

Memory T-Cell Remodeling Reveals Functional Immune Fitness Driving Durable Immunotherapy Response in NSCLC

Poster #
P3.114

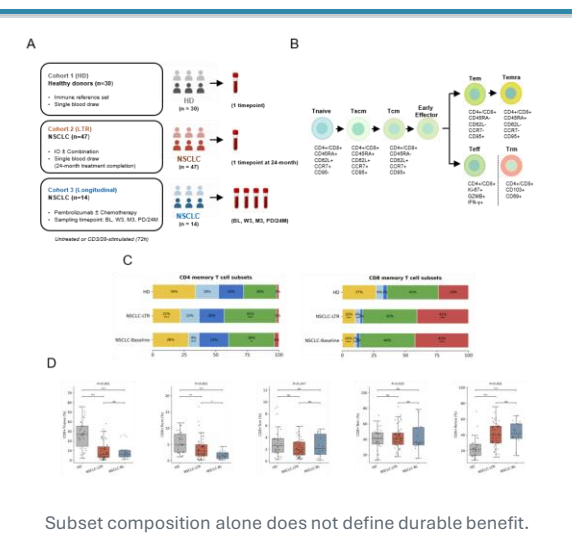
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BACKGROUND & OBJECTIVE

Immune checkpoint inhibitors (ICIs) targeting PD-1/PD-L1 have improved outcomes in advanced NSCLC, but durable benefit occurs in only a subset of patients, and tumor PD-L1 expression incompletely captures the immune competence required for sustained tumor control. We hypothesized that the functional responsiveness of circulating memory T cells to stimulation — rather than memory-subset composition alone — better reflects durable ICI benefit. To test this, we integrated flow-cytometric profiling of memory T-cell composition and function (before/after ex vivo CD3/CD28 stimulation) across healthy donors, long-term ICI responders, and a longitudinal NSCLC cohort, with complementary plasma proteomics and exploratory multiplex spatial imaging of pretreatment tumor tissue.

1 Memory T-cell composition is remodeled

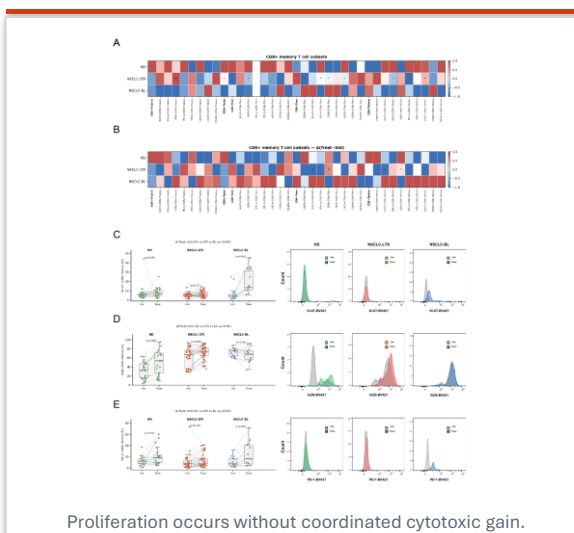


(A) Cohort & sampling overview. (B) Memory-subset gating schema. (C) CD4⁺CD8⁺ subset distribution by group. (D) CD8⁺ subset frequencies (HD vs LTR vs Baseline).

COMPOSITIONAL STABILITY

NSCLC is effector-skewed, but LTR and baseline NSCLC retain broadly similar memory-subset architecture.

2 CD8⁺ Temra activation is functionally uncoupled

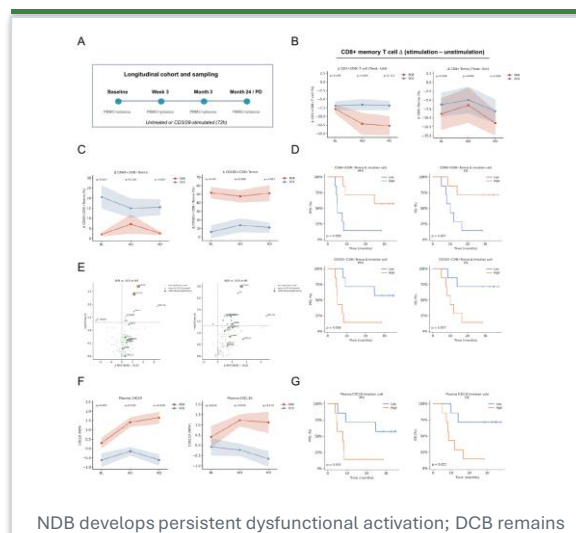


(A–B) CD8⁺ subset function heatmaps, unstimulated (A) and Δstimulation (B). (C–E) Paired Ki-67 (C), granzyme B (D), and PD-1 (E) in CD8⁺ Temra ± stimulation.

