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Detection of residual cancer cell signals through deconvolution of bulk RNA-Seq data with single-cell atlas in advanced lung cancer

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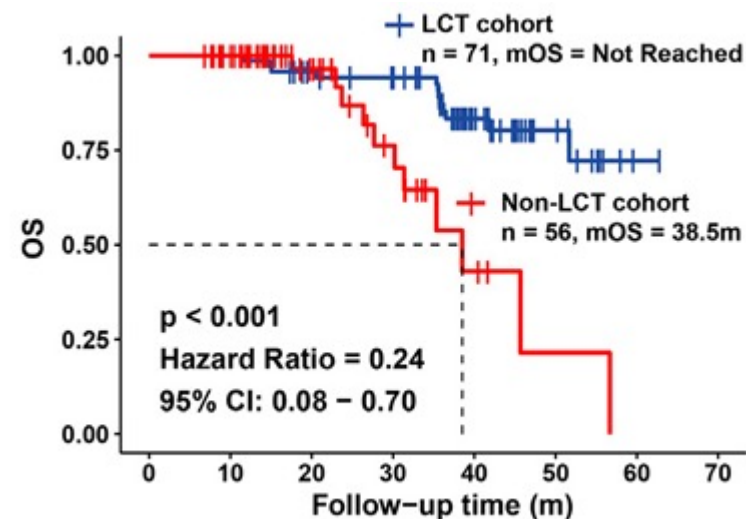
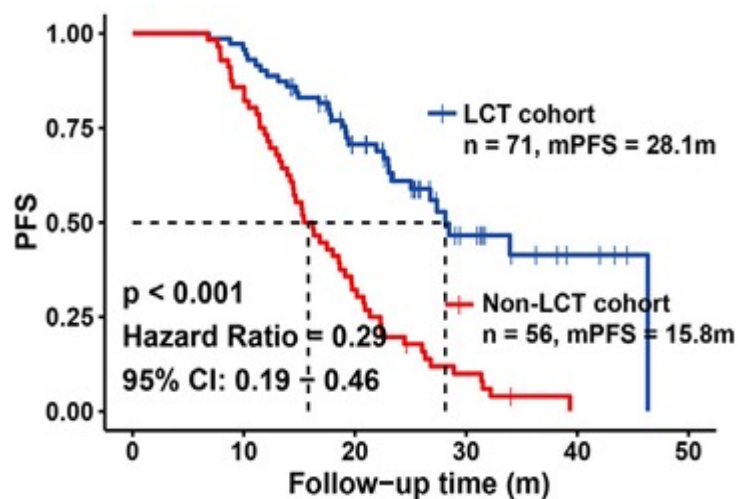
Disclosure

- I have no relevant financial conflicts of interest to disclose.
- No artificial-intelligence-generative tools were used to generate, write, or edit the content of this presentation slides.

