 53.5 |
|  N1 | 261 | 25.9 |
|  N2 | 207 | 20.6 |
| **M (metastasis)** |  |  |
|  M0 | 909 | 90.4 |
|  M+ | 97 | 9.6 |
| **Clinical stage** |  |  |
|  I | 120 | 11.9 |
|  II | 401 | 39.9 |
|  III | 384 | 38.2 |
|  IV | 101 | 10 |
| **Postoperative adjuvant therapy** |  |  |
|  Yes | 373 | 37.1 |
|  No | 620 | 61.6 |
|  Unknown | 13 | 1.3 |
| **CEA (ng/ml)** |  |  |
|  Median | 4.2 |
|  Range | 2.2-11.6 |
| **AFP (ng/ml)** |  |  |
|  Median | 2.4 |
|  Range | 1.6-3.4 |
| **CA199 (U/ml)** |  |  |
|  Median | 12.5 |
|  Range | 6.8-23.5 |
| **CA125 (U/ml)** |  |  |
|  Median | 9.6 |
|  Range | 5.3-16.1 |

**\*** Mucinous adenocarcinoma, neuroendocrine carcinoma, signet ring cell carcinoma

**Extended Data Table 1. Baseline clinical characteristics of CRC Patients (n=1006)**

TNM staging was performed according to AJCC 's (8th edition) instructions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP rs117518546** | **HCs (%)** | **CRC patients (%)** | **OR** | **95% CI** | ***P*** |
| **Allelic** | **C** | 813 (69.73) | 1450 (72.07) | 0.893 | 0.762-1.046 | 0.086  |
| **T** | 353 (30.27) | 562 (27.93) |
| **Genotypic** | **Dominant** | **CC** | 300 (51.46) | 537 (53.38) | 0.926 | 0.755-1.136 | 0.246  |
| **CT+TT** | 283 (48.54) | 469 (46.62) |
| **Recessive** | **CC+CT** | 513 (87.99) | 913 (90.76) | 0.747 | 0.538-1.037 | 0.049\*  |
| **TT** | 70 (12.01) | 93 (9.24) |
| **Additive** | **CC** | 300 (51.46) | 537 (53.38) | 0.902 | 0.775-1.049 | 0.180  |
| **CT** | 213 (36.53) | 376 (37.38) |
| **TT** | 70 (12.01) | 93 (9.24) |

|  |  |  |
| --- | --- | --- |
|  | **HCs** | **CRC Patients** |
| **Sample size** | 583 | 1006 |
| **Male** | 335 (57.46%) | 579 (57.55%) |
| **Female** | 248 (42.54%) | 427 (42.45%) |
| **Age (Mean± SEM)** | 35.18±18.57 | 66.26±12.41 |

**\***P value < 0.05

OR, odds ratio; CI, confidence interval

**Extended Data Table 2. The hIgG1-G396R variant allele frequency in HCs and CRC patients**

|  |  |  |
| --- | --- | --- |
| **rs117518546, OS** | **Univariable COX regression analysis** | **Multivariable COX regression analysis** |
| **Model** | **HR** | **95% CI** | ***P* value** | **HR** | **95% CI** | **P value** |
| **Additive (CT vs CC)** | 0.914 | 0.723-1.156 | 0.454 | 0.86 | 0.669-1.107 | 0.242 |
| **Additive (TT vs CC)** | 0.505 | 0.303-0.844 | 0.009\* | 0.467 | 0.27-0.81 | 0.007\* |
| **Recessive (TT vs CC+CT)** | 0.525 | 0.317-0.868 | 0.012\* | 0.497 | 0.289-0.853 | 0.011\* |
| **Dominant (CT+TT vs CC)** | 0.834 | 0.665-1.045) | 0.115 | 0.78 | 0.612-0.994 | 0.045\* |

|  |  |  |
| --- | --- | --- |
| **rs117518546, PFS** | **Univariable COX regression analysis** | **Multivariable COX regression analysis** |
| **Model** | **HR** | **95% CI** | ***P* value** | **HR** | **95% CI** | **P value** |
| **Additive (CT vs CC)** | 0.889 | 0.707-1.118 | 0.315 | 0.874 | 0.684-1.116 | 0.28 |
| **Additive (TT vs CC)** | 0.569 | 0.355-0.913 | 0.02\* | 0.591 | 0.358-0.977 | 0.04\* |
| **Recessive (TT vs CC+CT)** | 0.598 | 0.376-0.951 | 0.03\* | 0.625 | 0.382-1.023 | 0.062 |
| **Dominant (CT+TT vs CC)** | 0.827 | 0.664-1.03 | 0.09 | 0.821 | 0.649-1.037 | 0.098 |

