Leukocyte infiltrate in gastrointestinal adenocarcinomas is strongly associated with tumor microsatellite instability but not with tumor immunogenicity.

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PURPOSE: To analyze the correlation of genomic instability with leukocyte infiltrate in gastrointestinal carcinomas (GIACs) and with tumor immunogenicity, e.g., HLA class I cell surface expression defects and galectin-3 and PDL-1 expression.

EXPERIMENTAL DESIGN: Lymphocyte and macrophage infiltrations were immunohistochemically studied in HLA class I negative GIACs with sporadic high-level microsatellite instability (MSI-H) or microsatellite stability (MSS).

RESULTS: Tumors with MSI-H were associated with the following: dense infiltration (CD45, $P < 0.001$); cytotoxic CD8-positive lymphocytes ($P < 0.001$); and a complete absence of HLA class I cell surface expression, due to inactivating beta2-microglobulin (beta2-m) mutation in 50% of cases. In contrast, HLA class I negative tumors with MSS were significantly associated with fewer CD8-positive lymphocytes. There was no association between microsatellite instability and other molecular features of the tumor cells, including expression of galectin-3. Finally, macrophage infiltrate in the tumors was not correlated with microsatellite instability or HLA class I cell surface expression (CD64, $P = 0.63$; CD163, $P = 0.51$).

CONCLUSIONS: Microsatellite instability appears to be the most important factor determining the composition, density, and localization of leukocyte infiltrate, which is independent of other molecular features such expression of HLA class I cells, galectin-3, or programmed death ligand-1. Accordingly, the strong intratumoral CD8+ T infiltration of MSI-H tumors may be produced by elevated levels of specific inflammatory chemokines in the tumor microenvironment.

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