Background

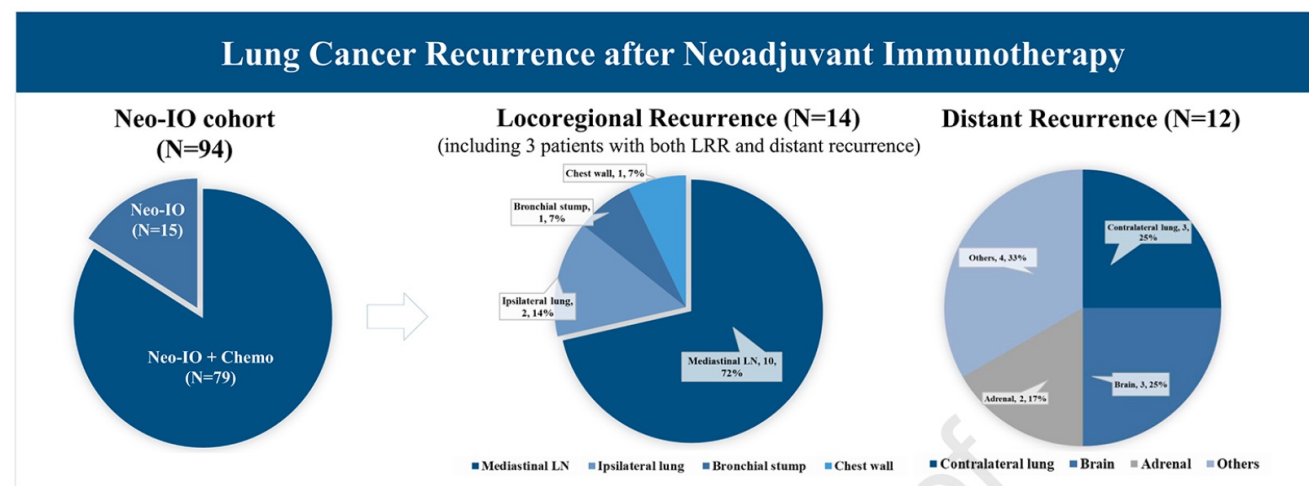
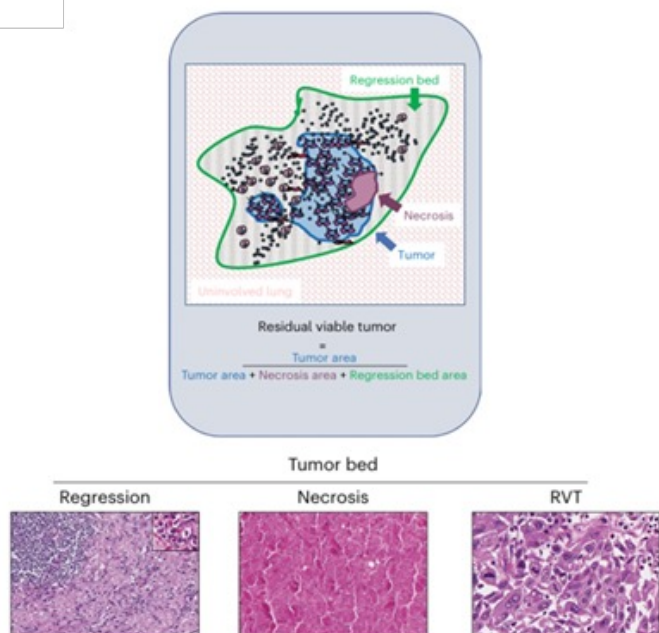
Local consolidative therapy (LCT) can improve both progression-free survival (PFS) and overall survival (OS) in patients with advanced NSCLC after 1st systemic therapy.

Surgical resection offers the opportunity to reassess the residual tumor.