DYSFUNCTIONAL ACTIVATION

Strong Ki-67 induction without matching GZB gain indicates impaired CD8⁺ Temra functional fitness.

3 Functional fitness tracks longitudinal benefit

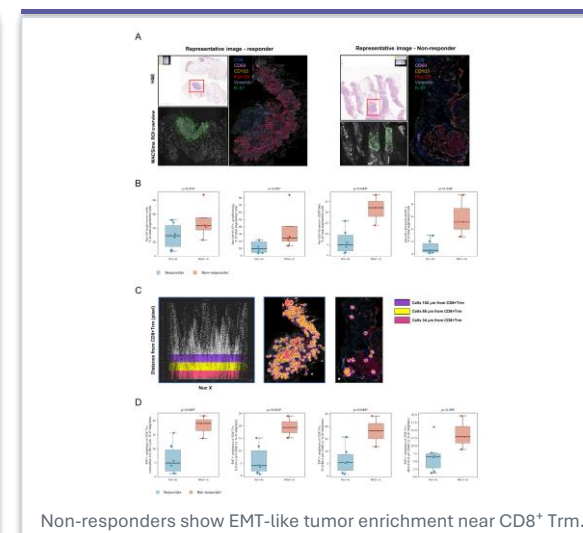


(A) Longitudinal sampling scheme. (B–C) ΔCD8/Temra and ΔCD69/CXCR3 dynamics (DCB vs NDB). (D) PFS/OS by ΔCD69/CXCR3. (E–G) Plasma CXCL9/CXCL10 dynamics and survival.

LONGITUDINAL SIGNAL

Dynamic inducible responses, rather than static composition, better separate durable from non-durable benefit.

4 Spatial context reveals a resistance phenotype



(A) Representative multiplex images (responder vs non-responder). (B) Tumor EMT/proliferation frequencies. (C–D) CD8⁺ Tmem neighborhood shells and EMT⁺ neighbor enrichment.

SPATIAL RESISTANCE

EMT-like tumor cells are enriched in non-responders and cluster near CD8⁺ Tmem, suggesting spatial immune constraint.

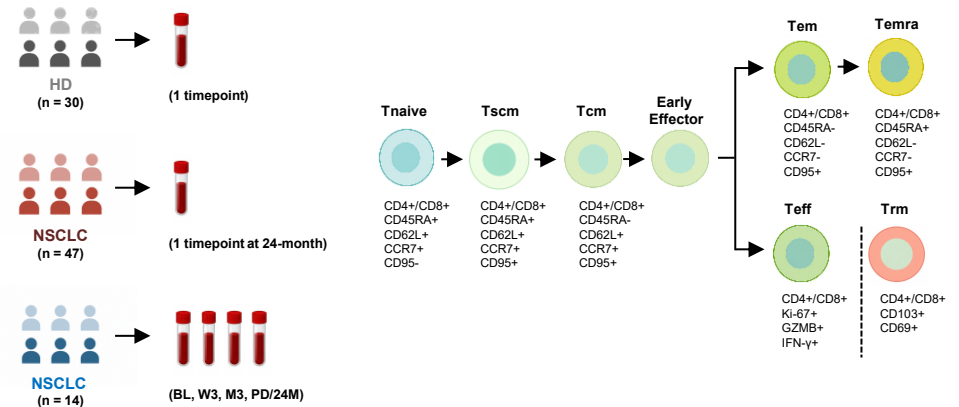
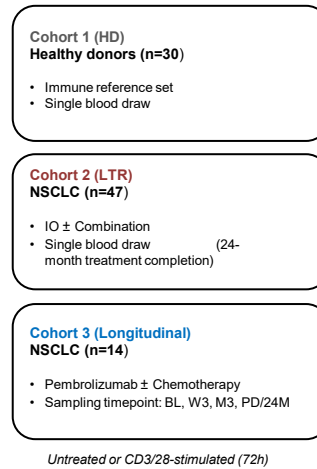
CONCLUSION

Durable benefit from ICI-based therapy in NSCLC was more clearly associated with subset-resolved functional responsiveness of circulating memory T cells than with memory-subset composition alone. CD8⁺ Temra cytotoxic responsiveness and CD69/CXCR3-related dynamics — mirrored by plasma CXCL9/CXCL10 — represent candidate predictive biomarkers of ICI response that warrant validation in larger cohorts. Exploratory spatial imaging further suggests that non-durable responders are accompanied by a distinct EMT-associated, proliferative tumor context spatially linked to CD8⁺ Tmem cells.

