UCSF Startups and Innovation in ***Diagnostics***

Advanced Gene Signature Biomarker Profile for Optimizing Bladder Cancer Treatment with PD-L1 Inhibitors

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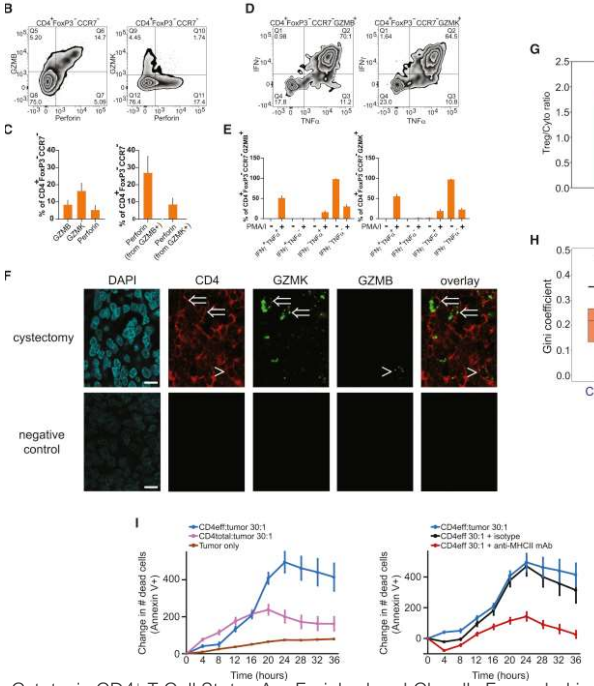


Multiple Cytotoxic CD4⁺ T Cell States Are Enriched and Clonally Expanded in Bladder Tumors and Possess Lytic Capacity against Tumors

DISEASE/INDICATION: Bladder cancer.

UNMET NEED: Bladder cancer presents a significant diagnostic challenge, with substantial variability in patient response to immunotherapies such as Programmed Death Ligand 1 (PD-L1) inhibitors. Current therapeutic approaches often follow a 'one-size-fits-all' strategy, lacking the precision required to predict individual responses effectively. This results in suboptimal treatment outcomes for a significant number of patients.

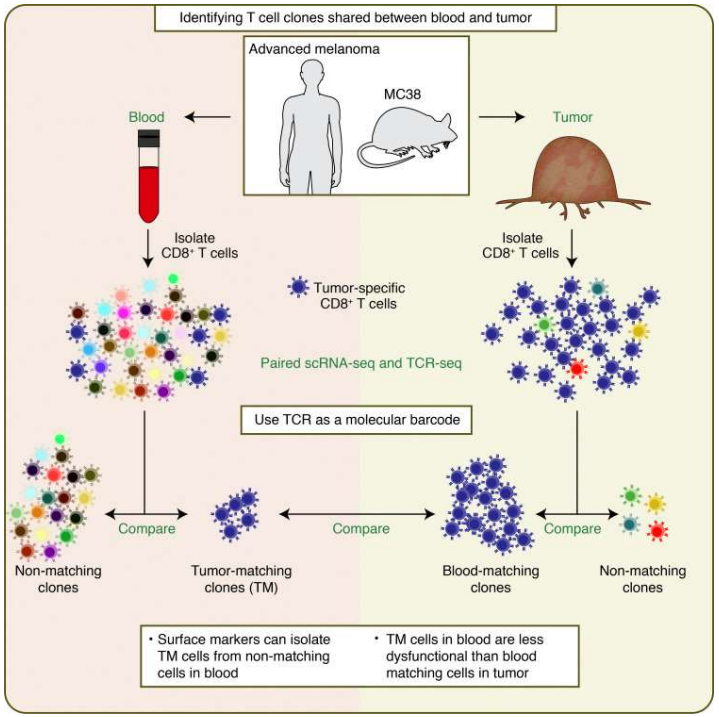
PRODUCT: A diagnostic system based on the detection of a specific gene signature biomarker in patients suspected of having bladder cancer. The system utilizes advanced genomic technologies to assess the expression levels of key genes identified in proliferating T cells among other markers, thereby predicting the responsiveness of an individual to PD-L1 inhibitors.

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Unlike traditional diagnostic methods that may rely on generalized biomarkers or invasive procedures, this invention employs a non-invasive, highly specific gene signature approach. It utilizes cutting-edge single-cell RNA sequencing and other molecular biology techniques to provide a precise, personalized prediction of treatment efficacy

DATA: The gene signature biomarker includes critical genes such as STMN1, KIAA0101, PKM, and TNFRSF18, all validated across various subtypes of bladder cancer including metastatic and non-metastatic forms. The presence of this gene signature in a biological sample, such as peripheral blood or directly from bladder cancer cells, is indicative of a higher likelihood of positive response to PD-L1 inhibitors like atezolizumab in metastatic bladder cancer patients.

