41 ASSESSMENT OF THE SPATIAL DISTRIBUTION OF CD4+ T CELLS SUBPOPULATIONS IN THE TUMOR MICROENVIRONMENT BY BRIGHTPLEX®, A SEQUENTIAL CHROMOGENIC MULTIPLEX ASSAY

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Background Cancer immunotherapy reinvigorates tumor-specific T cell responses of CD8+ cytotoxic T lymphocytes that detect intracellular antigens that are presented by MHC class I molecules expressed by all tumor cell types. Because most tumors do not express MHC class II, the potential antitumor protective role of CD4 T cells, which bind MHC class II molecules on target cells, has been less studied. However, CD4+ T cells are also required for efficacious antitumor immunity; they are core components of adaptive immunity that differentiate into lineages responsible for effector activities. Both TH1 and TH2 cell types mediate antitumor immunity, although TH1 cells may be more potent due to the production of large amounts of IFN-γ, as well as chemokines that enhance the priming and expansion of CD8 cells. TH1 cells help in recruiting natural killer cells and type I macrophages to tumor sites, which can act in concert toward tumor eradication. The ability of TH2 cells to mobilize innate cells, may represent a general pathway for their impact on the host antitumor response. Tumor infiltrating TFH cells play a key role in immune cell recruitment to the tumor and in the formation of intratumoral follicular structures, which correlate with a positive prognosis. On the contrary, cells from the TH17 subset induces inflammatory responses resulting in a tumor-promoting environment. CD4+ Tregs which are critically important for the maintenance of self-tolerance, impede effective immunity against the tumor when they are present in the tumor microenvironment (TME).Therefore, beyond the detection of total CD4+ T cells within the TME, it is of critical importance to determine to which subpopulation each CD4+ T cell belongs to decipher their roles in tumor rejection.

Methods We have developed a multiplex 7-plex panel of of antibodies against biomarkers to identify main types of CD4+ T cells

Results On a single FFPE tissue section, main types of CD4+ T cells: TH1, TH2, TFH, TH17 and Tregs are identified by a combination of antibodies against transcription factors and membrane proteins. Following images registration, complex cells phenotypes can be detected and quantified. Furthermore, digital pathology tools allow the evaluation of the spatial distribution of CD4+ T cells within the TME.

Conclusions This new tool unravels the diversity of CD4+ T cells in TME and could help clinical researchers to design more effective immunotherapies in cancer treatment. Integrated into an Immunogram, this new Brightplex® Panel will also be critical to understand the immune contexture of tumors.

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