Lineage Plasticity and Spatial Immune Redistribution Patterns in TTF-1/p40 Dual-Positive NSCLC: An Multi-Omics Study

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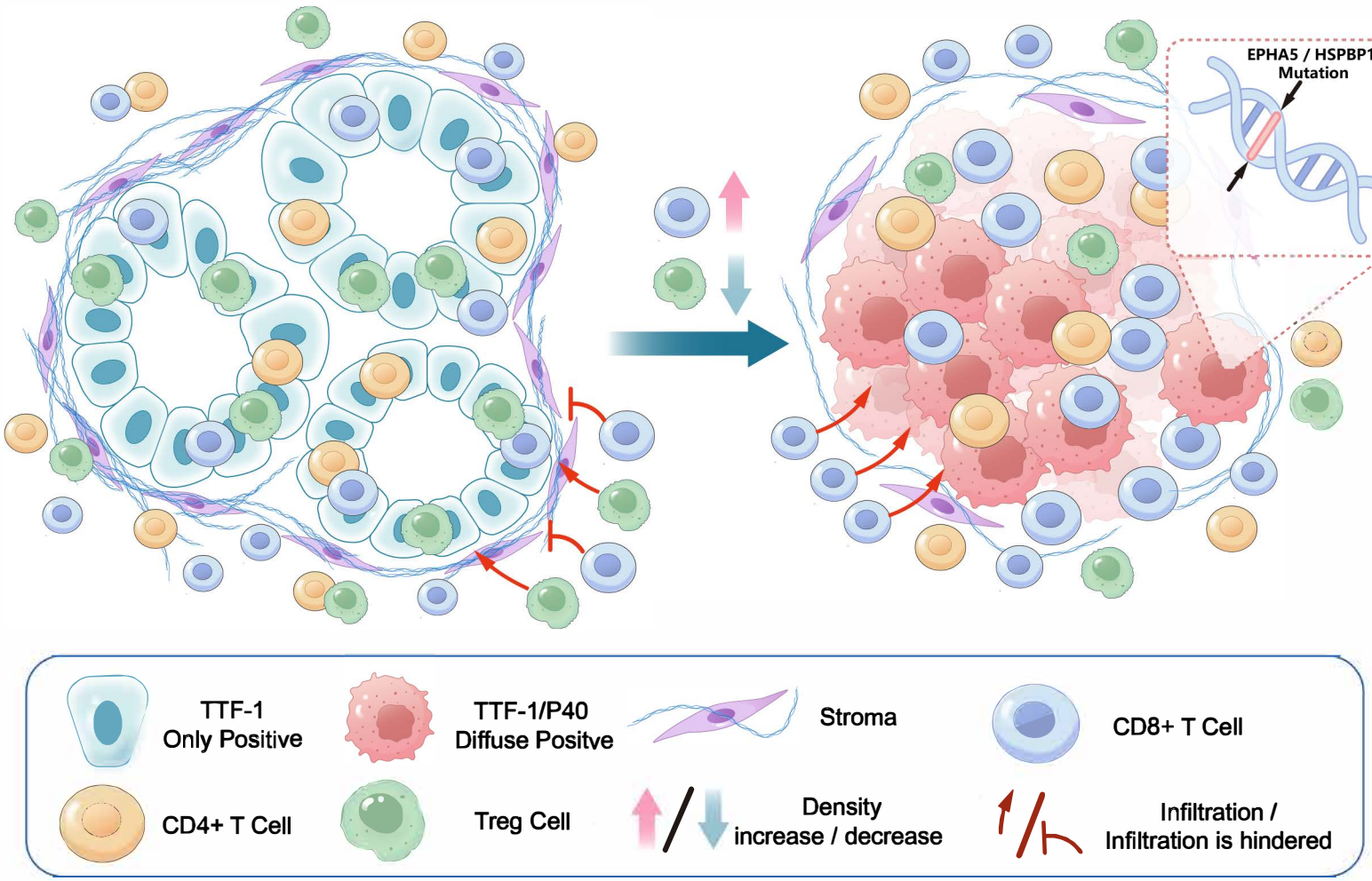

In Brief

(Left) Classic Adenocarcinoma: TTF-1 only NSCLC maintains a stable epithelial differentiation state. The TIME shows an "immune-excluded" phenotype, with Tregs infiltrating the parenchyma and relatively restricted CD8+ T cell proximity.

(Right) Lineage-Plastic State: In TTF-1/p40 diffuse-positive NSCLC, somatic variants (e.g., *EPHA5, HSPBP1*) were correlated with lineage plasticity and a biphenotypic morphology in exploratory analyses. The spatial organization differed descriptively: Tregs showed stromal-predominant distribution patterns at the region level (in mixed-effects sensitivity models, independent of stromal area fraction, $P < 0.001$). Parenchymal Treg density was reduced. CD8+ and CD4+ T cells were relatively closer to tumor cells. This spatial immune remodeling was associated with a favorable PFS trend in exploratory analyses.