Exosome Diagnostics for Cancer Patients on Immunotherapy

Prashanth Vallabhajosyula

Yale Life Sciences

PITCHFEST

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Team behind exosome diagnostics for precision oncology

We are innovators in exosome diagnostics

Transplant health

Heart

BLAVATNIK FUND FOR INNOVATION *FY2024*

Lung

Kidney

Oncology

Patient response to immunotherapy

Focus for today

Co-inventors

Prashanth Vallabhajosyula *MD, MS*

Laxminarayana Korutla *PhD*

Strategic Advisor

Lolahon Kadiri *PhD*

Scientific & Clinical Advisors

Ruth Halaban *PhD*

Benjamin Judson *MD, MBA*

Sara Pai MD, PhD

Immune checkpoint inhibitor “tsunami” in cancer therapeutics

Since 2011 when ICI was first introduced …

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11 new ICI drugs on the market

Examples

KEYTRUDA® (pembrolizumab) Injection 100 mg

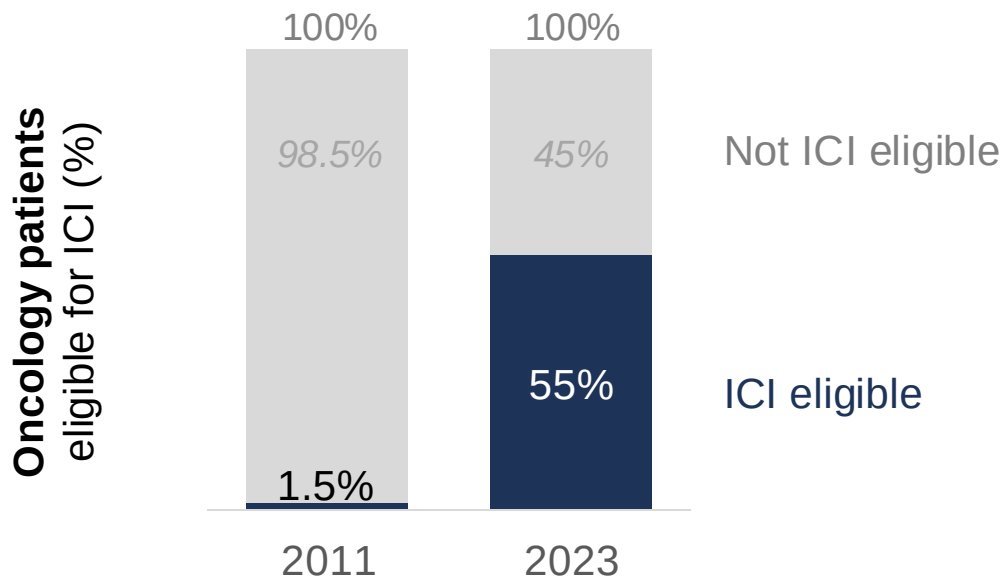
TECENTRIQ® atezolizumab

OPDIVO™ (nivolumab)

Approval in **20 general tumor types**

- 88 indications in cancer patients

… today, of the >2M new cancer patients per year in the United States, 55% have an indication for which ICI treatment is approved



But there are significant limitations to consider…

ICI treatment adoption has experienced big obstacles

Low response rates

≤ 20%
of patients
have cancer remission

Inability to identify responders prior to treatment selection

High risk of adverse events

As high as **70% of patients** experience complications (grade 3-5)

Inability to noninvasively monitor ICI response

The need for noninvasive biomarkers in this field is so critical that an entire Task Force for Immunotherapy Biomarkers was convened in 2014 (still active)

