“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

Brad Power
July 16, 2025

“These immune checkpoint blockade drugs are used very widely now, so over 40% of patients are now eligible for these therapies, meaning they have some kind of biomarker in their clinical workup, that means they are eligible to receive immune checkpoint blockade. Unfortunately, only about 20% of patients that receive these drugs actually have a durable clinical benefit from them, and this comes, oftentimes with a lot of pretty harsh side effects as well. So there's a trade-off in terms of a lack of efficacy and having a pretty substantial response baseline for the immune systems.” – Rob Kimmerling, PhD

“One of the big challenges when thinking about cancer is often this idea that within a tumor there's a lot of variability of every cell that's in that compact tumor. So a big challenge with therapies often is that a drug might only kill a few of those cells, not all the cells. For our version of testing, we take that tumor and break it down to all of its components, those single cells, those individual actors, and we're trying to test those cells to see which ones respond to therapies. That same concept of directly measuring individual cells can be applied to the immune system as well.” – Rob Kimmerling, PhD

“At its baseline, does a patient have T cells that are fit enough to actually mount a response to kill a tumor? And more specifically, are their immune cells specifically sensitive to different immune checkpoint blockade drugs? That's really the question we're trying to answer with our testing. For a patient's broad immune system, is it ready to actually respond to checkpoint blockade and mount a response to a tumor?” – Rob Kimmerling, PhD

Meeting Summary

Immune checkpoint inhibitors are transforming cancer therapy with expanding applications. These drugs help your immune system recognize and attack your cancer cells, some by blocking checkpoint proteins that inhibit your immune response to cancer. Today, more than 40% of cancer patients are eligible for these immune checkpoint blockade drugs, but fewer than 20% benefit, highlighting the need for better predictions of patient responses to these drugs. Current predictive tests leave opportunity for improvement in identifying whether you will likely benefit from this therapy. They focus on your tumor characteristics rather than your immune system readiness.

Rob Kimmerling, PhD, Co-Founder and their Chief Technical Officer at Travera, and Dennis Watson, Vice President of Business Development at Travera, are uniquely qualified to discuss ways you can personalize your immune checkpoint inhibitor treatments by predicting your likelihood of a positive response. Rob started in a lab at MIT where Travera’s unique weighing technology was developed for “functional testing”. Dennis has been working in genetics and genomics of cancer for nearly 20 years. Travera’s new immune system test is built on a novel advanced technology that analyzes the immune cells in your bloodstream to personalize treatment. It’s the first CLIA-approved test assessing baseline immune cell fitness, which can

provide insight on your immune system's readiness for activation, while also functionally measuring which of the most commonly used immune checkpoint inhibitor drugs will do the best job of activating your immune cells.

Why does knowing about your immune system health matter when you are considering immunotherapies, especially immune checkpoint inhibitors?

- Not all patients respond equally to immune checkpoint inhibitors. Currently, only about 20% of patients receiving these drugs experience a durable clinical benefit.
- Understanding your immune system's baseline fitness can help predict whether you're likely to respond to a specific immunotherapy drug.
- It can guide personalized treatment decisions, such as choosing between different checkpoint inhibitor drugs, deciding whether to combine drugs, and determining whether to continue or discontinue a particular therapy.
- It provides insights beyond traditional tumor-based biomarkers by assessing the functional capacity of your immune system to mount an effective response against cancer.
- It can help avoid unnecessary treatments with expensive drugs that are unlikely to be effective for your specific immune profile, potentially saving time, resources, and reducing side effects.
- It could help you monitor your immune system changes by taking longitudinal blood draws and measuring T-cell physical parameters like mass, volume, and density. By taking blood samples at different time points after interventions (like supplements, exercise, or lifestyle changes), you could track how these activities impact your immune cell fitness.
- Combining it with your molecular profiling and gene expression data, you can better understand the longitudinal profile of your immune system.

Who should ideally get a single cell immune system analysis of their blood?

- Melanoma patients considering immune checkpoint blockade therapy
- If your tumors are characterized by a high degree of DNA instability – microsatellite instability high (“MSI high”) – they are more likely to respond to certain immunotherapies, particularly checkpoint inhibitors like pembrolizumab. Your MSI status requires tumor tissue.
- Solid tumors that can be “MSI high” include: colon cancer, rectal cancer, esophageal cancer, gastric cancer, renal cancer, and bladder cancer.
- When you are considering multiple equally valid treatment options, such as different immunotherapy drugs,and there is no clear standard approach.
- When you want to understand your immune system's potential response to specific treatments.

How can you access this single cell immune system test? What does it cost?

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

Currently, Travera is offering the test through an Early Access program at no cost to patients. The goal is to collect real-world data while helping patients, so they're providing the test free of charge. They're particularly interested in patients with melanoma or other cancers where there are multiple immunotherapy options.

To access the test:

1. Reach out directly to Dennis Watson at dwatson@travera.com
2. The test requires a doctor's order
3. Travera will send a test kit
4. You get a blood draw
5. The sample is sent back to Travera
6. Results are returned to your doctor within about three days

How can you learn more about your immune system, immunotherapies, and tests for predicting your response to immune checkpoint inhibitors?

- Consult with your oncologist about existing biomarkers like tumor mutation burden, potential clinical trials for immune response testing, your specific cancer type and immunotherapy options.
- Explore resources to stay informed about the latest immunotherapy research, new diagnostic technologies, and personalized medicine approaches from cancer patient advocacy groups, the National Cancer Institute, academic cancer centers, and trustworthy online medical information sources.
- Consider emerging diagnostic tests like Travera's blood-based immune response test; reach out to Dennis Watson at dwatson@travera.com to discuss the test and potential applications
- See our previous discussions on blood-based tests (“liquid biopsies”), including:
    - "Liquid Biopsies" (Peter Kuhn and Stephanie Shishido) [#23]
    - “Testing Your RNA with Liquid Biopsies” (Alex Rolland) [#116]
    - “Using Predictive Biomarkers and Liquid Biopsies to Personalize Treatment for Prostate Cancer” (Andy Armstrong) [#64]
    - “The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]
    - “The Latest Tests for Personalized Cancer Care” (Tony Magliocco) [#89]
    - “Integrating Diverse Test Results for Cancer Patient Guidance” (Joe Lennerz, MD, PhD, MSc) [#142]
    - "Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

For the video recording of this conversation, please see here.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

Meeting Notes

KEYWORDS

Cancer diagnostics, immune system monitoring, immunotherapies, single cell assays, T cells, immune checkpoint blockade, tumor mutation burden, neoadjuvant therapy, clinical validation, biomarkers, patient response prediction, blood test, oncology drug spending, personalized medicine, clinical equipoise.

SPEAKERS

Rob Kimmerling (52%), Dennis Watson (29%), Brad Power (10%), Allen Morris (4%), Bill Paseman (2%), Richard Anders (2%)

CHAT CONTRIBUTORS

David Plunkett, Rick Davis, Bill Paseman, Allen Morris, Richard Anders, Ari Akerstein, Dennis Watson, Roger Royse

SUMMARY

Rob Kimmerling and Dennis Watson of Travera discussed their new diagnostic for monitoring immune system responses to immunotherapies. Travera's technology uses single-cell assays to measure T-cell activation and response to checkpoint blockade drugs, such as pembrolizumab (Keytruda). Early data from 21 melanoma patients showed an accurate predictive value (an “area under the curve” of 0.8), predicting 17 out of 21 responses. The test, currently available through a free early access program, aims to guide treatment decisions by predicting patient response to immunotherapies. Future plans include expanding the data set and exploring combinations with other drugs and targeted therapies.