Blood-based T cell Biomarkers to predict responsiveness to Immunotherapy

Adil Daud, MD
UCSF Clinical Professor, Medicine, PICI Member



DISEASE/INDICATION: Oncology

UNMET NEED: No FDA-approved blood-based biomarker tests for cancer in the U.S.

PRODUCT: Blood-based assay to predict a patient's response to immunotherapy

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Allows for non-invasive monitoring of the anti-tumor immune response in real-time without the need for single-cell sequencing

DATA: Validated preclinically in mice and clinically in patients with melanoma.

Short-cutting the Diagnostic Journey through Metagenomic Next-Generation Sequencing

UCSF Co-Founders

Joe DeRisi, PhD
UCSF Professor

Michael Wilson, MD
UCSF Professor

Charles Chiu, MD, PhD
UCSF Professor

PROBLEM:

- Hospitalization of a meningitis and encephalitis case can last up to 25 days, with average costs of nearly $20,000 per day.
- >60% of cases are due to infection, and patients often undergo 40+ different tests in the search for etiology.
- Each test takes days to weeks, and only detects a handful of pathogens, resulting in delayed treatment, unnecessary testing, and extended lengths of stay.

SOLUTION:

- Comprehensive detection of all viruses, bacteria, parasites, and fungi at once from a single sample.
- Rapid, powerful metagenomics testing platform that returns results to clinicians in 48h.

delvedetect
CEREBROSPINAL FLUID

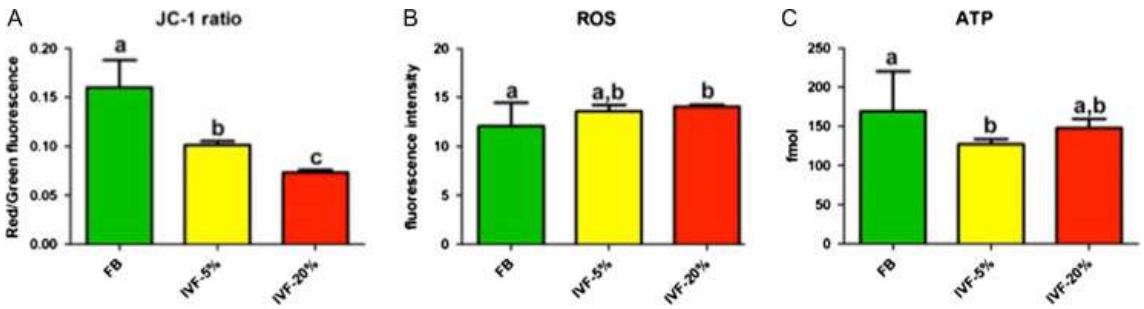
TRACTION:

- With $35M Series A, Delve Bio stands up a robust clinical and commercial operation to bring mNGS to more patients nationwide.
- Delve Bio launches Delve Detect, its flagship mNGS testing service that detects pathogens in cerebrospinal fluid.
- Premier top-tier customer base (~300 hospitals) with annual volumes increasing YoY (40% CAGR).
- Seven-year, real-world evidence of clinical adoption of mNGS published in Nature Medicine

LEARN MORE:

Improving IVF Success with Advanced Embryo Selection Technology

Paolo Rinaudo, MD, PhD
Cofounder, EmbryoDx Solutions
Obstetrics/Gynecology and Reproductive Endocrinologist at UCSF



PROBLEM:

- Inability to identify the healthiest embryos to transfer, leading to low success rates of IVF and need for multiple IVF cycles.

SOLUTION:

- Novel biomarkers indicative of embryonic health, laying the foundation for a safe and reliable device tailored for embryo selection.
- State-of-the-art technology that has the potential to dramatically increase IVF success rates.