There is a critical gap in diagnostics for ICI treatment today

FDA approved biomarkers are all based on biopsy of tumor tissue…

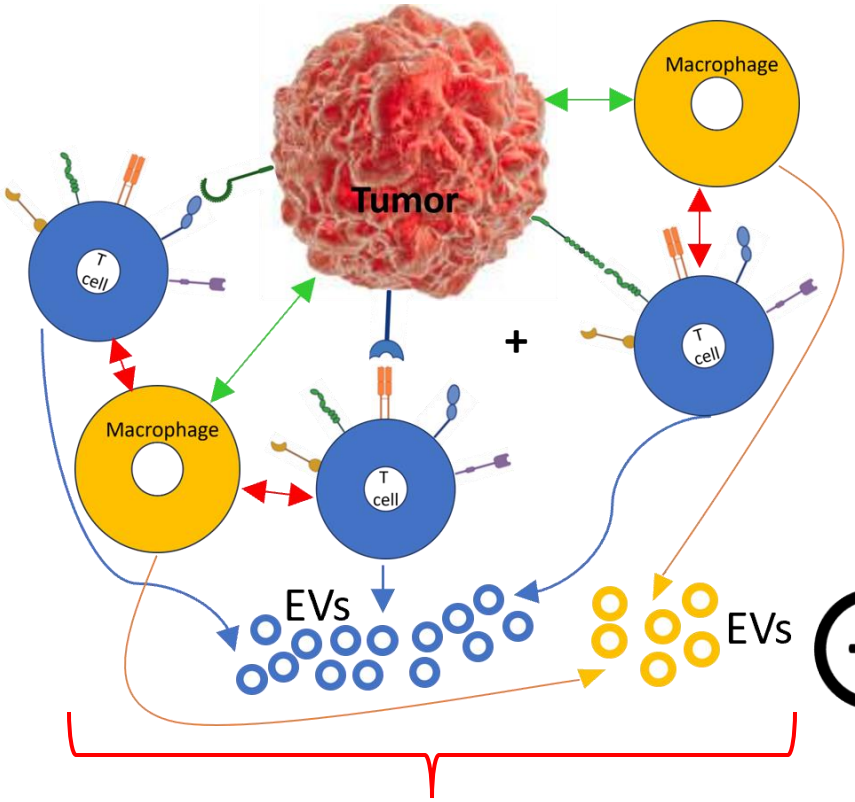
PDL1	MSI-H	TMB
Tumor protein expression	Tumor microsatellite instability	Tumor DNA mutational burden
Nonsmall cell lung cancer	Small subset of tumors have MSI (3.8%)	Pembrolizumab candidacy

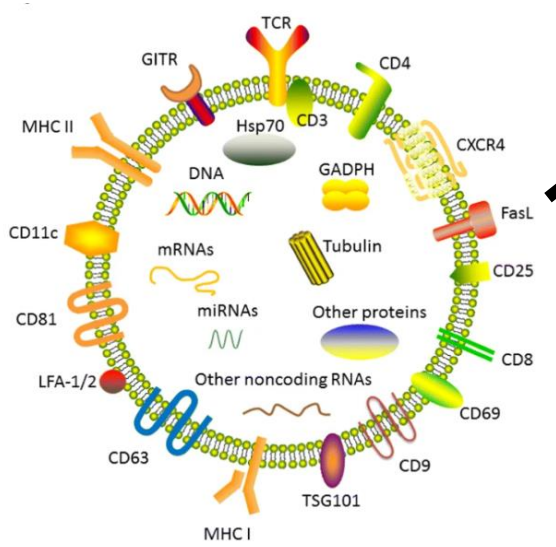
… and current solutions are lacking on multiple fronts