OUTLINE

Introductions and Overview of Travera

- This discussion was focused on diagnostics for monitoring the immune system and predicting responses to immunotherapies.
- Travera, had its origins at MIT, with a focus on functional medicine and cancer cell testing.
- Rob Kimmerling, one of the co-founders of Travera, has a background in assay (test) development, particularly single-cell assays for cancer.

Single-Cell Assays and Immune Response

- Single-cell assays are a set of techniques used to analyze individual cells, providing insights into cellular heterogeneity and gene expression patterns that are often masked when studying cell populations as a whole. These methods have revolutionized fields like developmental biology, cancer research, and immunology by allowing researchers to examine cellular processes at the most fundamental level.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

- Single-cell assays are important in understanding cancer variability and therapy response. They can be applied to the immune system, focusing on T cells and their role in targeting tumor cells.
- Immune checkpoint blockade drugs have a role in reactivating the immune system to fight tumors.
- Single-cell assays measure the physical parameters of T cells to gauge their functional response.

Travera’s Technology for Weighing Single Cells

- The test uses a suspended microchannel resonator to measure cell mass and density.
- The core platform can measure cell mass, volume, density, and shape.
- It provides a functional readout of a patient's immune cells.

Validation and Clinical Applications

- The early data from a cohort of 50 patients highlights the variability in T cell activation and response to immune checkpoint blockade drugs.
- Collaboration with MGH, focusing on melanoma patients undergoing neoadjuvant therapy and the correlation between blood test results and clinical outcomes.
- Early validation data from 21 melanoma patients shows the ability to predict response to immune checkpoint blockade using blood samples.
- The area under the curve (AUC) metric compares the performance of their biomarker with tumor mutation burden (TMB).
- There is potential to pair blood test results with existing tumor biomarkers to improve prediction accuracy.
- Potential applications for the test include advanced disease management, drug-specific functional readouts, and guiding drug combination strategies.

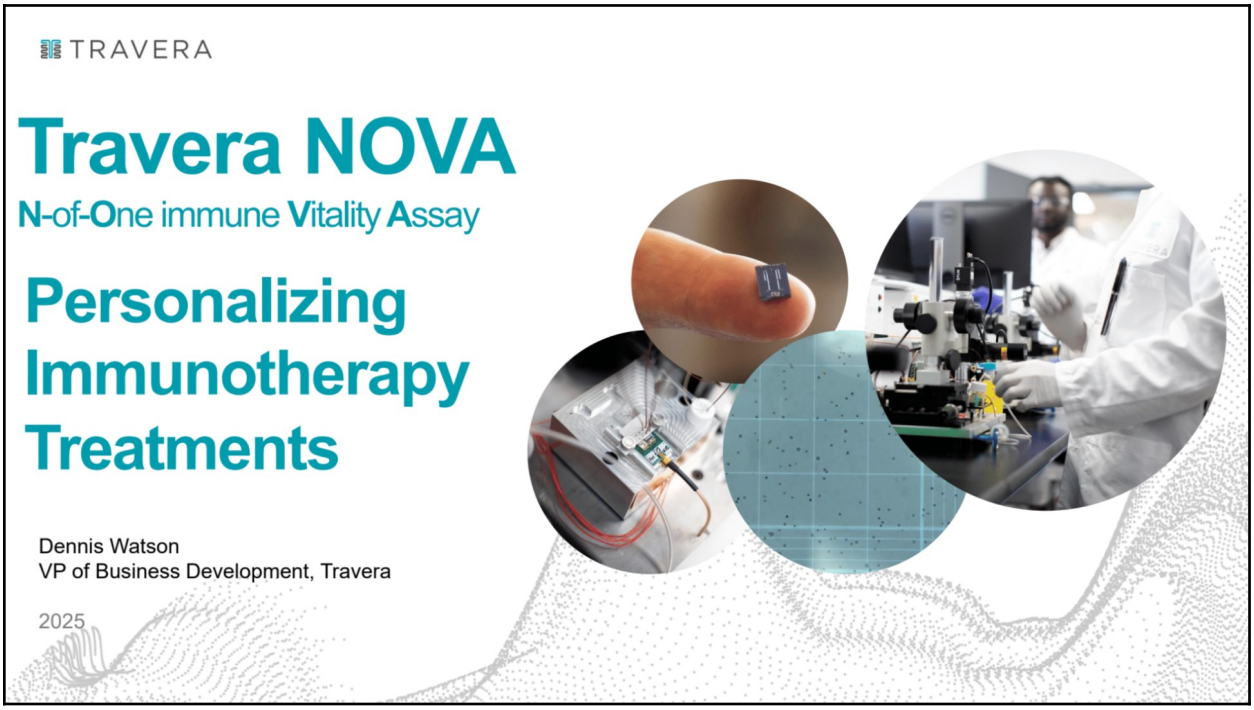
Future Directions

- Travera is running the test through an Early Access program, offering it at no cost to patients and collecting real-world data.
- The test has the potential to be used in various cancer types and the importance of building a larger data set to improve accuracy.
- There is a need for continued collaboration and data collection to refine the test and seek reimbursement.
- There is potential for isolating specific T-cell subsets and ongoing research to optimize the assay.
- The test can predict response to drug combinations.
- Functional tests require live cancer cells.
- The test can be used in non-cancer applications, such as autoimmune disease and transplant monitoring.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

TRANSCRIPT

Brad Power
This is the Cancer Patient Lab, and this is our weekly webinar.



Today, we're honored to have Rob Kimmerling and Dennis Watson of Travera with us. They've been working on diagnostics in an important new area, which is monitoring the immune system and doing things to describe whether people are going to be likely responders or responding, or something about the health of the immune system. Immunotherapies are an expanding area of cancer treatments, so knowing both who should get them and whether they're responding is an increasingly important area. I'm really looking forward to hearing about their new diagnostic and any help they may be providing cancer patients and caregivers in knowing whether immunotherapies are right for them.

This is, of course, for information purposes only. This is not medical advice. We try to arm our patients and caregivers in our community with information that they can take to their medical team.

We are a nonprofit 501(c)(3), and we depend on the kindness of donors who help fund our operations so we can bring you webinars like this. It's easy to donate. You can do so on our website, where there's a Donate button.