STATUS:

- Spinning out

LEARN MORE:

Exai Bio: A cell-free RNA- & AI-based liquid biopsy platform positioned to play a central role in the next phase of breast cancer management

Hani Goodarzi, PhD
Co-founder & Scientific Advisor, Exai Bio
UCSF Associate Professor and Arc Institute Core Investigator

PROBLEM:

- >40% of women over age 40 have dense breast tissue and these women have a higher overall risk of developing breast cancer
- Mammograms have significant limitations for women with dense breasts leading to missed cancers
- Growing awareness of mammogram limitations due to FDA guidelines
- ctDNA has clear plateaus in detecting early-stage breast cancer

SOLUTION:

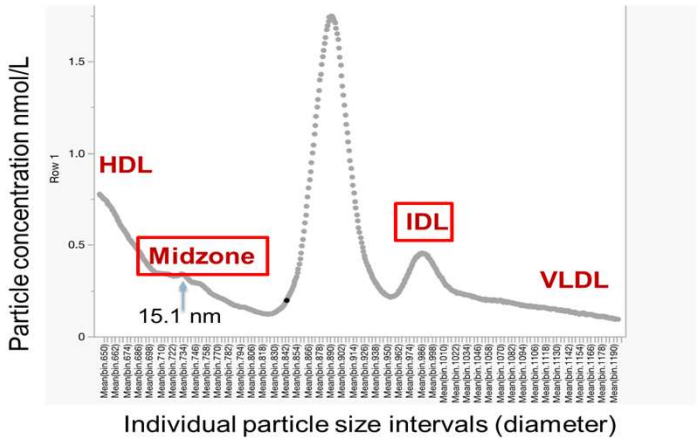
- Our co-founders at UCSF discovered a novel class of small RNA biomarkers, called oncRNAs, that are actively shed by living cancer cells into the blood.
- Generative AI Illuminates cancer specific patterns of RNAs in blood enabling a highly effective early detection solution.
- Exai's platform detects breast cancer at the earliest stages, surpassing ctDNA approaches. It is low cost and high performing.

LEARN MORE:

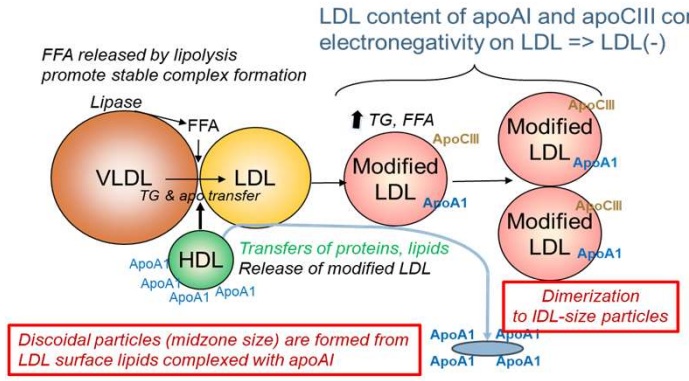
Improved cardiovascular risk factor diagnostic

Ronald Krauss, MD
Professor, Pediatrics
School of Medicine

Size and concentration of lipoproteins from ion mobility assay



LDL(-) production pathway and model for midzone and IDL-sized lipoproteins



DISEASE/INDICATION: cardiovascular diseases (CVD)

UNMET NEED:

- Current risk prediction via LDL and HDL measurement may not be accurate for all patients, e.g., some CVD patients LDL levels are normal. Other biomarkers (e.g., LDL-) is needed
- However, existing methodology of measuring LDL- (ion exchange chromatography) is time consuming and costly

PRODUCT: Diagnostic to measure LDL- in high-risk patients to assess and monitor risk and inform treatment decisions

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Potential use in clinical setting, as CV risk assessment
- Improved CV risk prediction vs. LDL and HDL measurements
- Ion-mobility based method complements existing advanced lipid panel (CardioIQ)

DATA:

- Growing research suggests that electronegative low-density lipoprotein (LDL-) is a key predictor of CVD, independent of total cholesterol level
- Validation studies of this assay ongoing

Precision Immunotherapy: Enhancing Cancer Treatment Efficacy through Advanced T-Cell Biomarker Analysis

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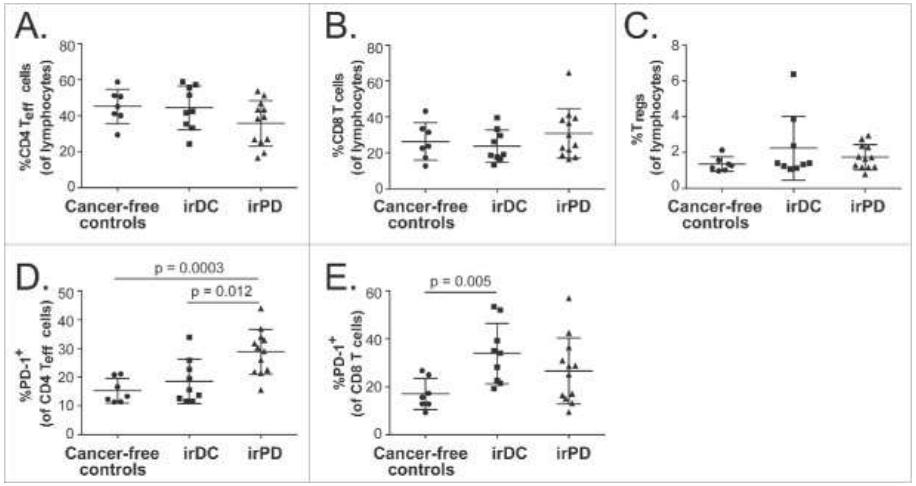

