SPATIAL-TRANSCRIPTOMIC ANALYSIS OF TUMOR-IMMUNE MICROENVIRONMENT IN AML PATIENTS RECEIVING PEMBROLIZUMAB AND DECITABINE

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Background Relapsed or refractory Acute Myeloid Leukemia (R-AML) is a deadly disease with an inadequate response rate to current treatments. Recent advances in immunotherapy shed light on R-AML, and several clinical trials have shown promising potential for combining immune checkpoint inhibitors (ICIs) with hypomethylating agents. A deeper understanding of the tumor-immune microenvironment in R-AML during combination ICI treatment is urgently needed for developing better therapeutics and stratifying treatment strategies.

Methods To dissect the tumor-immune interactions in the bone marrow microenvironment, we employed nanoString GeoMx Digital Spatial Profiler (DSP) and performed a spatial-transcriptomic analysis of patients with R-AML who received pembrolizumab and decitabine. We compared the transcriptomic profiles and TCR clonalities of tumor-interacting T cells, bystander T cells, and other cells at baseline, post-pembrolizumab treatment, and post-decitabine, which enable us to identify R-AML's suppressive immune microenvironment and immune cells' responses to ICI and hypomethylating agent.

Results We obtained the spatial-transcriptomic profiles of T cells, stromal cells, and leukemia cells in patients with R-AML at different treatment points. Our TCR-specific probes were able to track T cell clonal changes during treatments.

Conclusions R-AML harbored a complex tumor immune microenvironment and diverse T cell clonality.

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Ethics Approval This study is approved by NHLBI IRB.

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