



Detection of vCAF-EC niche as a novel diagnostic approach for lung cancer intrapulmonary metastasis

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INTRODUCTION

With the rising incidence of multiple lung cancers (MLCs), distinguishing between multiple primary lung cancers (MPLCs) and intrapulmonary metastasis (IPM) poses significant clinical challenges. Diagnosis of MPLC and IPM remains difficult due to insufficiently accurate criteria and ambiguous integration of genetic testing. Herein, we identified a IPM related PDGFR β ⁺ NOTCH3⁺ perivascular cancer associated fibroblast (vCAF)- endothelial cell (EC) niche, aim to improve the diagnosis of IPM.

METHODS

FFPE scRNA-seq was conducted using 3 paired FFPE samples of primary lung cancer lesions and intrapulmonary metastases. Paraffin sections of mice IPM model constructed by suspending mEGFP-CAF with LLC1 were selected for digital spatial profiler (DSP) analysis for further screening. Then multiple lung cancer (MLC) cohort with paired FFPE samples from 18 patients with IPM and 66 patients with MPLC was applied for mIF staining for validation. Moreover, NUMCH cohort, a TMA cohort with a total of 142 lung cancer patients, was used for further validation. The distance between PDGFR β ⁺ NOTCH3⁺ vCAFs and ECs was determined using Qupath v0.6.0.

DISCUSSION AND CONCLUSION

Detection of the novel vCAF-EC niche emerges potential significance in distinguishing between MPLCs and IPM. Application of the model could improve the accuracy of IPM diagnosis and optimize treatment plans.

RESULTS

Through single cell sequencing, digital spatial profiler and cohort validation, we characterized a distinct PDGFR β ⁺ NOTCH3⁺ vCAF subset, which is with higher abundance in IPM metastasis lesion than in IPM primary lesion and MPLC lesion. Detecting the abundance of PDGFR β ⁺ NOTCH3⁺ vCAF could robustly distinguishing IPM patients from MPLC patients (AUC=0.86, sensitivity=72.22%, specificity=84.85%), as well as distinguishing metastatic and non-metastatic LUAD patients. Cellchat analysis revealed that ECs drive notch signaling activation of PDGFR β ⁺ NOTCH3⁺ vCAF via JAG1-NOTCH3 interaction. Cell-cell distance analysis by Qupath v0.6.0 revealed that most PDGFR β ⁺ NOTCH3⁺ vCAFs distributed within 25 μ m from ECs, forming a PDGFR β ⁺ NOTCH3⁺ vCAF-EC niche. Moreover, detecting the mean distance of PDGFR β ⁺ NOTCH3⁺ vCAF from ECs achieve a robust performance on diagnosing IPM (AUC=0.89, sensitivity=88.89%, specificity=72.73%). Combining the abundance of PDGFR β ⁺ NOTCH3⁺ vCAF and mean distance of PDGFR β ⁺ NOTCH3⁺ vCAF from ECs, we determined the vCAF-EC niche score and achieve a better IPM diagnosis performance than traditional pathological standards (AUC=0.9495, sensitivity=94.44%, specificity=83.33%).

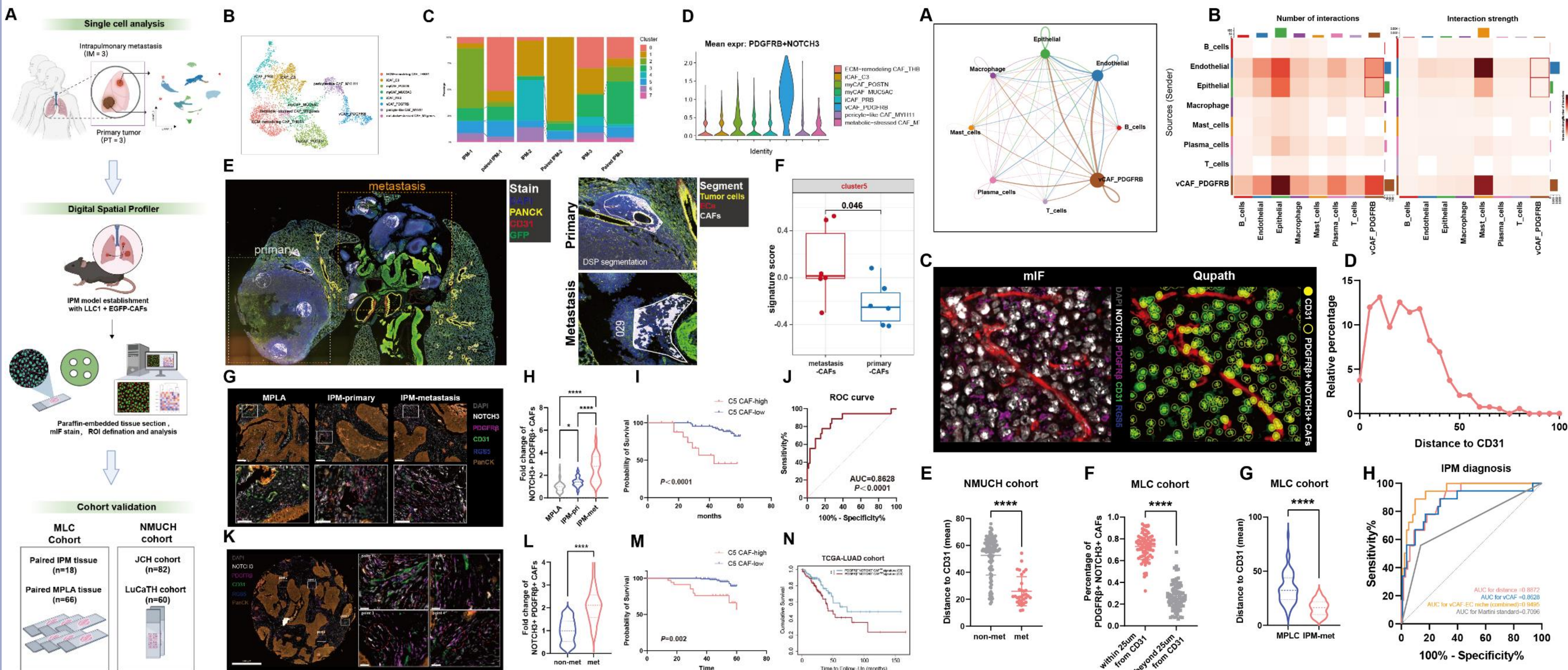


Figure1. Identification of IPM related CAFs as PDGFR β ⁺ NOTCH3⁺ vCAF subset.

Reference:

1. Cords, L et.al, Classifying cancer-associated fibroblasts-The good, the bad, and the target. Cancer Cell, 2024. 42(9): p. 1480-1485.
2. Ma, L., et al., Cellular neighborhoods in cancer. Nat Cancer, 2026. 7(1): p. 16-28.
3. Kalkavan, H., et al., Sublethal cytochrome c release generates drug-tolerant persister cells. Cell, 2022. 185(18): p. 3356-3374.e22.
4. Bankhead, P. et al. QuPath: Open source software for digital pathology image analysis. Sci Rep 7, 16878 (2017).

Figure 2. Endothelial cells drive shuttle-CAFs NOTCH activation.