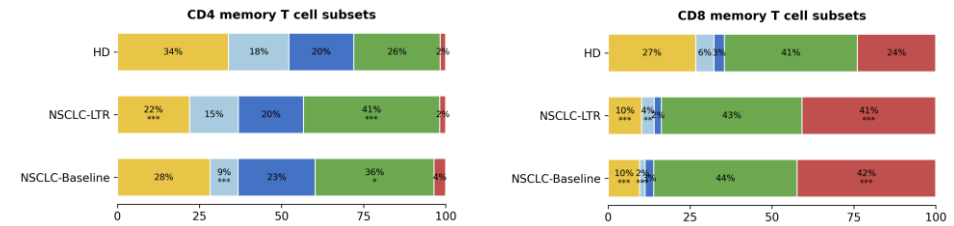
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Memory T-cell composition is remodeled

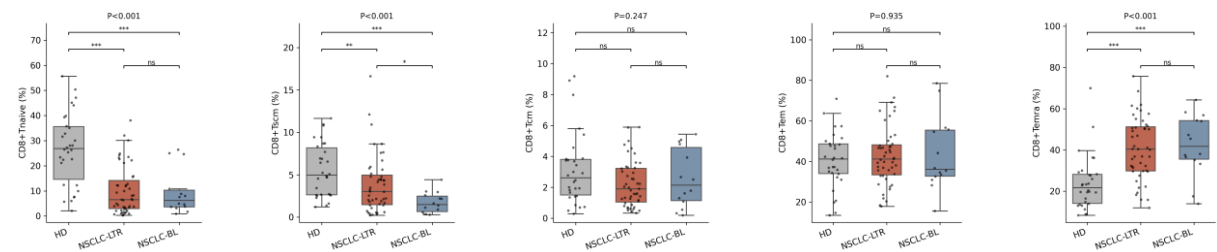
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C



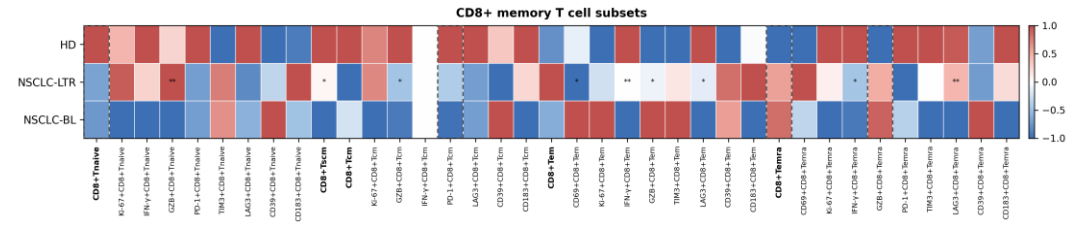
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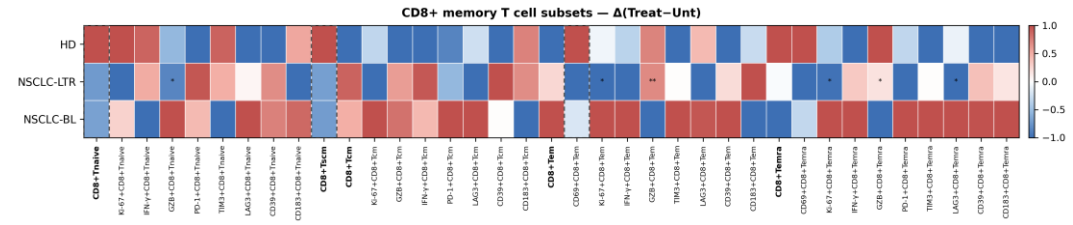
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CD8⁺ Temra activation is functionally uncoupled

