

Supplementary Table 1. Age-adjusted characteristics of cases by tumor CASR expression availability in the combined study

| | CASR unavailable cases (N = 2,957) | CASR available cases (N = 809) |
|---|------------------------------------|--------------------------------|
| Age, years* | 67.9(10.2) | 69.1(8.8) |
| White, % | 96.8 | 96.7 |
| Body mass index, ^a kg/m ² | 26.0(5.1) | 26.5(4.8) |
| Activity, ^b MET-hours/week | 17.4(20.3) | 17.8(21.0) |
| Tumor location* | | |
| Proximal colon, % | 38.8 | 49.6 |
| Distal colon, % | 29.8 | 29.1 |
| Rectum, % | 21.9 | 19.9 |
| Unspecified, % | 9.5 | 1.4 |
| Disease stage* | | |
| Stage I, % | 23.2 | 23.6 |
| Stage II, % | 19.8 | 31.4 |
| Stage III, % | 20.3 | 27.1 |
| Stage IV, % | 17.3 | 14.2 |
| In situ or unknown, % | 19.4 | 3.7 |
| Tumor differentiation* | | |
| Well, % | 12.0 | 12.0 |
| Moderate, % | 49.7 | 63.7 |
| Poor, % | 16.4 | 16.4 |
| Unspecified, % | 12.0 | 12.0 |

Values are means (SD) or percentages and are standardized to the age distribution of the study population.

Values of polytomous variables may not sum to 100% due to rounding.

^a Body mass index was calculated as weight in kilograms divided by the square of height in meters.

^b Hours of metabolic equivalent tasks.

* Value is not age adjusted

Supplementary Table 2. Association* of tumor CASR expression with colorectal cancer-specific mortality according to disease stage and tumor differentiation in the Nurses' Health Study and Health Professionals Follow-Up Study

| | Tumor CASR expression | | | p-trend | p-interaction |
|--|-----------------------|------------------|------------------|---------|---------------|
| | 0-1 No/weak | 2 Moderate | 3 Intense | | |
| Tumor differentiation (well to moderate) | | | | | |
| N death (151) | 28 | 91 | 32 | | |
| N patients (613) | 110 | 346 | 157 | | |
| Multivariable-adjusted* | 1 (reference) | 1.06 (0.66-1.70) | 0.70 (0.40-1.24) | 0.16 | 0.18 |
| Tumor differentiation (poor) | | | | | |
| N death (60) | 16 | 36 | 8 | | |
| N patients (131) | 33 | 77 | 22 | | |
| Multivariable-adjusted* | 1 (reference) | 0.79 (0.30-1.84) | 0.33 (0.07-1.31) | 0.16 | |
| Stage I-II | | | | | |
| N death (54) | 8 | 35 | 11 | | |
| N patients (448) | 88 | 249 | 111 | | |
| Multivariable-adjusted* | 1 (reference) | 1.39 (0.61-3.15) | 0.78 (0.29-2.13) | 0.49 | 0.42 |
| Stage III-IV | | | | | |
| N death (172) | 39 | 104 | 31 | | |
| N patients (331) | 61 | 198 | 72 | | |
| Multivariable-adjusted* | 1 (reference) | 0.67 (0.43-1.00) | 0.52 (0.31-0.88) | 0.02 | |

** Cox model were stratified by age groups at diagnosis, study (for the pooled analysis), and disease stage; we further adjusted for age at diagnosis, year of diagnosis, family history of colorectal cancer, tumor grade of differentiation, tumor subsite, LINE-1, MSI, CIMP, PTGS2, *KRAS*, *BRAF*, and *PIK3CA* mutations, nuclear expression of VDR and CTNNB1. There were 65 missing in tumor differentiation analysis and 30 missing in stage analysis.