**\***P value < 0.05

**Extended Data Table 3. Univariable and multivariable COX regression analyses to investigate the effects of hIgG1-G396R variants on OS or PFS**

|  | **All cases** | **CC** | **CT** | **TT** | ***P*** | **CC+CT** | **TT** | **P** | **CC** | **CT+TT** | ***P*** | **CC** | **TT** | ***P*** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gender, n(%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Female | 427 | 240(56.2) | 159(37.2) | 28(6.6) | 0.032\* | 399(93.4) | 28(6.6) | 0.012\* | 240(56.2) | 187(43.8) | 0.123 | 240(89.6) | 28(10.4) | 0.009\* |
|  Male | 579 | 297(51.3) | 217(37.5) | 65(11.2) | 　 | 514(88.8) | 65(11.2) | 　 | 297(51.3) | 282(48.7) | 　 | 297(82) | 65(18) |  |
| **Age, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
| ≤70 | 587 | 333 (56.7) | 207(35.3) | 47(8.0) | 0.031\* | 540(92.0) | 47(8.0) | 0.109 | 540(92.0) | 254(43.3) | 0.012\* | 333(87.6) | 47(12.4) | 0.037\* |
|  >70 | 419 | 204(48.7) | 169(40.3) | 46(11.0) | 　 | 373(89.0) | 46(11.0) | 　 | 373(89.0) | 215(51.3) | 　 | 204(81.6) | 46(18.4) |  |
| **BMI, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  <18.5 | 61 | 27(44.3) | 27(44.3) | 7(11.5) | 0.47 | 54(88.5) | 7(11.5) | 0.646 | 27(44.3) | 34(55.7) | 0.282 | 27(79.4) | 7(20.6) | 0.568 |
|  18.5-23.9 | 542 | 288(53.1) | 207(38.2) | 47(8.7) | 　 | 495(91.3) | 47(8.7) | 　 | 288(53.1) | 254(46.9) | 　 | 288(86) | 47(14) |  |
|  >24 | 355 | 196(55.2) | 123(34.6) | 36(10.1) | 　 | 319(89.9) | 36(10.1) | 　 | 196(55.2) | 159(44.8) | 　 | 196(84.5) | 36(15.5) |  |
| **Native place distribution, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Northern Region | 823 | 475(57.7) | 302(36.7) | 46(5.6) | <0.001\* | 777(94.4) | 46(5.6) | <0.001\* | 475(57.7) | 348(42.3) | <0.001\* | 475(91.2) | 46(8.8) | <0.001\* |
|  Southern Region | 183 | 62(33.9) | 74(40.4) | 47(25.7) | 　 | 136(74.3) | 47(25.7) | 　 | 62(33.9) | 121(66.1) | 　 | 62(56.9) | 47(43.1) |  |
| **Tumor location, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Right colon | 291 | 156(53.6) | 105(36.1) | 30(10.3) | 0.71 | 261(89.7) | 30(10.3) | 0.457 | 156(53.6) | 135(46.4) | 0.926 | 156(83.9) | 30(16.1) | 0.531 |
|  Left colon and rectum | 715 | 381(53.3) | 271(37.9) | 63(8.8) | 　 | 652(91.2) | 63(8.8) | 　 | 381(53.3) | 334(46.7) | 　 | 381(85.8) | 63(14.2) |  |
| **Tumor size, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  ≤5cm | 526 | 278(52.9) | 199(37.8) | 49(9.3) | 0.94 | 477(90.7) | 49(9.3) | 0.935 | 278(52.9) | 248(47.1) | 0.725 | 278(85) | 49(15) | 0.87 |
|  >5cm | 480 | 259(54) | 177(36.9) | 44(9.2) | 　 | 436(90.8) | 44(9.2) | 　 | 259(54) | 221(46) | 　 | 259(85.5) | 44(14.5) |  |
| **Gross morphology, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Ulcer type | 720 | 386(53.6) | 269(37.4) | 65(9) | 0.73 | 655(91) | 65(9) | 0.402 | 386(53.6) | 334(46.4) | 0.659 | 386(85.6) | 65(14.4) | 0.568 |
|  Eminence type | 272 | 142(52.2) | 102(37.5) | 28(10.3) | 　 | 244(89.7) | 28(10.3) | 　 | 142(52.2) | 130(47.8) | 　 | 142(83.5) | 28(16.5) |  |
|  Infiltration type | 14 | 9(64.3) | 5(35.7) | 0(0) | 　 | 14(100) | 0(0) | 　 | 9(64.3) | 5(35.7) | 　 | 9(100) | 0(0) |  |