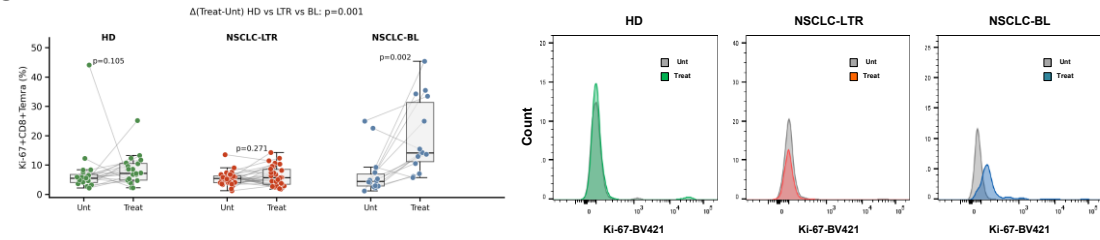
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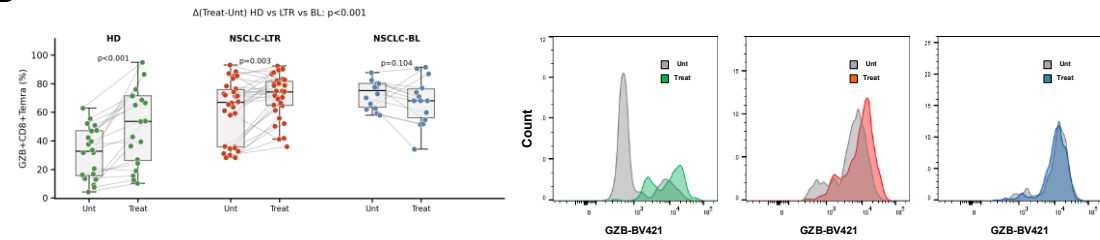
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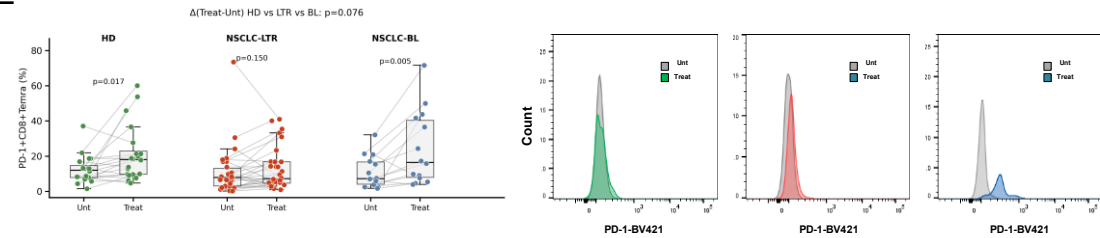
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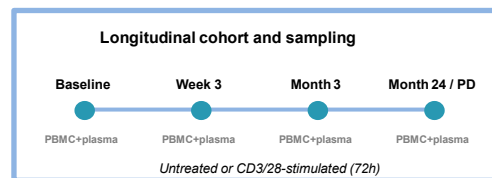
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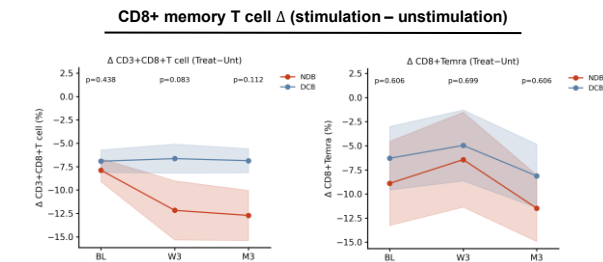
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Functional fitness tracks longitudinal benefit

