

SUPPLEMENTARY MATERIAL**SUPPLEMENTARY TABLES****Supplementary Table 1:** HLA class I expression combinations

| HLA-A | HLA-B/C | Resulting total HLA class I combination |
|--------------|----------------|--|
| negative | negative | loss |
| negative | 1-50% | loss |
| negative | >50% | loss |
| 1-50% | negative | loss |
| 1-50% | 1-50% | downregulation |
| 1-50% | >50% | downregulation |
| >50% | negative | loss |
| >50% | 1-50% | downregulation |
| >50% | >50% | expression |

| Immunoreactivity score | Resulting total HLA class I combination |
|-------------------------------|--|
| 0-3 | loss |
| 4-6 | downregulation |
| 7-12 | expression |

Supplementary Table 2: Characteristics of included studies

| Study | Country | Period | N | Female (%) | Age (y) | Location | Antibodies | Scoring method | Outcomes |
|------------------|-------------|-----------|------|------------|---------|---------------|---------------------------------------|-------------------------------|--------------|
| Watson, 2006 | UK | 1994-2000 | 462 | 42 | 57-93 | colon, rectum | HC10 | 0%, 1-50%, >50% stained cells | DSS, OS |
| Speetjens, 2008 | Netherlands | 1996-1999 | 1008 | 35 | 26-92 | rectum | HCA2, HC10 | % stained cells | DFS, OS |
| Kasajima, 2010 | Germany | 1995-2007 | 290 | 47 | 17-90 | colon, rectum | Mouse antihuman MHC class I mAb (MBL) | IRS (0-12) | OS |
| Reimers, 2014 | Netherlands | 2002-2008 | 920 | 48 | 26-96 | colon | HCA2, HC10 | 0%, 1-50%, >50% stained cells | DFS, DSS, OS |
| Zeestraten, 2014 | Netherlands | 1991-2001 | 283 | 52 | 22-93 | colon | HCA2, HC10 | % stained cells | DFS, DSS, OS |

DFS: disease-free survival, DSS: disease-specific survival, IRS: immunoreactivity score, mAb: monoclonal antibody, OS: overall survival

Supplementary Table 3: Clinicopathologic characteristics of 2,863 patients who underwent resection of a colon or rectal tumor, by tumor location