| **Histological type, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Adenocarcinoma | 910 | 487(53.5) | 338(37.1) | 85(9.3) | 0.88 | 825(90.7) | 85(9.3) | 0.746 | 487(53.5) | 423(46.5) | 0.789 | 487(85.1) | 85(14.9) | 0.827 |
|  Other\*\* | 96 | 50(52.1) | 38(36.9) | 8(8.3) | 　 | 88(91.7) | 8(8.3) | 　 | 50(52.1) | 46(47.9) | 　 | 50(86.2) | 8(13.8) |  |
| **Tumor differentiation, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Well amd Moderate | 783 | 414(52.9) | 289(36.9) | 80(10.2) | 0.14 | 703(89.8) | 80(10.2) | 0.046\* | 414(52.9) | 369(47.1) | 0.546 | 414(83.8) | 80(16.2) | 0.053 |
|  Poor | 223 | 123(55.2) | 87(39.0) | 13(5.8) | 　 | 210(94.2) | 13(5.8) | 　 | 123(55.2) | 100(44.8) | 　 | 123(90.4) | 13(9.6) |  |
| **Lymphovascular invasion, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  Positive | 728 | 390(53.6) | 270(37.1) | 68(9.3) | 0.96 | 660(90.7) | 68(9.3) | 0.89 | 390(53.6) | 338(46.4) | 0.849 | 390(85.2) | 68(14.8) | 0.943 |
|  Negative | 276 | 146(52.9) | 105(38) | 25(9.1) | 　 | 251(90.9) | 25(9.1) | 　 | 146(52.9) | 130(47.1) | 　 | 146(85.4) | 25(14.6) |  |
| **T, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  T1+T2 | 145 | 76(52.4) | 53(36.6) | 16(11) | 0.72 | 129(89) | 16(11) | 0.421 | 76(52.4) | 69(47.6) | 0.801 | 76(82.6) | 16(17.4) | 0.442 |
|  T3+T4 | 861 | 461(53.5) | 323(37.5) | 77(8.9) | 　 | 784(91.1) | 77(8.9) | 　 | 461(53.5) | 400(46.5) | 　 | 461(85.7) | 77(14.3) |  |
| **N, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  N0 | 538 | 278(51.7) | 208(38.7) | 52(9.7) | 0.51 | 486(90.3) | 52(9.7) | 0.621 | 278(51.7) | 260(48.3) | 0.245 | 278(84.2) | 52(15.8) | 0.46 |
|  N+ | 468 | 259(55.3) | 168(35.9) | 41(8.8) | 　 | 427(91.2) | 41(8.8) | 　 | 259(55.3) | 209(44.7) | 　 | 259(86.3) | 41(13.7) |  |
| **M, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  M0 | 909 | 478(52.6) | 343(37.7) | 88(9.7) | 0.18 | 821(90.3) | 88(9.7) | 0.143 | 478(52.6) | 431(47.4) | 0.122 | 478(84.5) | 88(15.5) | 0.098 |
|  M+ | 97 | 59(60.8) | 33(34) | 5(5.2) | 　 | 92(94.8) | 5(5.2) | 　 | 59(60.8) | 38(39.2) | 　 | 59(92.2) | 5(7.8) |  |
| **Clinical stage, n(%)** | 　 | 　 |  |  | 　 | 　 |  | 　 | 　 |  | 　 |  |  |  |
|  I+II | 521 | 266(51.1) | 203(39) | 52(10) | 0.29 | 469(90) | 52(10) | 0.403 | 266(51.1) | 255(48.9) | 0.126 | 266(83.6) | 52(16.4) | 0.256 |
|  III+IV | 485 | 271(55.9) | 173(35.7) | 41(8.5) | 　 | 444(91.5) | 41(8.5) | 　 | 271(55.9) | 214(44.1) | 　 | 271(86.9) | 41(13.1) |  |
| **CEA(ng/ml), median(range)** | 4.2(2.2-11.6) | 4.4(2.2-12.7) | 3.8(2.1-10) | 4.4(2.2-11.1) | 0.44 | 4.2(2.2-11.6) | 4.4(2.2-11.1) | 0.24 | 4.4(2.2-12.7) | 3.8(2.2-10) | 0.37 | 4.4(2.2-12.7) | 4.4(2.2-11.1) | 0.2 |
| **AFP(ng/ml), median(range)** | 2.4(1.6-3.4) | 2.4(1.5-3.4) | 2.3(1.6-3.3) | 2.6(1.8-3.6) | 0.62 | 2.4(1.6-3.4) | 2.6(1.8-3.6) | 0.522 | 2.4(1.5-3.4) | 2.4(1.6-3.4) | 0.642 | 2.4(1.5-3.4) | 2.6(1.8-3.6) | 0.685 |
| **CA199(U/ml), median(range)** | 12.5(6.8-23.5) | 12.5(6.5-23.3) | 12.3(7-25.1) | 13.4(7.1-22.1) | 0.61 | 12.3(6.8-23.9) | 13.4(7.1-22.1) | 0.458 | 12.5(6.5-23.3) | 12.6(7-24.2) | 0.38 | 12.5(6.5-23.3) | 13.4(7.1-22.1) | 0.381 |
| **CA125(U/ml), median(range)** | 9.6(5.3-16.1) | 9.9(5.4-16.3) | 9.3(5.2-16) | 9.3(3.7-14.6) | 0.68 | 9.7(5.3-16.1) | 9.3(3.7-14.6) | 0.615 | 9.9(5.4-16.3) | 9.3(5.2-15.9) | 0.395 | 9.9(5.4-16.3) | 9.3(3.7-14.6) | 0.514 |