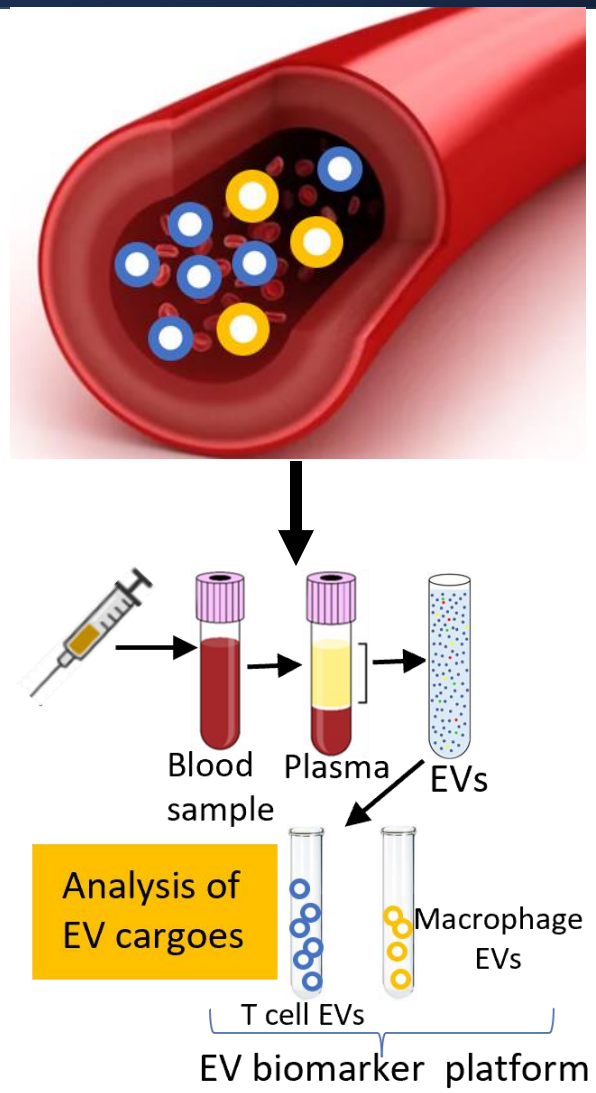
- **Static** | One-time readout of tumor
- **Not repeatable**
- **No molecular window** into the patient's immune response
- **Narrow application** | Approved for only a few tumor types
- **Inadequate sensitivity** and **specificity**
- **Invasive** | Requires biopsy of the tumor

We propose a blood test that can improve on all these limitations

SOLUTION: Immune cell-specific extracellular vesicle (EV) profiling







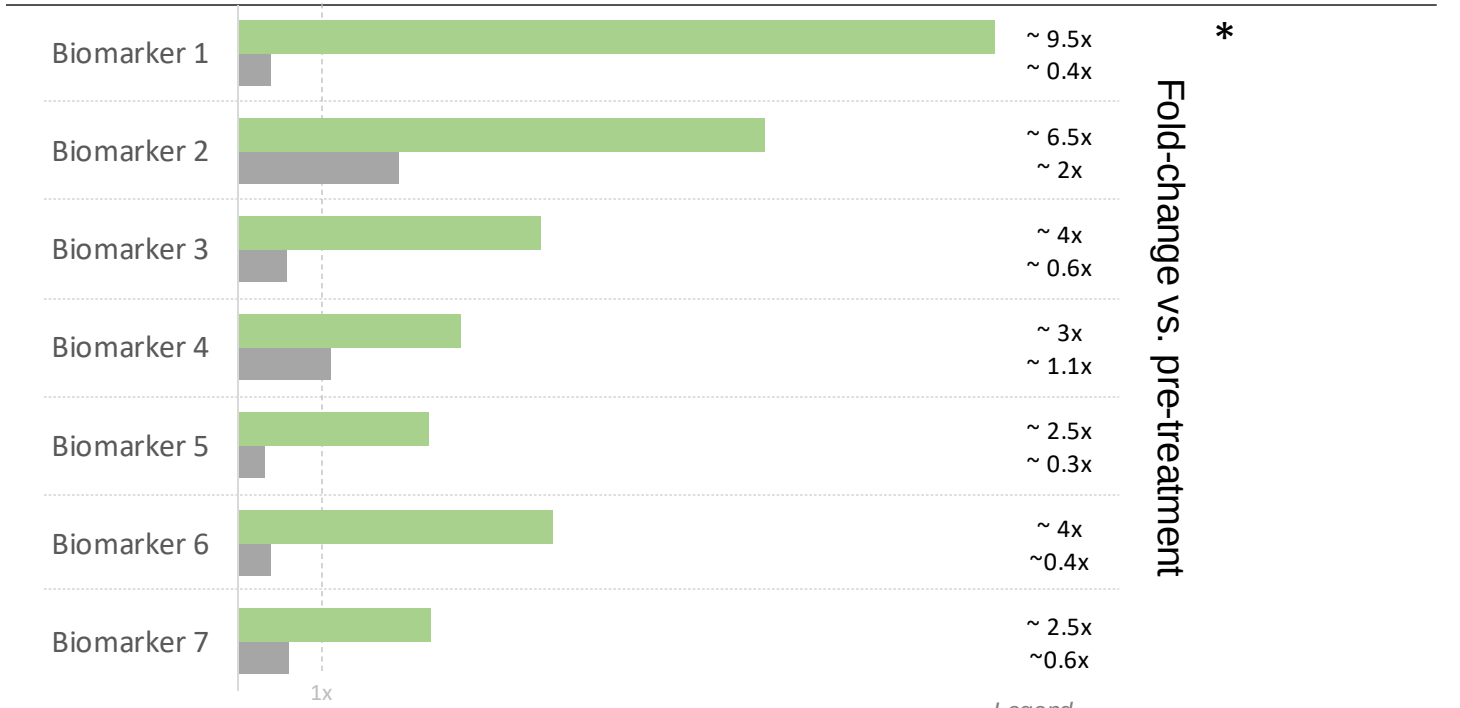
Clinical pilot study in melanoma patients shows predictive value of biomarker assay