Background

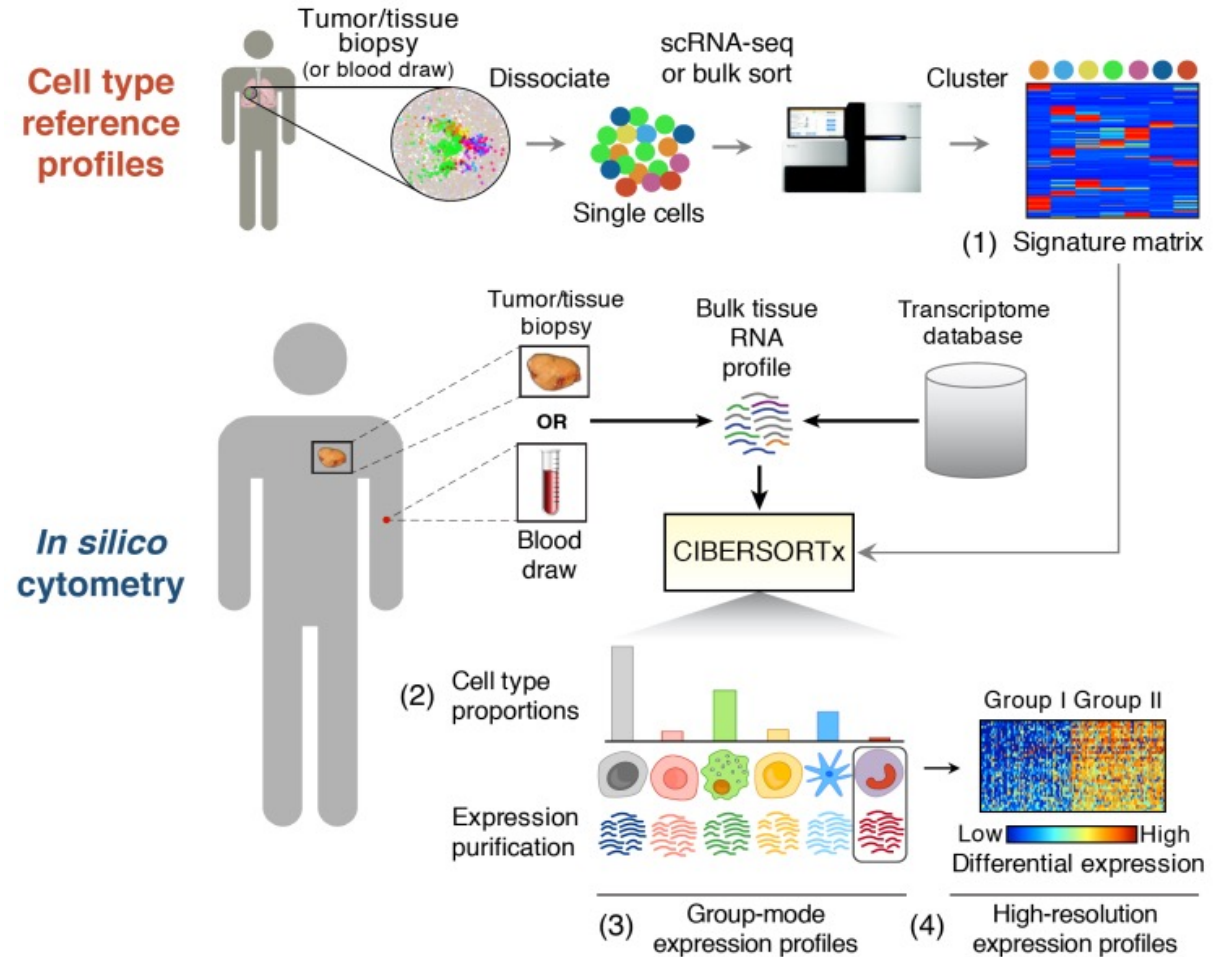
- Even patients who achieve pathological complete response (pCR) or major pathological response (MPR) after surgery can still experience recurrence.
- An unmet clinical need: we lack a good transcriptomic biomarker to capture hidden residual tumor lesions in surgical samples.



Patients with pCR (12.5%) developed recurrence; all were distant recurrences.