Dennis Watson 1:59
I'm going to start us off real quick, and then I'll turn it over to Rob, just with a couple of sort of quick, quick notes from our side.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

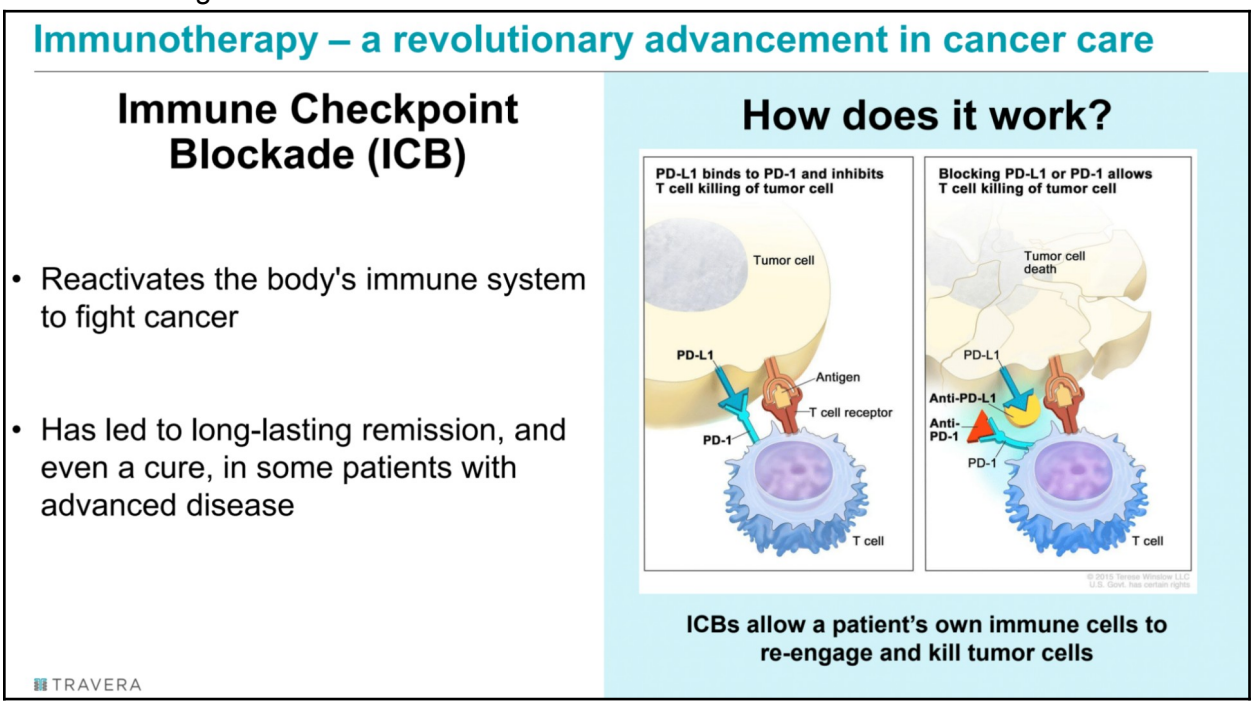
For those of you that are unfamiliar with us, Travera spun out of MIT. Rob will introduce himself in a minute, but he is one of the technical co-founders of the company. I've been here for a little over three years myself. It's a functional medicine company that started in cancer cell testing, and we have expanded our platform and technology into what we're going to introduce today. Rob's going to go through the science, the assay, and a lot of those descriptions. At the end, I'm going to close with just a couple of quick slides, outlining some potential utility applications for where the test is at this time, and what drugs we offer, how a patient or a provider could gain access to the test, and just the logistics of all of that will look like.

Rob Kimmerling 3:25
As Dennis mentioned, I'm one of the co-founders and the CTO of Travera. My background is pretty heavily focused in assay development, single cell assay development, especially for cancer. A lot of the work we've been doing at Travera has focused on exactly that. How can we use single cell assays to help guide therapy selection? And recently, we've been working quite a bit on applying this to the immune system as well, and getting a sense of whether or not we can capture the functional response of a patient's immune system and use that to inform their therapy selection.

A bit more to dive into the actual therapy space.

Brad Power 4:08
Rob, could you just explain single cell assays? Because I don't think that “single cell" is necessarily something everybody understands.

Rob Kimmerling 4:17



“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

One of the big challenges when thinking about cancer is often this idea that within a tumor there's a lot of variability of every cell that's in that compact tumor. So a big challenge with therapies often is that a drug might only kill a few of those cells, not all the cells. For our version of testing, we take that tumor and break it down to all of its components, those single cells, those individual actors, and we're trying to test those cells to see which ones respond to therapies. That same concept of directly measuring individual cells can be applied to the immune system as well.

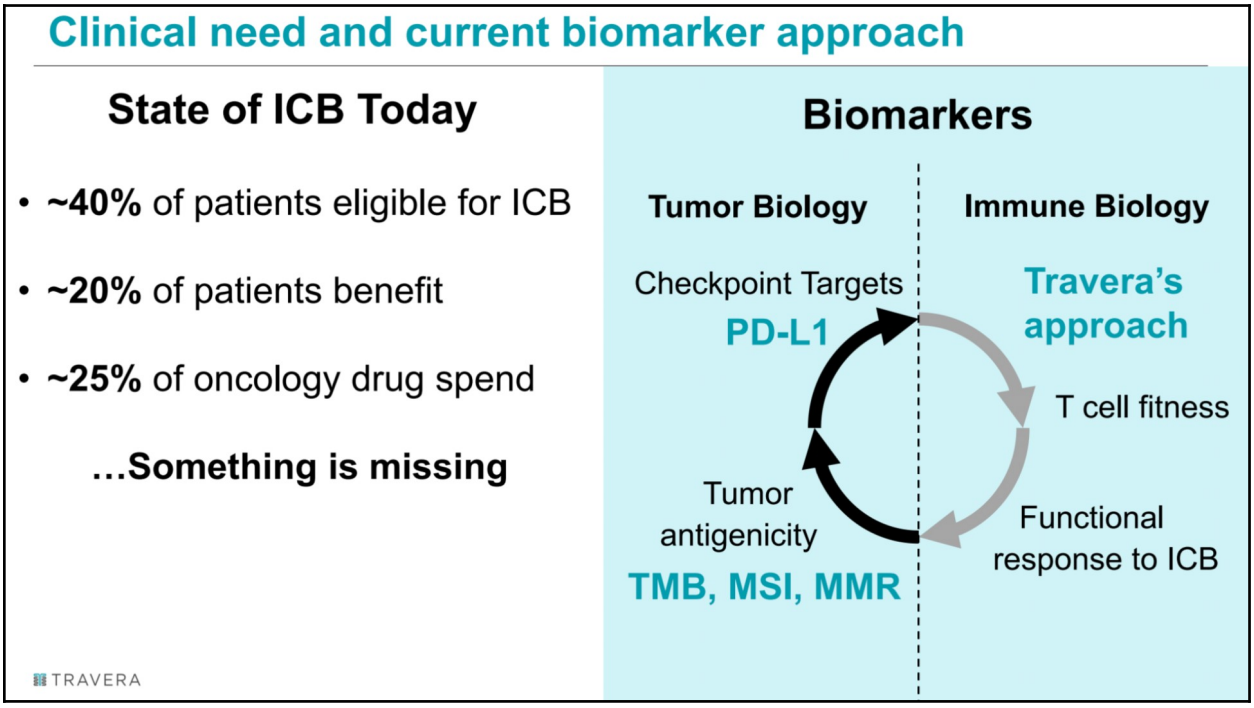
For what we're going to be talking about today, this is primarily thinking about a blood draw. So from a patient's blood you can isolate these single cells. These are things like T cells or B cells or monocytes, and all of these individual components kind of give the full activity of what a patient's immune system can perform. So when I'm talking about single cell assays, in this context, we're really talking about T cells most of the time. These are the cells that within a body can target cells that are infected by a virus, for example, or they can target tumor cells, and these T cells perform the killing.

That's a good lead into the background on the therapy space when we're talking about immunotherapy here. What we're really referring to primarily are immune checkpoint blockade drugs. So these are drugs that have really come around in the last decade or so into really wide clinical usage, and essentially, at their core, what they are capable of doing are reactivating a patient's own immune system to fight a tumor. And in some contexts, these drugs have been really transformative.

