Cyclic multiplex imaging insights into type 3 dendritic cells and CD4$^+$T cell dynamics in lung adenocarcinoma

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Abstract:
Advancements in multiplex imaging techniques have provided a comprehensive spatial understanding of immune components within the microenvironment of mouse and human lung adenocarcinomas. Employing cyclic multiplexing analysis, we investigated the distribution of conventional dendritic cells type 2 (DC2 and DC3) and their interactions with T cells in adenocarcinomas. Human tissue sections were stained using the Multiple Iterative Labeling by Antibody Neodeposition (MILAN) technique, which is optimized for formalin-fixed, paraffin-embedded (FFPE) tissues. Conversely, mouse sections were subjected to the Iterative Bleaching Extends Multiplexity (IBEX) method, which excels in fresh-frozen tissues.

Notably, DC2s were predominantly located outside murine tumors, while DC3s exhibited a distinct intra-tumoral distribution, particularly in close proximity to CD4$^+$T cells, which included regulatory T cells (Tregs). These findings were corroborated in human tumors, highlighting the relevance of our murine model to clinical scenarios.

Analyzing sections of non-small cell lung cancer (NSCLC) patients, DC3s emerged as the predominant subpopulation among cDC2s, shedding light on the specific role of DC3s in the tumor microenvironment. Furthermore, a comprehensive analysis of whole-slide sections revealed remarkable heterogeneity in the spatial distribution of T cells and dendritic cells within individual tumors. Specific regions exhibited enrichment in DC3s and CD4$^+$T cells, contrasting with other areas characterized by a prevalence of CD8$^+$T cells but a lack of cDC2s. This heterogeneity underscores the complexity of the immune landscape within lung adenocarcinomas.

Our study not only delineates the distinct spatial organization of immune cell subsets within the tumor microenvironment but also underscores the potential clinical implications of these intricate dynamics in shaping the immune response against lung adenocarcinoma.