Supplemental Note 2

Some samples, especially subsets of CRC and GC, exhibited few detectable SCNAs (Fig. 1A-D). Indeed, 19% of CRC, 14% of GC and 6% of EA had no detectable arm-level SCNAs. The absence of SCNAs in specific samples could be attributed to tumors with more bland copy-number profiles as occurs with, for example, tumors characterized by microsatellite instability (MSI). Alternatively, it is possible that bland SCNA profiles be a sign that samples have low tumor content due to substantial contamination by DNA from non-cancer tissues. Although all tumors were reviewed by a pathologist to select cases with estimated tumor content of >70%, it remained possible that some of these cases were much more stromally contaminated than thought. To evaluate for the possibility of high stromal admixture, we evaluated many of these 'quiet' cases, those without arm-level SCNAs, for the presence of cancer-associated mutations or evidence of MSI. For this analysis, we focused on cases of CRC and GC given the greater aneuploidy seen in the EA tumors.

Starting with the CRC collections, we first evaluated the quiet cases for evidence of mutations in classic 'hot-spot' genes as these cases had been evaluated with mass spectrometric genotyping for mutations in *KRAS, BRAF, PIK3CA* and *PTEN* among other genes (1). Among the 37 CRC tumors in our study without arm-level SCNAs, we identified colorectal cancer-associated mutations in 21 (57%). Among those 'quiet' cases without mutations found, we performed MSI testing in those 7 additional cases for which sufficient DNA was available PCR-testing for markers D2S123, D5S346, D17S250, BAT25, BAT26, BAT4, D18S55, D18S56, D18S67, and D18S487 using established techniques (2). Among these MSI was detected in 3 of 7 cases. For the GC tumors, DNA

from the 14 cases without arm-level SCNAs were evaluated with MSI testing. Two of these showed MSI and a third case upon MSI testing had no evidence of MSI but was found to have LOH of chromosome 18, another marker of the presence of tumor DNA. Beyond these three cases, another two cases had evidence of somatic mutations (*KRAS* and *PIK3CA* mutations) upon review of genotyping data. These data demonstrate clear evidence of significant tumor content in a majority (~65%) of the CRC cases and 36% of the GC tumors with more quiet SCNA profiles.

Supplemental Note 2 References

1. MacConaill LE, Campbell CD, Kehoe SM, Bass AJ, Hatton C, Niu L, et al. Profiling critical cancer gene mutations in clinical tumor samples. PLoS One. 2009;4:e7887.

2. Ogino S, Kawasaki T, Kirkner GJ, Yamaji T, Loda M, Fuchs CS. Loss of nuclear p27 (CDKN1B/KIP1) in colorectal cancer is correlated with microsatellite instability and CIMP. Mod Pathol. 2007;20:15-22.