Melanoma is an example where patients with very late stage disease have had curative readouts with these kinds of treatments. Just to take a quick detour into how they work, this at a high level, what often happens is a patient’s tumor will have “checkpoint” signals, which are effectively signals expressed on the surface of a tumor that tells the patient's immune cells to effectively ignore the tumor. These are the tumor's way of protecting itself from a patient's immune system. This is problematic because the patient can no longer mount an effective immune response and kill off that tumor themselves. So these checkpoint blockade drugs are doing if they're targeting that checkpoint signal. They're antibodies that effectively turn off a tumor's ability to block T cells. As a result, by targeting that axis, you're able to have T cells that, once again, can recognize a patient's tumor. These cells can grow. They can actually start to kill the tumor again.

Effectively, what we are trying to get a sense of is, how can we read out with a high level of certainty, what is happening with these T cells? And that's really what we've been focusing on.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]



So as a sort of baseline context for this: These immune checkpoint blockade drugs are used very widely now, so over 40% of patients are now eligible for these therapies, meaning they have some kind of biomarker in their clinical workup, that means they are eligible to receive immune checkpoint blockade. Unfortunately, only about 20% of patients that receive these drugs actually have a durable clinical benefit from them, and this comes, oftentimes with a lot of pretty harsh side effects as well. So there's a trade-off in terms of a lack of efficacy and having a pretty substantial response baseline for the immune systems.

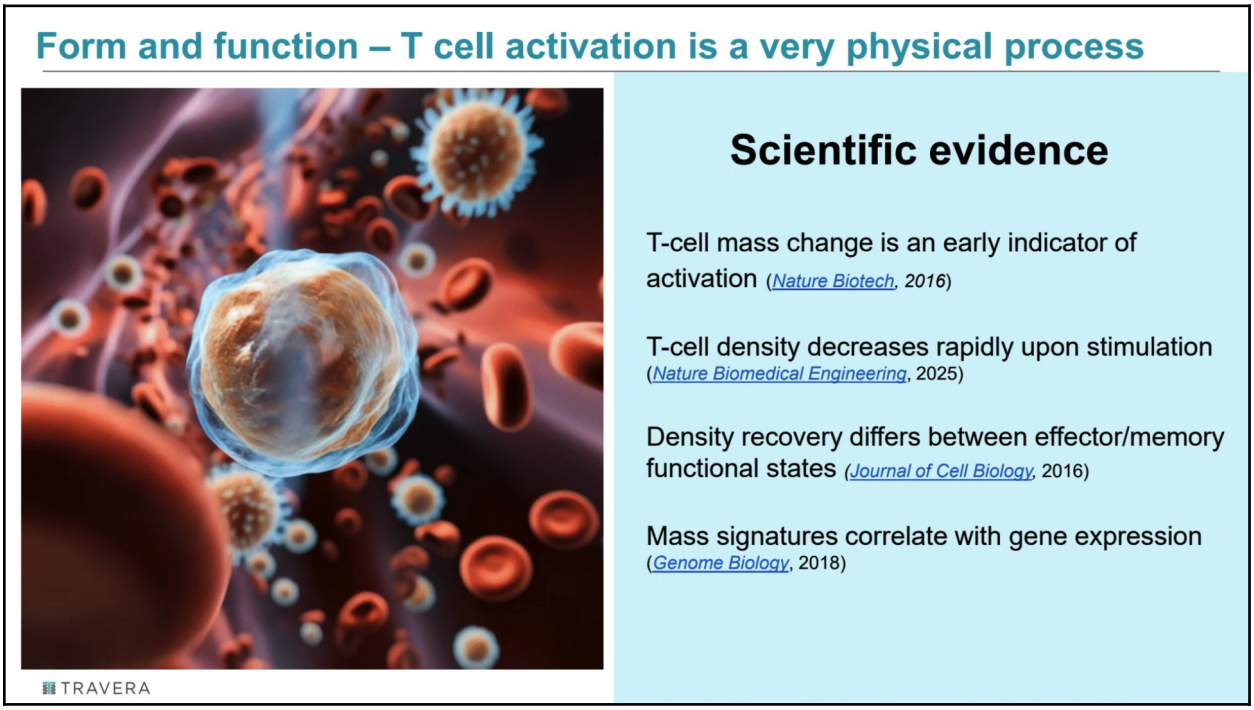
Finally, this is a really big portion of oncology drug spending. This is something where almost a quarter of all drug spending is going towards these checkpoint blockade drugs for managing cancer.

Clearly, there's a pretty big mismatch between the number of patients that are getting these, the number of patients that are benefiting, and the patients that are unfortunately seeing side effects without having any real potential improvement of the cancer. For those reasons, there's been a really big focus on developing biomarkers to help predict which patients will respond best to these drugs.

There are two key pieces to what these biomarkers are focusing on. Currently, the largest focus is on the tumor biology side. So in order for a patient's immune system to actually respond to a tumor, it has to be sort of recognized as a foreign body, the same way you recognize a viral infection or bacterial infection. A tumor has to present some kind of antigen or signal that is not actually supposed to be there. And so a current readout for that are things like the mutation status of a tumor, things like tumor mutation burden and MSI status. These give an indication

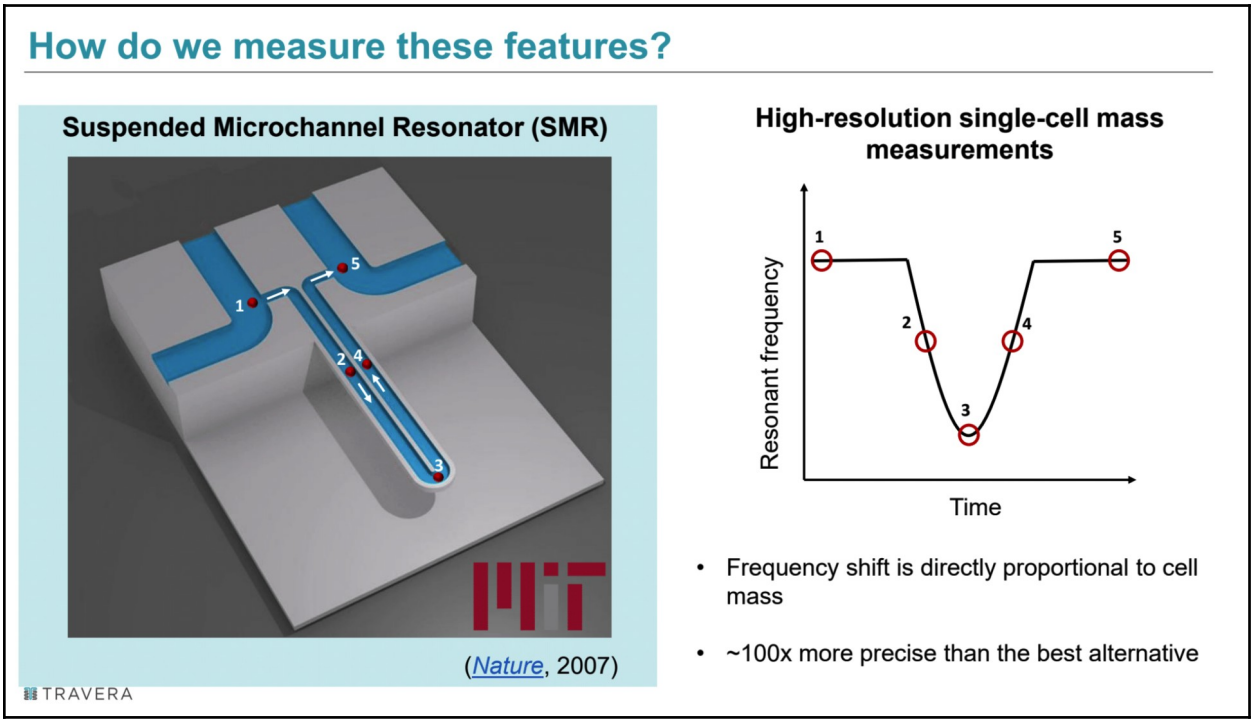
about how unstable that tumor's genome is, and these are an estimate of how well that tumor will present itself as being foreign to the patient's immune system. Similarly, within the tumor biology, are these direct checkpoint targets. So PDL-1 is one example of protein that's expressed on tumor cells that tells the immune system to turn off. And if a tumor is expressing a higher amount of that molecule, it's a good predictor of whether or not that patient might respond. So these are the current offerings that are clinically used pretty commonly. But the other side of the coin for having an immune response to a tumor is the patient's immune system.