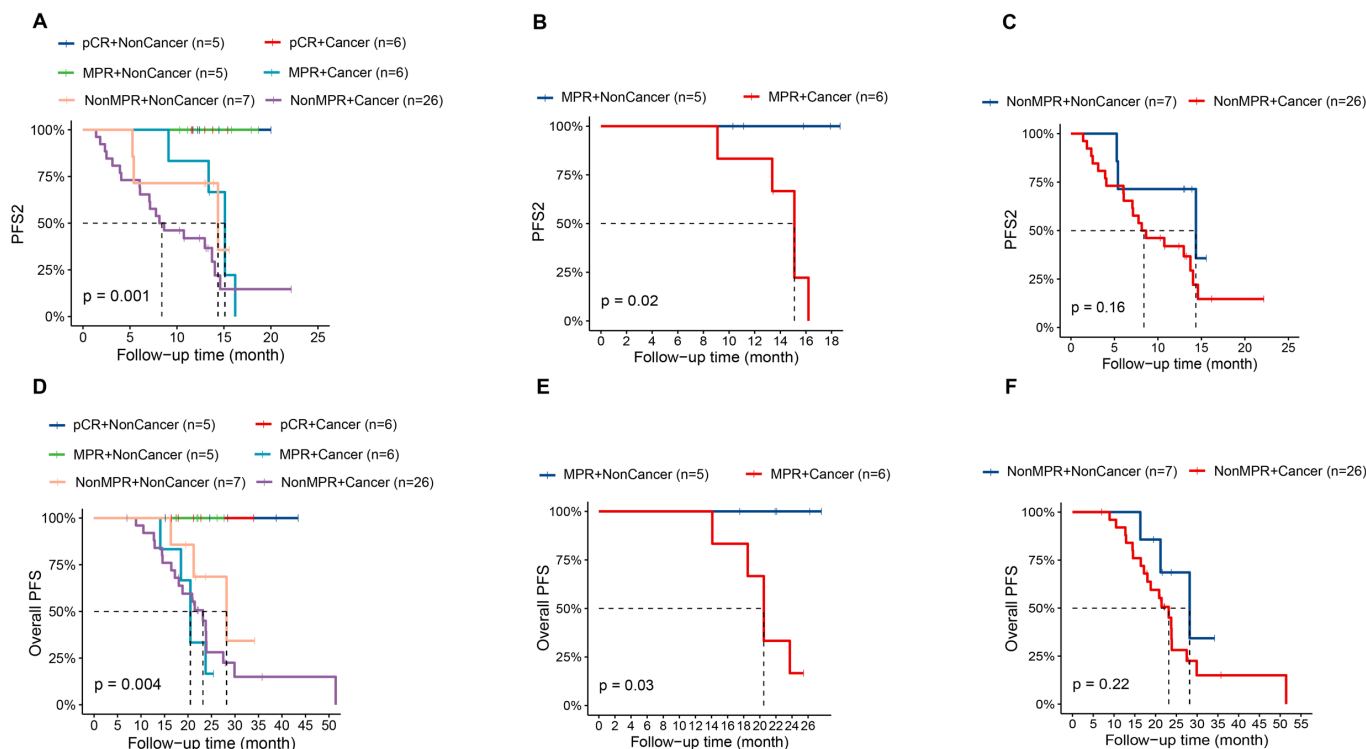
Methods

- Bulk RNA-seq on 55 primary tumors from 55 induced oligometastatic NSCLC patients underwent surgery following 1st line therapy.
- **CIBERSORTx digital cytometry: lung-cancer-specific single-cell reference profiles - a signature matrix**
- **Deconvolved bulk RNA-seq data to identify patients w/ and w/o residual cancer-cell signals: determining cell type abundance and expression**
- Tumor cells ✓



