Next Generation Cancer Therapeutics 2026

Poster #: B-6

Ex Vivo Live Tumor Fragment Profiling to Predict Immune Checkpoint Inhibitor Response Across Solid Tumor Types

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Introduction

- Existing biomarkers are inaccurate and fail to capture the dynamics of the tumor microenvironment (TME)[1,2]
- Functional precision medicine addresses this gap by enabling the measurement, not prediction, of immune response[3]
- The elive™ platform retains the native TME in live tumor fragments (LTFs) through 72 hours of ex vivo culture, allowing for rapid characterization of immunotherapies and targeted therapies[4,5]

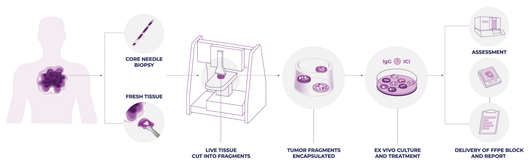
Methods

Cytokine profiling and clinical correlation: Patients with immune checkpoint inhibitor (ICI)-eligible solid tumors were enrolled in observational trials (NCT05478538, NCT05520099, NCT06349642, NCT07327489). Biopsies and resections were cut into LTFs, encapsulated in hydrogel, and treated sequentially with IgG control followed by ICI for cytokine profiling. Cytokine production was assessed longitudinally by a multiplexed bead-based immunoassay.

Cytotoxicity assessment: MIA PaCa-2 cells were implanted in immunocompromised mice to establish cell line–derived xenografts. Tumor tissue was cut into LTFs, encapsulated in hydrogel, and treated with DMSO control or varying concentrations of daraxonrasib through 72 hours (or staurosporine as positive control for cell killing). Cell viability was assessed via assay measuring cellular reducing capacity.

Downstream analyses included flow cytometry, multiplex immunofluorescence, immunohistochemistry, and transcriptional profiling.

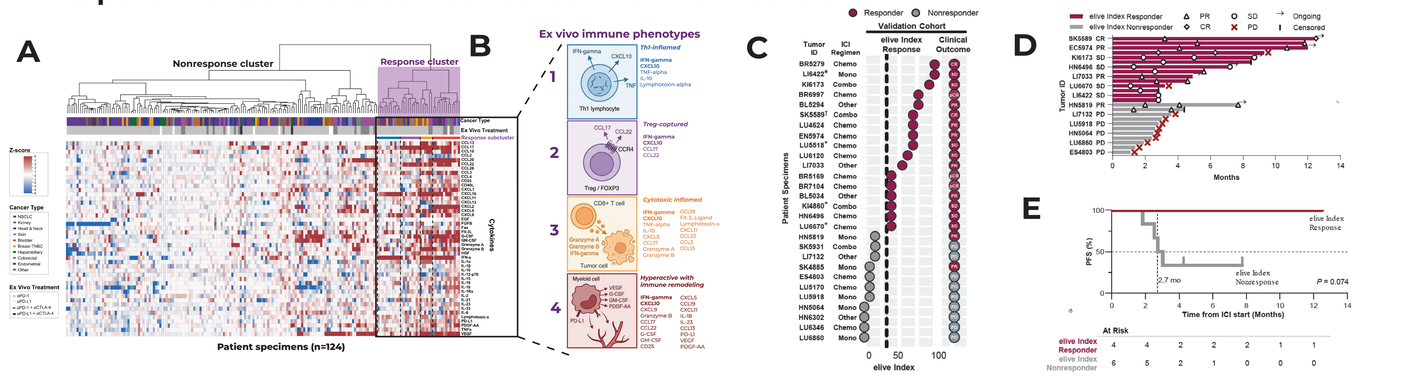
Platform workflow for ICI response profiling:



Live tumor tissue from core needle biopsies or resections is cut into LTFs using an automated cutting instrument and encapsulated in hydrogel. LTFs are treated sequentially with IgG control followed by ICI, and cytokine secretion is assessed longitudinally through 72 hours. Tissue can be formalin-fixed, paraffin-embedded (FFPE) for downstream

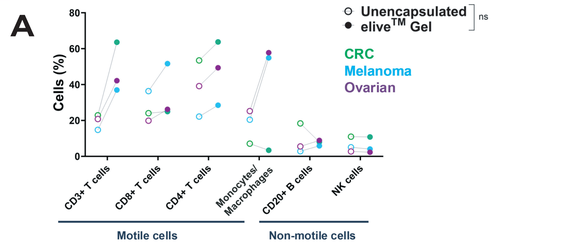
Results

1 Functional profiling on the elive platform enables the measurement of ex vivo immune response to ICIs and is 93% concordant with clinical outcomes



