Comment re: Intratumoral Immune Reaction in Human Colorectal Cancer

To the Editor: The recent article by Camus and coworkers (1) is in line with their previous reports on immune cell infiltration in colorectal cancer (CRC). They showed the presence of a high density of immune effector cells in tumors of patients without metastases, whereas these cells were absent in the primary tumor or did not have an effector phenotype in metastasized patients (1). Although we agree that these results are highly interesting, we feel that this group thus far ignores a hallmark in CRC that is pivotal to the discussions on immune interactions in CRC, namely its genetic background. Two major types of genomic instability are recognized as mechanisms of carcinogenesis in CRC: chromosomal instability (CIN) and microsatellite instability (MSI). MSI is present in ∼20% of CRC, has a prevalence for right-sided CRC, and is associated with a better prognosis than CIN (2). CIN is associated with rather gross DNA aberrations. MSI, in contrast, is characterized by an accumulation of mutations in microsatellites due to failing mismatch repair. Deletions or insertions of base pairs in microsatellites of coding sequences result in shift of the reading frame downstream of the microsatellite and, from here, translation to an abnormal protein product, foreign to the immune system. The better patient prognosis in MSI compared with CIN may be based on expression of these aberrant proteins, resulting in better functioning of immune surveillance. Moreover, MSI has been shown to correlate with higher intratumoral numbers of CD3⁺, CD8⁺, and Granzyme B⁺ T cells; a more Th1-associated cancer microenvironment; and increased incidence of MHC class I loss by tumor cells (3, 4). CIN tumors have less prominent targets for the immune system in comparison with the highly aberrant proteins in MSI tumors. Up to now, for CIN-associated CRC, it is unclear if immunologic interactions play any role of significance in survival of patients. Several methods, both immunohistochemical and PCR based, are available for rather easy identification of CIN and MSI in CRC. Therefore, in our opinion, any study on immunologic interaction in CRC should stratify for CIN/MSI. By considering this genetic background, Camus and colleagues could make a major contribution to the discussion of involvement of immunologic interaction in CRC. This is important, as it will direct future immunologic treatment of CRC (5).

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References


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