Results

1. Residual cancer signal predicts clinical prognosis

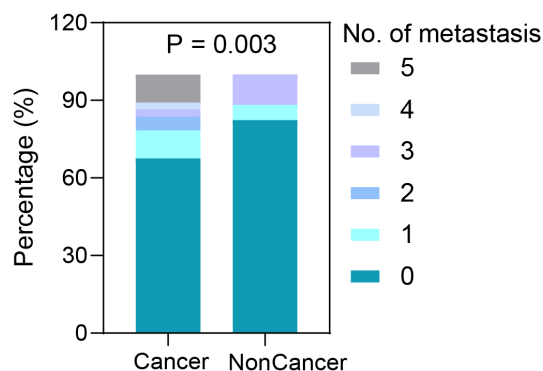
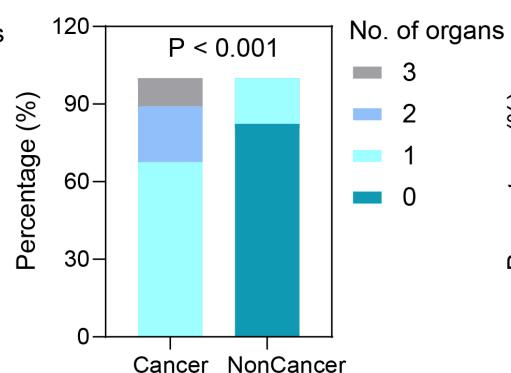
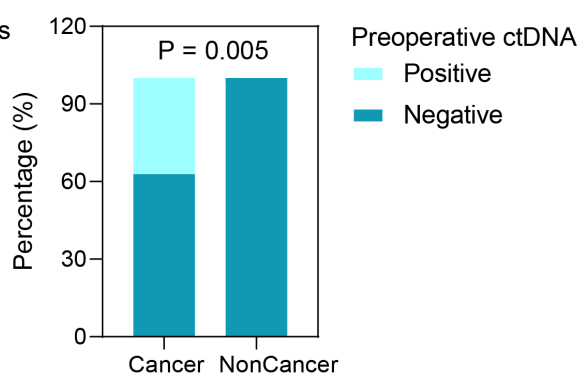
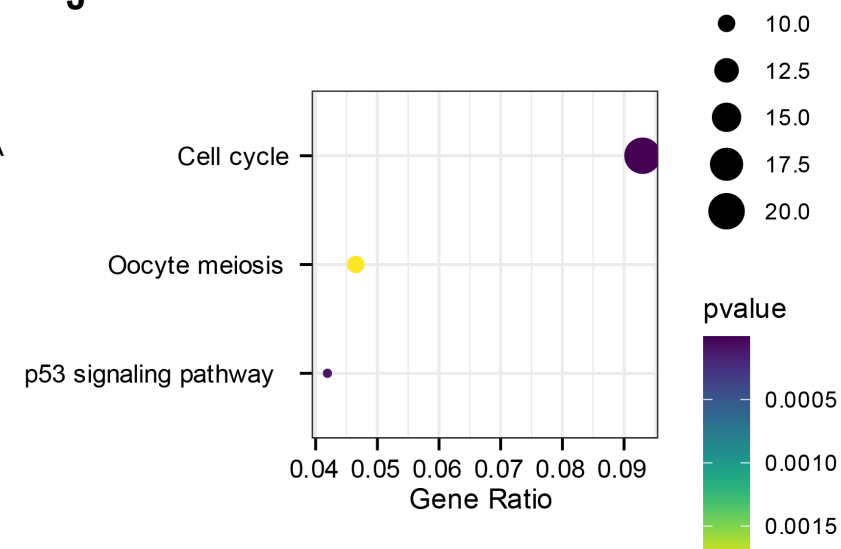


PFS2= PFS

- Patients with detectable cancer cell signals had shorter PFS ($p = 0.001$ for PFS2, Figure A; $p = 0.004$ for overall PFS, Figure D) compared to those without detectable signals, a similarly shorter PFS was found in the MPR groups (Figure B and E).
- In the Non-MPR subgroup, there was no significant difference in PFS between patients who had detected cancer cell signals and those who did not (Figure C and F).
- More informative among patients with favorable pathological tumor response.

Results

2. Residual cancer signals reflected heavier pre-treatment tumor burden.

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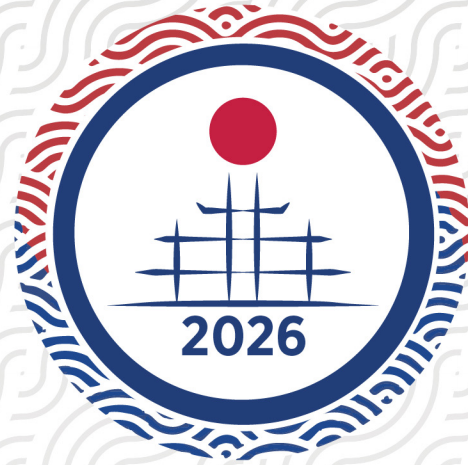
Patients with detectable cancer cell signals exhibited more preoperative metastatic sites ($p = 0.003$, Figure G), more metastatic organs ($p < 0.001$, Figure H), and a higher preoperative ctDNA positivity rate ($p = 0.005$, Figure I), as well as elevated gene expression enriched in cell cycle and P53 signaling pathways (Figure J).

Actionable Take Away Message

- Residual cancer cell signals detected through transcriptomic deconvolution can identify patients at higher risk of disease progression in patients with induced oligometastatic NSCLC after 1st line therapy following by LCT.

Future Direction for Research

- A deconvolution of bulk RNA-seq data with scRNA-seq atlas references can serve as a useful tool to understand the residual tumor signals.



Thank You.●