Comparisons of immune subsets between cancer-free controls and pre-treatment levels of patients with metastatic melanoma. Scatter plots of the following immune subsets for cancer-free controls, irDC and irPD: (A) Percentage of $CD4^+$ T_{eff} cells of lymphocytes; (B) Percentage of $CD8^+$ T cells of lymphocytes; (C) Percentage of T_{regs} of lymphocytes; (D) Percentage of $CD4^+$ T_{eff} cells expressing surface PD-1; (E) Percentage of $CD8^+$ T cells expressing surface PD-1. Error bars show standard deviations.

DISEASE/INDICATION: For patients with melanoma and metastatic castration-resistant prostate cancer (mCRPC), focused on those undergoing immune checkpoint inhibitor therapies.

UNMET NEED: Current immunotherapies, such as anti-CTLA-4 and anti-PD-1 treatments, show promising results but often face challenges like varying patient response and severe side effects. There is a critical need for precise patient selection to enhance treatment efficacy and minimize unnecessary exposure to potentially harmful therapies.

PRODUCT: This precision medicine approach leverages a biomarker-based method to identify cancer patients who are most likely to benefit from specific immunotherapies. Using a minimal-invasive blood sample, the product measures levels of PD-1, PDL1, CTLA4 and CD127 T cells (including subsets of CD4+ and regulatory T cells) to determine a patient's amenability to immunotherapy.

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Provides: a) Specificity and Sensitivity: Utilizes specific biomarkers that are clinically validated for predicting therapy response; b) Adaptability: Can be used before and during treatment to monitor response, allowing for dynamic treatment adjustments; c) Ease of Use: Employs flow cytometry, a widely used technique in clinical labs, ensuring integration into existing diagnostic workflows without additional equipment or extensive training; d) Enhanced Efficacy and Safety: Early clinical data indicate that patients matching specific immunological profiles show better responses to the combined therapy, thus allowing more personalized and effective treatment plans.

DATA: Validated in patients.

Precision Immunotherapy: Enhancing Treatment Efficacy through PBMC and Intratumoral Myeloid Cell Profiling

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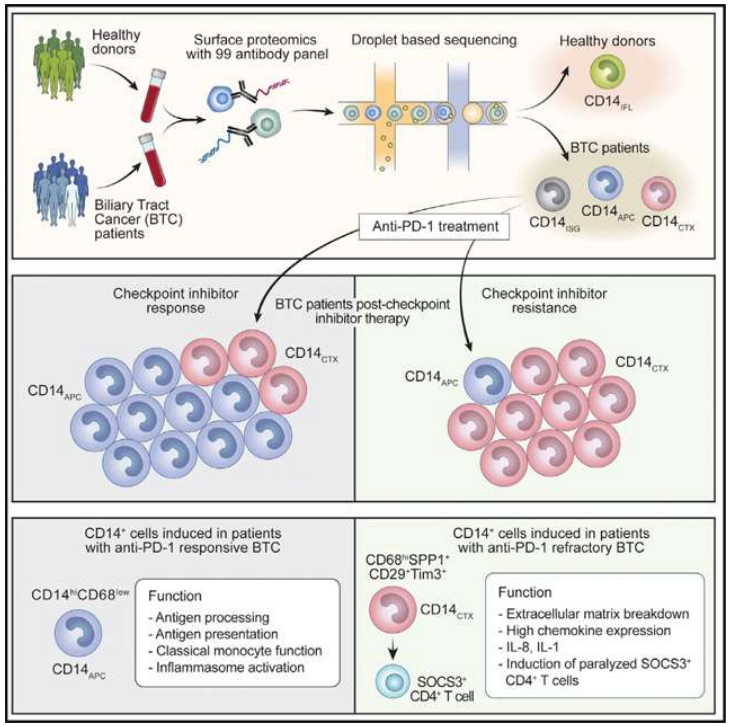

DISEASE/INDICATION: Cancer, including but not limited to biliary tract cancer, prostate cancer, colon cancer, kidney cancer, and skin cancer.