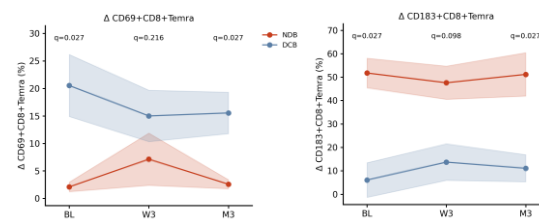
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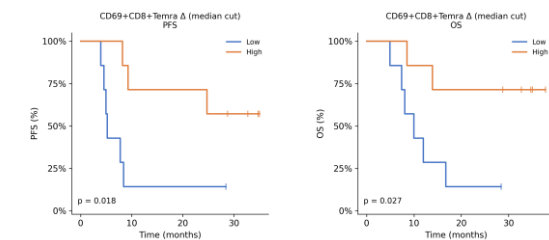
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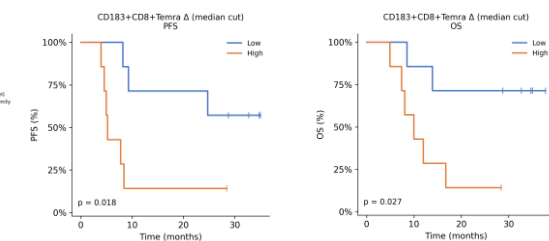
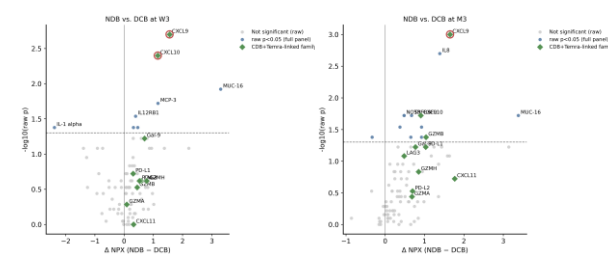
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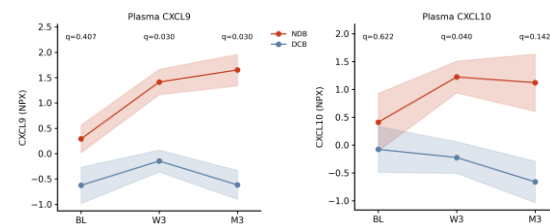
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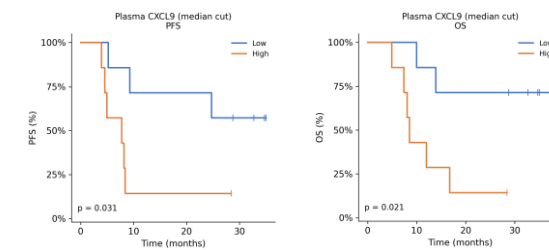
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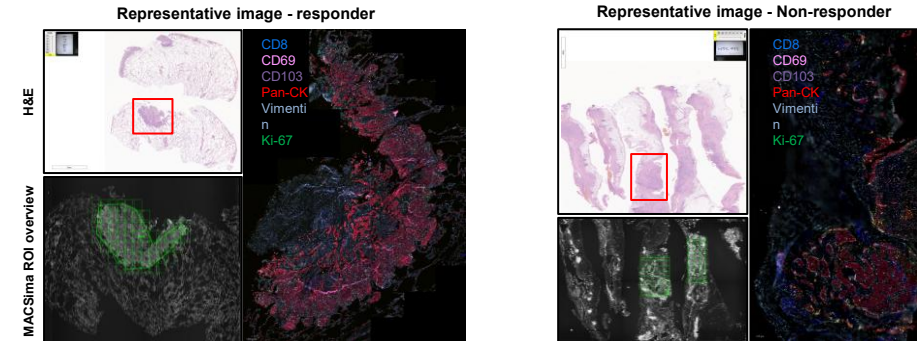
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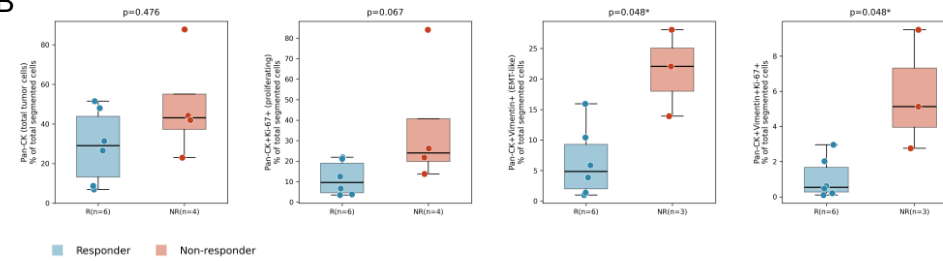
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Spatial context reveals a resistance phenotype

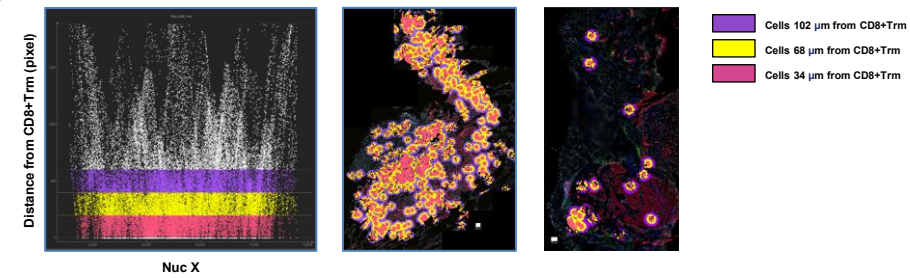
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