At its baseline, does a patient have T cells that are fit enough to actually mount a response to kill a tumor? And more specifically, are their immune cells specifically sensitive to different immune checkpoint blockade drugs? That's really the question we're trying to answer with our testing, is for a patient's broad immune system, is it ready to actually respond to checkpoint blockade and mount a response to a tumor?



The way we think about this is very physically. The reason we do that is, it turns out for T cells, there's a pretty tight linkage between their form and function. So when you think about a T cell that's in its naive state, this is before it's activated by anything like a tumor or infection, it's this really small and tight, almost spore-like cell. These are really dense, really tightly packed cells. As soon as those cells become activated, when they see a signal, like a tumor, like an infection, the first thing they do is they take in a bunch of water, and those cells have their volume increase very dramatically and slightly after that, a few hours after that, it cells start to do things like turn on protein production, and as a result, their mass starts to increase as well. And so what we found, based on some of the literature back when we were at MIT, we were first doing this research is these physical parameters are really good readouts for biologically, what's

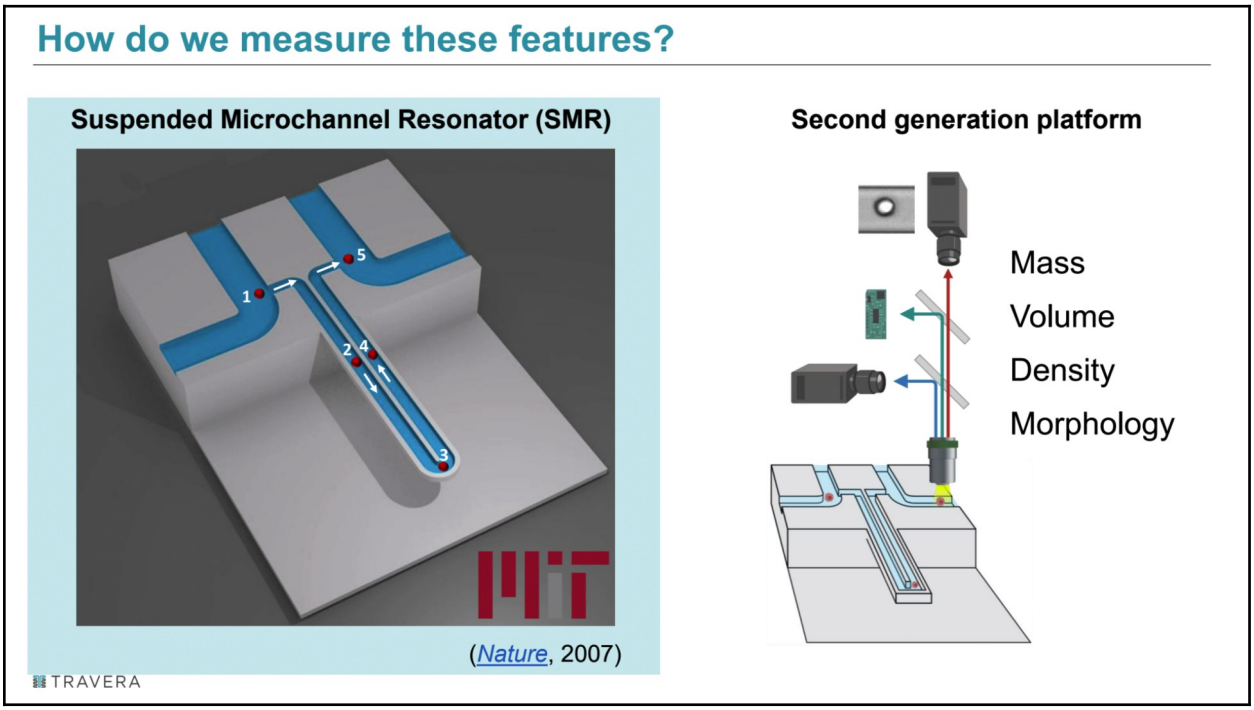
happening in those immune cells. So for example, when a T cell is exposed to stimulation, its mass increases very quickly. We know that the density drops very quickly. And we also know that those changes in those physical parameters correspond to the function of those immune cells as well. So for example, T cells often have two different roles. Some are meant to clear the active threat. These are kind of the effector T cells that are actually doing the killing. There's other T cells that are there for the reserves. In the case there's another event they have to react to in the future. These are the memory T cells. Both of those subsets of cells have very distinct physical characteristics associated and this is something, again, we have quite a bit of research back in the MIT lab to really flesh out what these mean, these physical parameters mean, but that kind of gets to how we measure these so these physical measurements are quite useful for characterizing biology, but how do we actually read them out? And so the core platform that we use is something called a suspended micro channel resonator at a very high level.



This is a very sensitive scale. So what we can do is we can actually weigh individual cells that are coming through this sensor in terms of how it actually works. This is what's called a microfluidic device, essentially a very, very small scale fluidic circuit that has a little diving board feature in there. And so this diving board is vibrating constantly, and then as a cell passes through this fluidic channel across that diving board, the additional weight of that cell changes the frequency with which that diving board is oscillating. So the concept here is very similar to when you're sort of diving off a diving board, when you're standing at the end, it kind of goes pretty slow, and as soon as you dive off, because it's losing your mass, it starts to vibrate very quickly. That same physical principle is at work here, except on a much, much smaller scale. And so what we're able to do is we can track that change in frequency, and as a result, we can back out the weight of each one of those individual cells that's passing through the device. This