Biomarker Assay

Panel of 7 markers
in T cell EVs that reflect ICI mediated changes in the T cells in the tumor microenvironment

- Noninvasive
- Repeatable
- Dynamic
- Wide application | Tumor agnostic, for any ICI
- Molecular window into tumor immune microenvironment

T cell EV biomarkers show distinct profile changes to ICI therapy in responders



Preliminary results based on 20 patients with melanoma stage III receiving anti-PD1 antibody ICI therapy

* All biomarkers were statistically significant in responders

A diagnostic that reliably distinguishes responders from non-responders would disrupt the treatment paradigm

The global ICI market is already a $50B market …

ICIs approved by FDA for over 20 cancer types

USD 50 B Market
(expected USD 150B by 2030)

~ 80%	**~20%**
spent on non-responders	improves patient's lives

70% of these patients have ICI-associated adverse complications

… with strong reasons for <u>HCPs</u> to use the Dx

- Minimize risk of adverse events in non-responders
  - *80% of non-responsive patients are exposed to adverse events*
- Help HCPs determine the appropriate treatment (if predictive)

… and for <u>Payers</u> to reimburse

- Reduce healthcare burden in terms of cost and resource utilization

Blavatnik Fund support will be critical for the next important stage of biomarker development

	Clinical pilot	Extended validation study		
When	**Summer – Fall 2024**	**Stage 1** *(2 months)*	**Stage 2** *(2 months)*	**Stage 3** *(8 months)*
Steps	**Pilot study of approach** 20 patients with melanoma receiving ICI therapy Cross validated for other cancer types – head and neck cancer	• **Validate clinical correlation** Study 30 patients to achieve robust statistical confidence and clinical correlation	• **Optimization of biomarker panel.** Explore additional biomarkers to improve accuracy and sensitivity (in 30 patients)	• **External validation of the optimized biomarker panel** - analyze 100 pts • **Correlate EV biomarkers to tumor immuno-histology** - analyze 20 pts
		Yale Melanoma SPORE – **258 melanoma patients** treated with ICIs with pre- and post-treatment blood samples.		
Outcomes	POC T cell EV biomarker panel distinguishes responders versus non-responders	• Validated diagnostic accuracy of EV platform	• Finalized set of biomarkers for full scale study	• Validated T cell EV profiles reflect tumor immune microenvironment • FDA pre-submission
	Completed	*$50k*	*$50k*	*$200k*
		$300k total funding		