**\*** P value < 0.05

**\*\*** Mucinous adenocarcinoma, neuroendocrine carcinoma, signet ring cell carcinoma

**Extended Data Table 4. Characteristics of CRC patients in different genotypes (n=1006)**

|  |  |
| --- | --- |
| **CRC patients, number** | **rs117518546 genotype** |
| P0413 | CC |
| P1228 | CC |
| P0411 | CC |
| P0825 | CC |
| P0202 | CC |
| P0720 | CC |
| P0123 | CT |
| P1212 | CT |
| P0309 | CT |
| P0104 | CT |
| P0305 | CT |
| P0323 | CT |
| P0408 | CT |
| P0410 | CT |
| P0613 | CT |
| P0728 | CT |
| P1026 | CT |
| P1025 | TT |

**Extended Data Table 5. Genotypes of 18 CRC patients involved in scRNA-seq analyses**

The rs117518546 genotypes of 18 CRC patients using in the scRNA-seq assays are shown, which were verified via either Taqman-probe-based genotyping or bulk WES.

|  |  |  |
| --- | --- | --- |
| **Species** | **Target gene** | **Sequences (5'-3')** |
| **Human** | *GAPDH* | Forward | ACCTCAACTACATGGCTGAGAAC |
| Reverse | CATGGTGGTGAAGACGCCAG |
| *IGHG1* | Forward | AATGGGCAGCCGGAGAACAACT |
| Reverse | TGCTCTTGTCCACGGTGAGCTT |
| *IGHG2* | Forward | AATGGGCAGCCGGAGAACAACT |
| Reverse | TGCTCTTGTCCACGGTGAGCTT |
| *IGHG3* | Forward | TAAGCCCACCCCAAAGGCCAAA |
| Reverse | ACCGTGGGCATGTGTGAGTTGT |
| *IGHG4* | Forward | AATGGGCAGCCGGAGAACAACT |
| Reverse | TTGTCCACGGTTAGCCTGCTGT |
| *IGHA* | Forward | CGCTGGCCTTCACACAGAA |
| Reverse | CGCCATGACAACAGACACA |
| *CXCL12* | Forward | ACTGGGTTTGTGATTGCCTCTGAA |
| Reverse | GGAACCTGAACCCCTGCTGTG |
| *CXCL13* | Forward | GAGGCAGATGGAACTTGAGC |
| Reverse | CTGGGGATCTTCGAATGCTA |
| *CCL19*  | Forward | CCAGCCCCAACTCTGAGTG |
| Reverse | ATCCTTGATGAGAAGGTAGTGGA |
| *CCL21*  | Forward | CGCAGCTACCGGAAGCAG |
| Reverse | CTGCCTGAGAGCGCTTGC |
| **Mouse** | *GAPDH*  | Forward | AGTATGACTCCACTCACGGCAA |
| Reverse | TCTCGCTCCTGGAAGATGGT |
| *TGFB*  | Forward | AGAGAAGAACTGCTGTGTGC |
| Reverse | GGGTTGTGTTGGTTGTAGAG |
| *IL1B* | Forward | CAACCAACAAGTGATATTCTCCATG |
| Reverse | GATCCACACTCTCCAGCTGCA |
| *IL6*  | Forward | ACCAGAGGAAATTTTCAATAGGC |
| Reverse | TGATGCACTTGCAGAAAACA |
| *IL23p19*  | Forward | CCAGCGGGACATATGAATCT |
| Reverse | AGGCTCCCCTTTGAAGATGT |
| *CXCL13* | Forward | AACTCCACCTCCAGGCAGAATG |
| Reverse | TGTGTAATGGGCTTCCAGAATACC |
| *CCL21* | Forward | GCAAAGAGGGAGCTAGAAAACAGA |
| Reverse | TGGACGGAGGCCAGCAT |
| *CXCR5* | Forward | GACTCCTTACCACAGTGCACCTT |
| Reverse | GGAAACGGGAGGTGAACCA |

**Extended Data Table 6. Primers for RT-qPCR analyses**