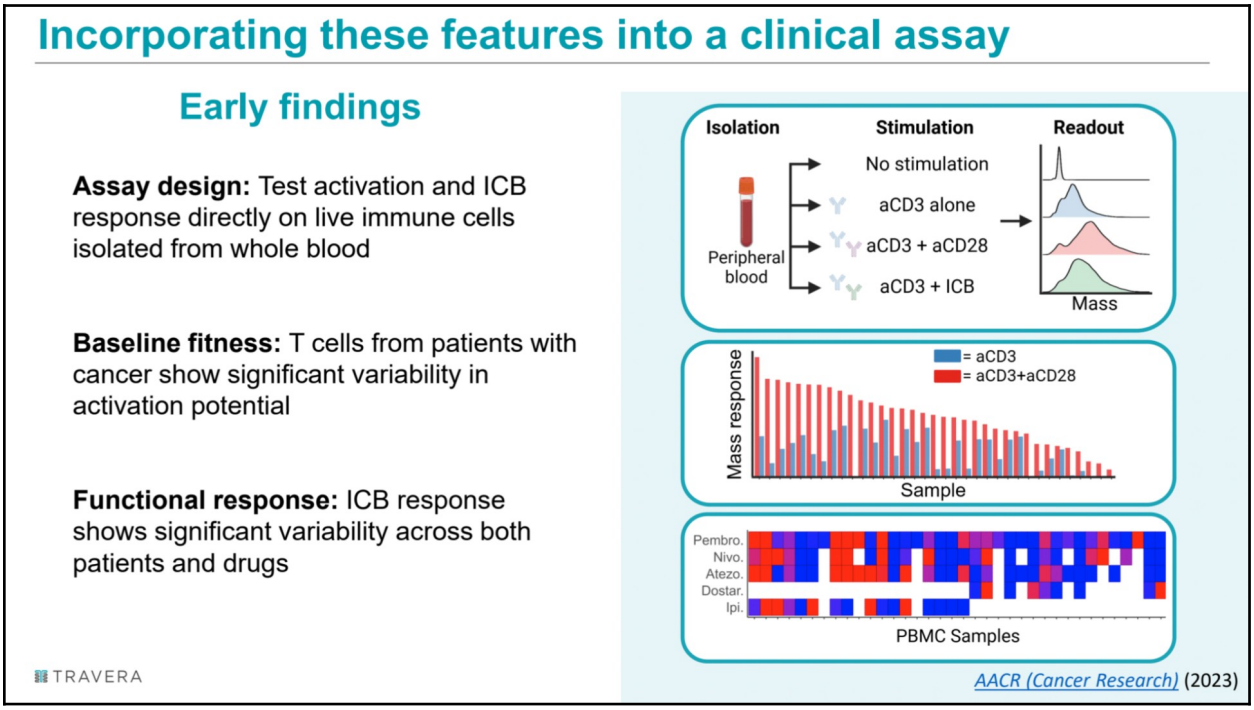
turns out to be about 100 times more precise than other methods of looking at cell size, things like imaging or or colder counter, which is more of an electrical readout of cell sizing.

Rob Kimmerling 13:23



What we've also been working on is: how can we take this sort of core readout of cell mass and start to get additional information about these other physical parameters that we're interested in measuring? I mentioned we also want to look at the density of these cells, the volume of these cells. So in addition to this kind of core mass readout sensor, what we've been building at the company is a way to layer in things like imaging. How can we take pictures of each of these cells as they're going through, and layer on additional information that captures the activation state and the functional state of these immune cells. So at the end of the day, what we end up with is this set of different biophysical properties, including the mass, the volume, the density, and the shape and texture, the morphology of these single cells. That's really what we are using to get a functional readout of a patient's immune cells. So the next step for us was with this kind of core technology in hand, was how can we use these physical readouts of patients immune cells to guide how they might respond to something like a checkpoint blockade drug?

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]



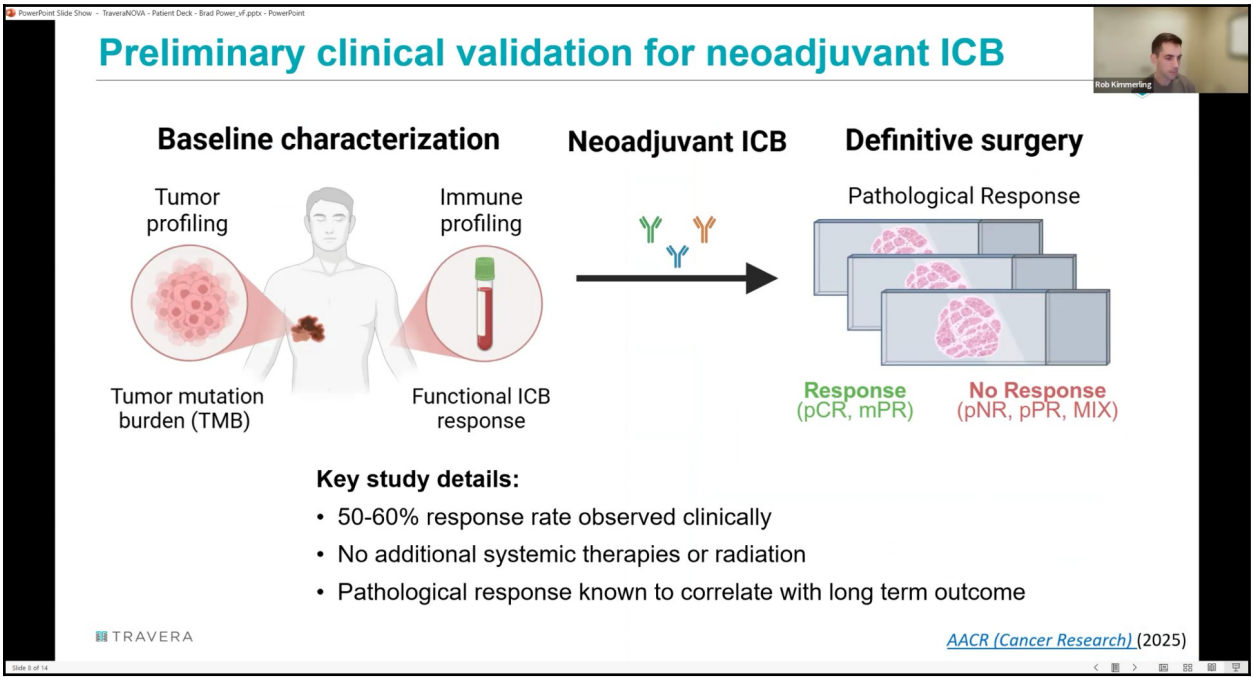
A few years back, we presented our core assay structure. This is the design of the test that we're actually running from a blood sample. What we're able to do is we can get a sample of peripheral blood from a patient. We isolate all of the immune cells from that blood, and then we test a few different stimulation conditions on those cells. We're getting a sense of how strongly these cells activate just in response. Stimulation, but also we're trying to measure how much that activation improves if we also treat those cells with an immune checkpoint drug. And so early on, what we're able to do is for a cohort of about 50 patients or so, we found that at baseline, there's quite a bit of variability in how well a patient's immune cells activate. So what we're looking at is, that's the second panel down here. We're looking at across individual patients, how strongly do their T cells activate in response to stimulation. And we're looking at the direct quantitative physical change in those cells. To really read this out. So what this indicated is that there does seem to be quite a bit of just baseline fitness difference for patients' immune systems. And then the other piece that we're able to get from this early cohort is that at an individual patient level, there's also quite a bit of variability in response to these immune checkpoint blockade drugs. So for some patients, when you activate those cells in the presence of something like pembrolizumab, which is an example of these ICB drugs, those cells activate much more strongly, whereas for other drugs, or for other patients, I should say, pembrolizumab doesn't really have any meaningful activation for for those patients.

Bill Paseman 16:17
You're describing basically your test as of a couple of years ago. What I'm confused about is, as I recall, your trays wound up requiring, in essence, a tumor to go on and function. But the way you're describing it here, in terms of T cell activation of the rest of it, seems like it could have been done with a blood test?

