HIGH PREVALENCE OF IMMUNE EXCLUSION IN EPITHELIAL TUMORS

Antoine Italiano, Jean-Philippe Guégan, Xinwei Sher, Laura Dillon, Tamas Oravecz, Thomas Schürpf, Guy Clifton.

Institut Bergonie, Bordeaux, France; Explicyte, Bordeaux, France; Parthenon Therapeutics, Inc, Boston, MA, USA

Abstract

Background Immune infiltrated tumors have high levels of lymphocytes in contact with tumor cells and are more responsive to immune checkpoint inhibitors. Tumors with a paucity of lymphocytes contacting tumor cells can be divided into immune deserted and immune excluded phenotypes. Immune exclusion is characterized by lymphocytes restricted to the periphery of cancer nests, typically to the peritumoral stroma. Mechanisms that prevent lymphocyte infiltration in immune exclusion may be distinct. Understanding the immune phenotype landscape across tumors is necessary to ensure novel therapies targeting immune exclusion are directed at optimal indications.

Methods Samples from colorectal cancer (CRC), non-small cell lung cancer (NSCLC), ovarian cancer (OC), pancreatic cancer (PDAC), triple-negative breast cancer (TNBC), leiomyosarcoma (LMS), and undifferentiated pleomorphic sarcoma (UPS) were evaluated. Slides were stained with a multiplex IHC assay for CD8 and CK and evaluated by two pathologists who characterized the tumors as: deserted, characterized by a paucity/absence of CD8+ T cells (<1%); excluded, characterized by the presence of CD8+ T cells that do not penetrate the tumor parenchyma; and infiltrated, characterized by the presence within the tumor parenchyma of CD8+ T cells.

Results Overall, 143 samples were evaluated with 18.9% of tumors defined as deserted, 46.9% as excluded, and 34.3% as infiltrated (Table 1). In the 103 epithelial tumors, 19.4% (n=20) were defined as deserted, 63.1% (n=65) as excluded, and 17.4% (n=18) as infiltrated. Of the 40 sarcoma samples, 17.5% (n=7) were defined as deserted, 5% (n=2) as excluded, and 77.5% (n=31) as infiltrated. Immune exclusion was highest in CRC (70.0%), PDAC (71.4%), and TNBC (71.4%).

Conclusions Immune exclusion is the most prevalent immune phenotype in CRC, NSCLC, OC, PDAC, and TNBC. LMS and UPS have a low rate of immune exclusion and are predominantly infiltrated. Further research is warranted to understand and target the mechanisms underlying immune exclusion.

Ethics Approval Ethics approval obtained at Institut Bergonie.