

colorectal oncogenesis and progression by causing a possible chronic inflammatory mucosal damage, thereby promoting colorectal (CRC) invasion, metastasis, and mortality. *H. pylori* positive CRC patients undergoing positron emission tomography/computed tomography (PET/CT) imaging had a higher rate of metastatic disease associated with a higher mortality rate [1]. As for the possibility that current *Hp-I* induces humoral and cellular immune responses that provoke potential oncogenic sequelae including metastases and mortality, we agree with Dr. Kountouras, and we made this point clear in our article [1]. We demonstrated [2] that fecal shedding of viable *H. pylori* and *H. pylori* antigens occurs, under certain circumstances, and are detected in the stool. We agree that histology is the gold standard for current *Hp-I* diagnosis, nevertheless, as discussed in our article [1], measurement of circulating *H. pylori* antibodies by an ELISA test is sensitive and specific for detecting *H. pylori* infection. Serology may remain positive even after curing the infection. The latter is an advantage, as the past infection may be even more important for carcinogenesis. *H. pylori* antibodies may persist in patients with chronic *H. pylori* infection over decades or throughout life, even if *H. pylori* is no longer detectable in biopsy specimens. In patients treated with antisecretory drugs, *H. pylori* antibodies persist. Positive antibody levels were found in 86%

of patients with chronic atrophic gastritis; however, positive histology was only apparent in 33% of the subjects [3]. There are a few other possible physiopathological mechanisms for the association between *Hp-I* and complicated colorectal neoplasia. Large prospective studies with additional measurements of possible mediators would be desirable.

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The Association of *Helicobacter pylori* Seropositivity and Colorectal Cancer

To the Editor:

We thank Dr. Kountouras and colleagues for their comments, which are published in this issue of the *Israel Medical Association Journal (IMAJ)*. We agree with them that *Helicobacter pylori* infection (*Hp-I*) has an impact on

Capsule

Signatures of T cell dysfunction and exclusion predict cancer immunotherapy response

Cancer treatment by immune checkpoint blockade (ICB) can bring long lasting clinical benefits, but only a fraction of patients respond to treatment. To predict ICB response, Jiang et al. developed TIDE, a computational method to model two primary mechanisms of tumor immune evasion: the induction of T cell dysfunction in tumors with high infiltration of cytotoxic T lymphocytes (CTL) and the prevention of T cell infiltration in tumors with low CTL level. The authors identified signatures of T cell dysfunction from large tumor cohorts by testing how the expression of each gene in tumors interacts with the CTL infiltration level to influence patient survival.

They also modeled factors that excluded T cell infiltration into tumors using expression signatures from immunosuppressive cells. Using this framework and pre-treatment RNA-Seq or NanoString tumor expression profiles, TIDE predicted the outcome of melanoma patients treated with first-line anti-PD1 or anti-CTLA4 more accurately than other biomarkers such as *PD-L1* level and mutation load. TIDE also revealed new candidate ICB resistance regulators, such as *SERPINB9*, demonstrating utility for immunotherapy research.

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