UNMET NEED: Efficacy of immune checkpoint inhibitors (ICIs) for the treatment of some cancers varies significantly among patients due to the complex interplay of individual immunological landscapes. The current challenge in oncology is not only the identification of effective treatments but also the selection of appropriate patients who are most likely to benefit from specific therapies like ICIs.

PRODUCT: An advanced biomarker-based approach for the selection and treatment of cancer patients using ICIs. This method involves isolating peripheral blood mononuclear cells (PBMCs) and intratumoral myeloid cells, quantifying specific cell types (CD14CTX, CD4SOCS3, and MacSPP1), and using these data to determine patient eligibility for ICI therapy. This approach is poised to become an integral part of personalized cancer treatment plans.

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Unlike traditional methods that often rely on generalized biomarkers or indirect indicators of treatment efficacy, our approach provides a direct, quantifiable measure of tumor and systemic immunological profiles. This method allows for: a) High specificity and sensitivity in selecting patients who will respond to ICIs, using the identification of unique cell surface markers like Tim3 and CD29 on CD14CTX cells; b) Use of advanced sequencing technologies (e.g., scRNAseq, CITE-seq) to ensure precise and comprehensive analysis; c) Potential to significantly increase disease-free survival (DFS) rates by tailoring treatments based on individual immunological data rather than a one-size-fits-all approach.

DATA: Validated in patients.

Predictive assay for meningioma risk stratification and radiotherapy response

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William C. Chen, MD
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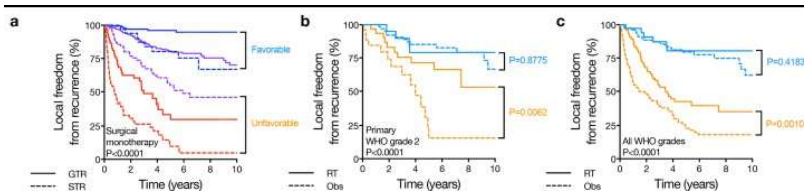


DISEASE/INDICATION: Meningioma

UNMET NEED: To date, no clinically tractable biomarkers are available to guide patient selection for adjuvant radiation therapy

PRODUCT: Targeted gene expression assay

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

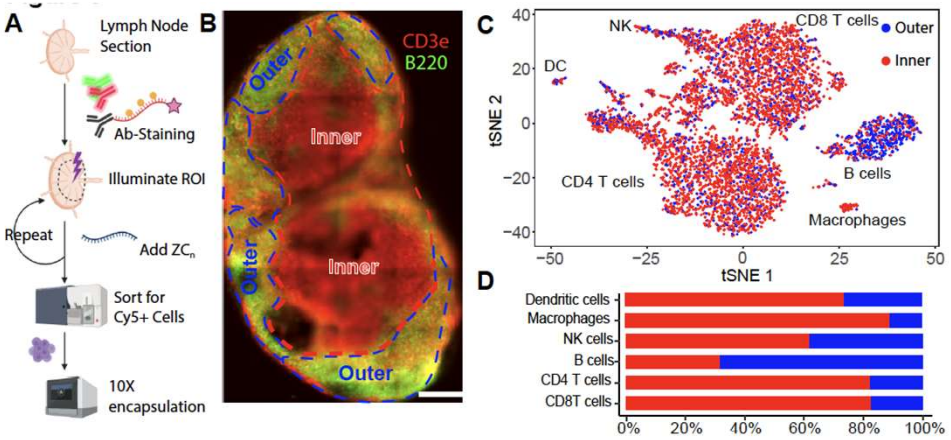
- Favorable risk score indicates patients could avoid adjuvant radiotherapy.
- Use of the biomarker may alter management in one-third of cases

DATA: External validation of biomarker, including prospective clinical trial. Link: https://pubmed.ncbi.nlm.nih.gov/37944590/

Further prospective validation is planned from ongoing Phase 3 randomized trial, anticipated accrual completion in 2024.

ZipSeq: Single-cell RNA-sequencing with in situ spatiotemporal information

Max Krummel, PhD
UCSF Professor,
Pathology



Adoptive transfer of CD8 T cells from CD2-RFP mouse and CFSE labelled B cell

DISEASE/INDICATION: Research tool that can be used to study tissue development, wound healing, cellular interactions in cancer immunotherapy treatments, cellular therapies (such as adoptive cell and stem cell), gene therapies, immune cell targeted therapeutics (such as T cell engagers)

UNMET NEED: Spatial single-cell sequencing that is compatible with live tissue

PRODUCT: Reagent kits, instrumentation, software

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Enables capturing of cellular spatial and time-varying information within the tissue prior to scRNA-seq analysis

DATA: Proof of concept data on wound healing, lymph node tissue, tumors