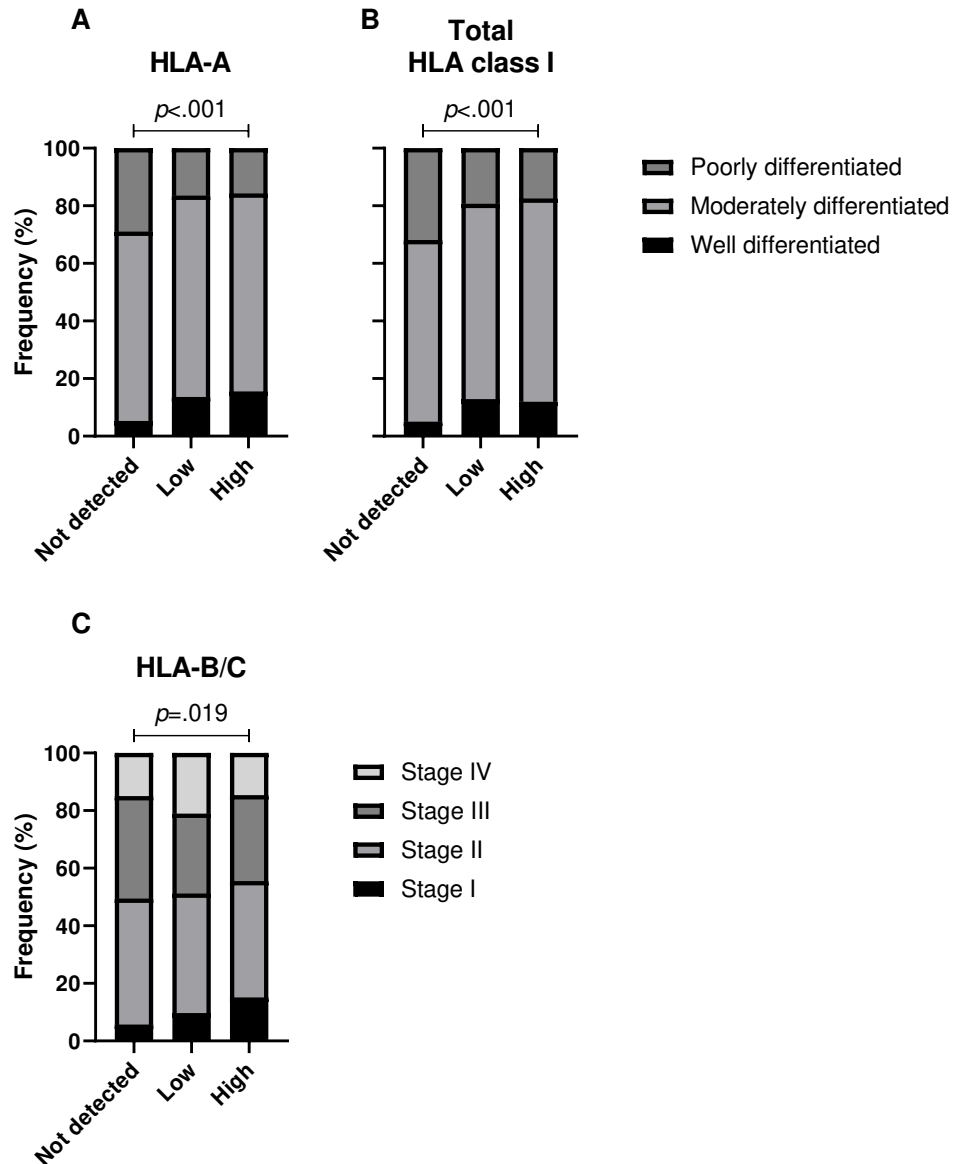
| | | Location | | | | | |
|-----------------------------|---------------------------|-----------------|-------|------------------|-------|-----------------|-------|
| | | Colon (N=1,620) | | Rectum (N=1,243) | | Total (N=2,863) | |
| | | N | % | N | % | N | % |
| Study | Watson | 233 | 14.4% | 179 | 14.4% | 412 | 14.4% |
| | Kasajima | 223 | 13.8% | 56 | 4.5% | 279 | 9.7% |
| | Speetjens | 0 | 0.0% | 1008 | 81.1% | 1008 | 35.2% |
| | Reimers | 920 | 56.8% | 0 | 0.0% | 920 | 32.1% |
| | Zeestraten | 244 | 15.1% | 0 | 0.0% | 244 | 8.5% |
| Age, y (median, IQR) | | 70 | 62-76 | 66 | 58-74 | 68 | 60-75 |
| Gender | Male | 826 | 51.0% | 806 | 64.8% | 1632 | 57.0% |
| | Female | 794 | 49.0% | 437 | 35.2% | 1231 | 43.0% |
| T stage | Tis | 2 | 0.4% | 3 | 1.3% | 5 | 0.7% |
| | T1 | 13 | 2.9% | 16 | 7.0% | 29 | 4.2% |
| | T2 | 53 | 11.6% | 45 | 19.6% | 98 | 14.3% |
| | T3 | 288 | 63.3% | 141 | 61.3% | 429 | 62.6% |
| | T4 | 99 | 21.8% | 25 | 10.9% | 124 | 18.1% |
| N stage | N0 | 247 | 54.5% | 120 | 53.6% | 367 | 54.2% |
| | N1 | 114 | 25.2% | 55 | 24.6% | 169 | 25.0% |
| | N2 | 92 | 20.3% | 49 | 21.9% | 141 | 20.8% |
| M stage | M0 | 403 | 88.4% | 213 | 91.4% | 616 | 89.4% |
| | M1 | 53 | 11.6% | 20 | 8.6% | 73 | 10.6% |
| Stage | 0 | 1 | 0.1% | 1 | 0.1% | 2 | 0.1% |
| | I | 224 | 13.9% | 365 | 29.4% | 589 | 20.6% |
| | II | 642 | 39.8% | 352 | 28.4% | 994 | 34.8% |
| | III | 496 | 30.7% | 441 | 35.5% | 937 | 32.8% |
| | IV | 252 | 15.6% | 82 | 6.6% | 334 | 11.7% |
| Histologic grade | Well differentiated | 162 | 10.8% | 59 | 4.8% | 221 | 8.1% |
| | Moderately differentiated | 1024 | 68.1% | 844 | 68.2% | 1868 | 68.2% |
| | Poorly differentiated | 317 | 21.1% | 327 | 26.4% | 644 | 23.5% |
| | Undifferentiated | 0 | 0.0% | 8 | 0.6% | 8 | 0.3% |
| Vascular invasion | No | 306 | 72.2% | 133 | 68.9% | 439 | 71.2% |
| | Yes | 118 | 27.8% | 60 | 31.1% | 178 | 28.8% |

| | | | | | | | |
|--------------------------------|-----|-----|-------|----|-------|-----|-------|
| Lymphovascular invasion | No | 110 | 47.0% | 26 | 46.4% | 136 | 46.9% |
| | Yes | 124 | 53.0% | 30 | 53.6% | 154 | 53.1% |
| KRAS mutation | No | 519 | 66.3% | 62 | 66.0% | 581 | 66.2% |
| | Yes | 264 | 33.7% | 32 | 34.0% | 296 | 33.8% |
| BRAF mutation | No | 501 | 84.2% | - | - | 501 | 84.2% |
| | Yes | 94 | 15.8% | - | - | 94 | 15.8% |
| MS status | MSS | 980 | 90.0% | - | - | 980 | 90.0% |
| | MSI | 109 | 10.0% | - | - | 109 | 10.0% |

IQR: inter-quartile range; MS: microsatellite; MSS: microsatellite stable; MSI: microsatellite instable.

SUPPLEMENTARY FIGURES

Supplementary Figure 1



Supplementary Figure 1. Association of HLA class I expression level in colon malignant tumors with pathologic characteristics. Stacked bar graphs demonstrate the association of higher HLA-A (A) and total HLA class I (B) expression levels in colon malignant tumors with lower histologic grade, and the association of higher HLA-B/C expression level in colon malignant tumors with lower stage (C). P values were derived from Fisher's exact test.