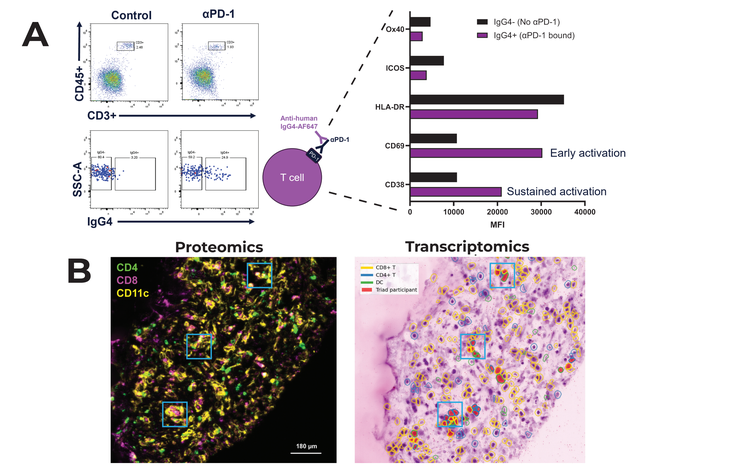
A) Unsupervised hierarchical clustering of cytokine profiling data from 124 specimens showed a subset of specimens that exhibit increased cytokine production (red boxes) following treatment with ICI. Significant upregulation of 26 cytokines differentiated the response cluster (purple) from the nonresponse cluster. The response cluster was further divided into 4 subclusters of response (blue, purple, orange, and red bars), distinguished by unique cytokine signatures. **B)** The biological states reflected in each of the 4 subclusters was determined according to the cytokine signature exhibited. Subcluster 1 represents a classic Th1-inflamed TME, while subcluster 2 exhibits a Treg-captured state. Subcluster 3 reflects cytotoxic T-cell activity, and subcluster 4 shows a TME that has reached full activation and is now displaying evidence of adaptive resistance. **C)** A validation cohort of 28 patients shows the elive Index–predicted ICI response is 93% concordant with clinical outcomes (*<6 months SD; †Tier 2 Validation ICI combinations)[5]. **D)** Swimmer plot showing time to progression analysis of elive Index-predicted responders and nonresponders for the validation cohort. **E)** Progression-free survival of elive Index–predicted responders (red) and nonresponders (grey) for the pure-ICI treated validation patients only.

2 Retention of native TME



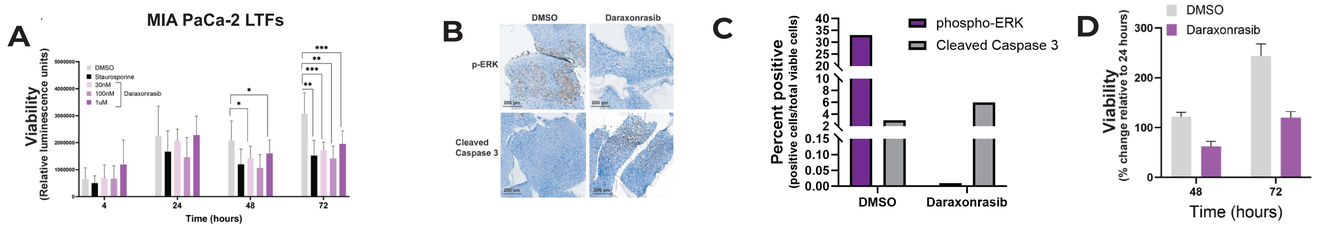
A) Flow cytometry of elive hydrogel-encapsulated LTFs (filled dots) and unencapsulated LTFs (open dots) following ex vivo ICI treatment shows improved retention of T cells, macrophages, and monocytes in encapsulated fragments. **B)** Multiplex immunofluorescence of a cervical LTF shows CD8+ T cells (magenta), CD4+ T cells (red), and activated T cells (CD69, green; CD137, orange), with 68% of CD8+ T cells showing CD69 activation.

3 Detection of T-cell activation and immune triads



A) Flow cytometry analysis of αPD-1–bound T cells shows the presence of early (CD69) and sustained (CD38) T-cell activation markers. **B)** Spatial proteomics (left) and transcriptomics (right) show evidence of immune triads (CD4+ T cell, CD8+ T cell, and dendritic cell within ~20 µm) in a non-small cell lung cancer LTF treated with αPD-1 .

4 Expansion to targeted therapies



A) LTFs from a cell line derived xenograft pancreatic cancer model show decreased cellular reducing capacity (viability) following treatment with KRAS inhibitor daraxonrasib, expanding the platform's application to targeted therapies. **B)** IHC of MIA PaCa-2 LTFs treated with daraxonrasib shows decreased ERK phosphorylation (p-ERK) and increased cleaved caspase 3 (CC3) levels compared to DMSO-treated control. **C)** Percentage of viable cells positive for p-ERK and CC3 in MIA PaCa-2 LTFs following treatment with daraxonrasib or DMSO control. **D)** Proof-of-concept experiment in a human pancreatic ductal adenocarcinoma (PDAC) specimen shows decreased cell viability in LTFs treated with 10 µM daraxonrasib compared with DMSO control.

Conclusions

- elive retains the native TME
- elive enables the functional measurement of immune response and has 93% concordance with clinical outcomes
- elive offers broad utility across translational pharmaceutical development and biomarker discovery by recapitulating clinically relevant immune phenotypes of ex vivo response

Acknowledgments

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Scan to learn more

References

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