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

Rob Kimmerling 16:43
You're absolutely right that this portion is done with a blood test. So one thing that's very different about this assay versus our old assay is our old assay was looking primarily at tumor cells, like you mentioned. So that was looking at something like a biopsy or section tissue and directly tracking the effect of cytotoxic drugs on those tumor cells. This is a new assay that's focused entirely on blood, and what we're looking at is just immune cell function and using that as a way to predict whether or not a patient will respond to these ICB drugs. So you're not misinterpreting. You're absolutely right that this only requires a blood draw for this burden assay.

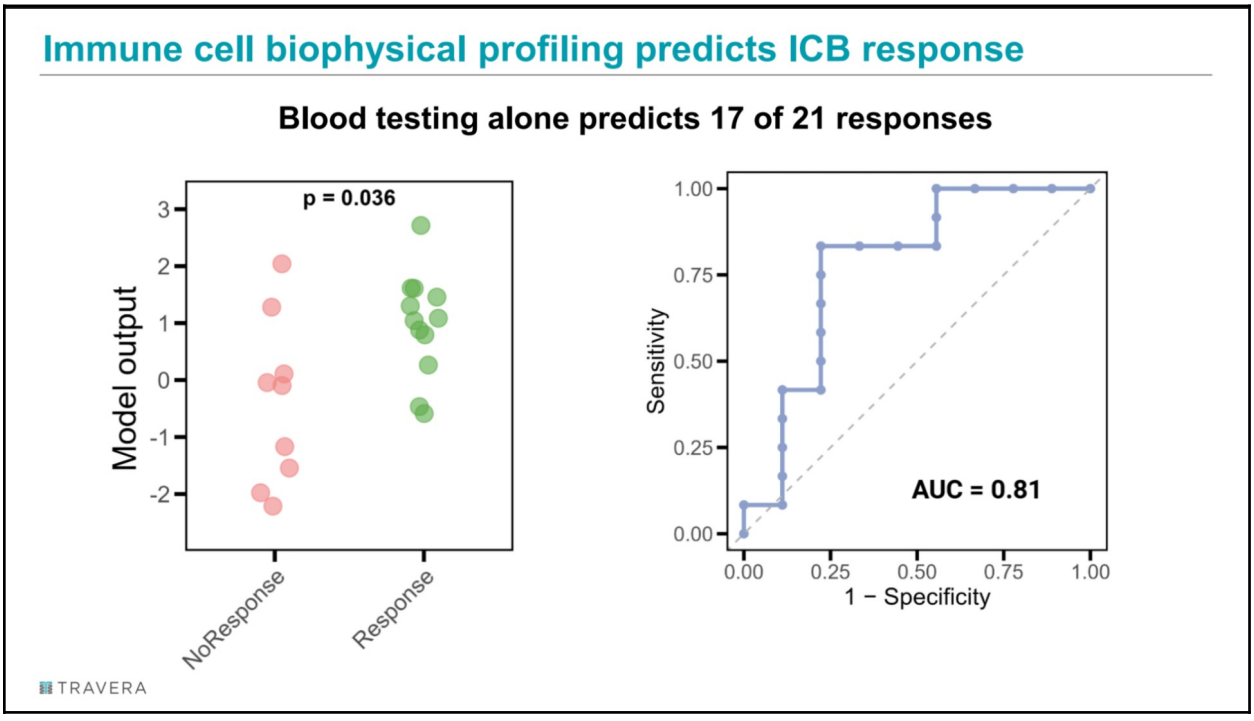
So in addition to the variability in activation, I mentioned there's also variability in response to these individual drugs with patients. So that was a really interesting takeaway for this early set of patients, was that across 50 there's there's differences among patients, but really the key question is whether or not those differences are meaningful. So when we measure a different immune response from a patient, does that actually correspond to how they would respond clinically?



That's a question we've been able to get at more recently with the collaboration we have with Genevieve Boland's group at MGH, and they are focusing primarily on melanoma. These are patients that are eligible for surgery, but prior to them receiving their surgery, they undergo a course of immune checkpoint blockade therapies called neoadjuvant therapy.

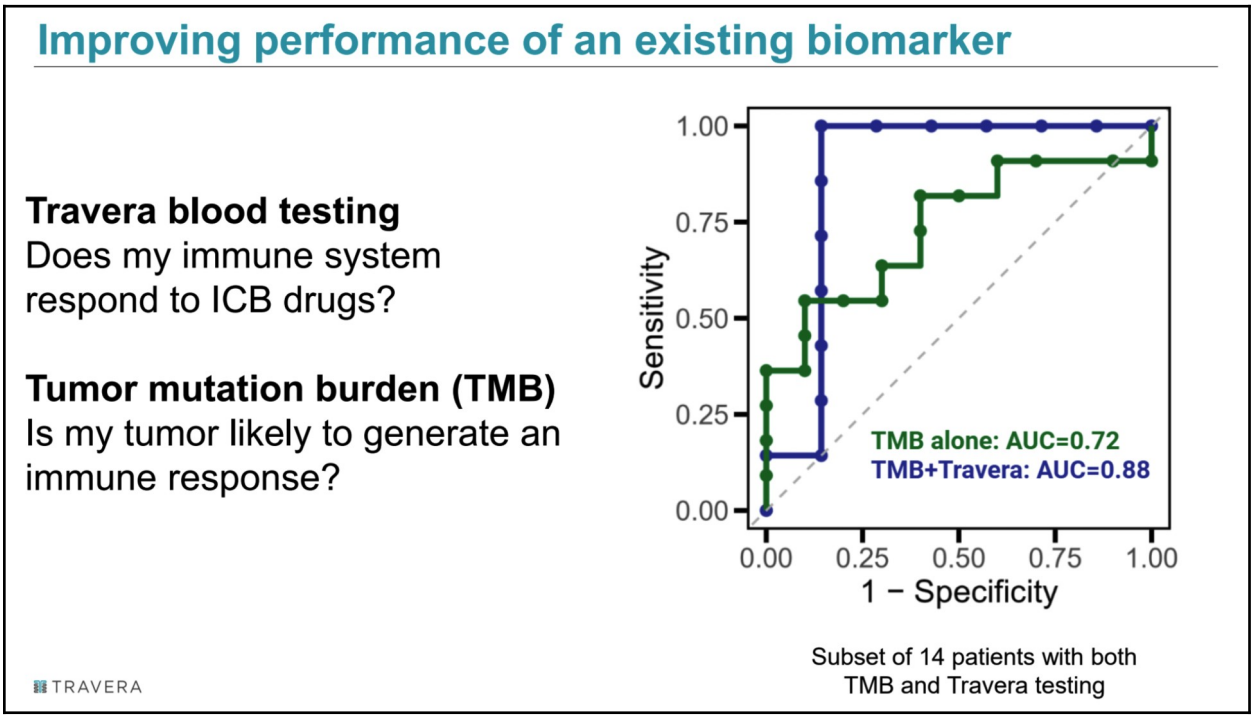
The main idea here is to shrink the tumor in advance of that surgery. And what's really helpful about this context for us is that we're able to collect both tumor profiling and immune profiling

prior to those patients receiving therapy. So the idea here is that at baseline, before patients get the immune checkpoint blockade, we can take a blood draw and we can look at whether or not we see a functional response to these ICB drugs and how well that that patient's immune system is performing. And then they undergo their neoadjuvant treatment. This is about six weeks of therapy that they receive, and then at that point, they undergo definitive surgery. So this would be them having their what's remaining of their tumor, hopefully fully removed. And then at the time of surgery, the pathologists are actually able to determine whether or not these patients responded to that course of truth. And so essentially, what they're doing is just the fraction of tumor cells that have been killed within the sample that's coming out, and from that readout, get a sense of whether or not the patient, in fact, was responsive or non responsive, to the checkpoint blockade drug. What's helpful here, about a validation context is that unfortunately, only about 50 to 60% of patients will respond to this neoadjuvant ICB. So what that means is that we are expecting to have both positive and negative predictions that we're trying to find from this blood draw. The other piece that is relevant here is that these patients are only receiving the checkpoint blockade therapy during that new ladder window. So one thing that is tricky in other clinical contexts is when a patient is receiving both checkpoint blockade as well as radiation or systemic chemotherapy, it's really difficult to back out what the effect of just the ICB treatment was in the context of all these other therapies, whereas for this melanoma context, we have a pretty clean way to read out our test versus a clinical outcome.



