

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1. Proximity between cells of interest detected by Digital Pathology. (A) Examples of the distribution of PD-L1+ cells and CD8+ cells within the tumor microenvironment. (B) Example of dual staining obtained with Immunoscope IC test, raw image, top left. Automatic detection of cells and identification of PD-L1+ cells (blue nucleus and brown plasma membrane) and CD8+ cells (purple nucleus and grey plasma membrane), top right. Materialization of a 20µm circle around the centroid of two PD-L1+ cells, bottom left. Identification (red nucleus) of a PD-L1+ cell with at least one CD8+ within a 20µm around its centroid, bottom right. (C) Distribution of the proximity index in 132 NSCLC patients from the Charlie/Delta cohort.

Supplementary Figure S2. Univariate Cox analysis on continuous or dichotomized variables of the progression free survival (PFS). Upper panel: Training set, Lower panel: validation set. Variables measured in the Tumor Stroma Interface (TSI) are reported but were not used to establish the Immunoscope IC model since that compartment was missing in more than a third of the biopsy samples. Significant logrank P-values are marked as *** $p < 0.005$, ** $0.005 > p < 0.01$, * $0.01 > p < 0.05$.

Supplementary Figure S3. PD-L1 TPS is not associated with improved PFS or OS of patients (A, B) Kaplan-Meier curves describing PFS at 1% PD-L1 TPS on the training set and the validation set respectively (C, D) Kaplan-Meier curves describing PFS at 50% PD-L1 TPS on the training set and the validation set respectively.

Supplementary Figure S4. Hierarchical clustering of patients according to the five variables contributing to the LASSO model. (A) Training set in three-category Immunoscope-IC. (B) Training set in two-category Immunoscope-IC, (C) Validation set in three-category Immunoscope-IC, (D) Validation set in two-category Immunoscope-IC.

Supplementary Figure S5. Distribution of Immuscore-IC in the training cohort. Dashed lines represent the cutoffs used to dichotomize the score into two- (top panel) or three-category (bottom panel) Immunoscore IC.

Supplementary Figure S6. Distributions of variables measured in Immunoscore-IC test. The figure shows the distribution of variables in both training and test cohorts. The x-axis (in log scale) represents marker values and the y-axis indicates the density distribution.