And so in looking at the early data, what we found is that for the first 21 patients that were through now, in 17 out of these 21 patients, we were able to predict their response to immune checkpoint blockade using just the blood draw. So effectively, what we're doing is, prior to the patient receiving therapy, we take a blood sample, we measure the response of those T cells to

the immune checkpoint blockade that patient receives, and then we correlate that with how well that patient responded clinically, based on the pathological response. And what we can see is that when doing this combined measurement of the physical readout, there's a significant difference between the patients that responded and that did not respond. And what's interesting here is it seems like we're able to pick out both of these so we are able to predict both responders and non responders, which is quite helpful, something that is very relevant for a sort of clinical biomarker framework. Another way to look at this kind of data is called the area under the curve. This is essentially getting a readout of how much better than random your biomarker is performing. So this AUC read out for context, something like tumor mutation burden, which is kind of the gold standard of predictive biomarkers, especially for melanoma, has a clinical AUC value of about point seven, and one is perfect. Point five is effectively a coin toss and not a very good biomarker. So TMB is right around point seven. And for us, the blood readout as of now is an AUC right around point eight, which, again, is a standalone biomarker, is very valuable. It's something that is performing quite well compared to TMV. But from our perspective, I don't think we view this as the most valuable piece being a standalone biomarker. We do think that the blood test is really capturing immune function, the patient's immune fitness, but it does miss some of that tumor detail I mentioned earlier, and doesn't think about mutation burden. Can't capture whether or not a patient will have sort of a signal for the immune system to respond to.



The next piece we tried to look at is: how can we take this blood test and pair it with existing biomarkers that are really more focused on the tumor? For melanoma, this is an example where there's kind of two questions that can be answered with the biomarkers. The first one from the blood testing is, does my immune system actually respond to ICB drugs? For my T cells, do

they become more strongly activated if I activate them in the presence of these different ICB drugs?

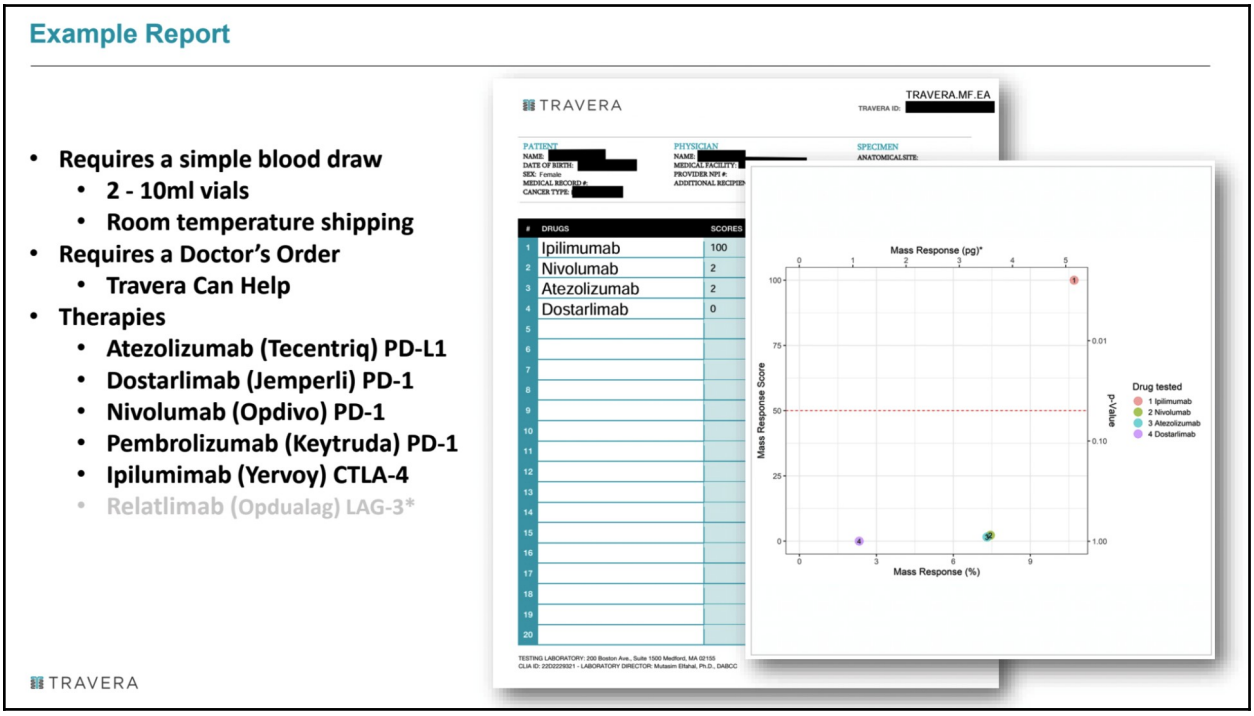
But the second question is whether that tumor is likely to generate an immune response. This is really the core focus of the existing tumor mutation burden readout. The theory there is that when a tumor has a higher mutational burden, is more likely to generate these kind of dysfunctioning proteins that look different to the patient's immune system, and as a result, can then mount a response against those so what we did is for this first cohort of patients, there was a subset of 14 of them that had both our blood testing performed as well as tumor mutation burden read out. And what we found is that TMB alone kind of performed similarly to how we would expect it to based on the clinical results at large, was an area under the curve around point seven. There's only about eight out of those 14 cases that were predicted with TMB alone. But if you take the TMB data and you pair it with the functional blood measurement for each one of those patients that combined, biomarker now has an AUC of about point eight, eight. And in this case, I was able to predict 13 of those 14 cases. So for us, this is still early data. We're really trying to build this out now to get more and more of these cases and examples here. But at a high level, the takeaway is that when we pair a functional readout from blood with these more tumor specific markers, it appears we're able to perform a little bit better for predicting patient response.

Brad Power 24:05
We know that you're getting your data from a blood draw. Is the tumor mutational burden also from a blood draw? Or is that from histopathology, some kind of tissue sample, or how's that done?

Rob Kimmerling 24:21
For this cohort, it was from a tissue sample. It was from a biopsy of the melanoma earlier on, I will say that we are speaking with some potential collaborators that also get TMB from blood. So there's potentially an appealing kind of biomarker that could be developed there where you're getting TMB from blood, as well as the immune marker. But for everything we're showing here, the TMB was coming from the tumor measurement. So at a high level, this is the main piece of excitement for us, is that it appears we have a differentiating biomarker to help make the decision for whether or not a patient will respond to ICP. And so that was really the COVID. Four of us are now launching this in our CLIA lab and starting a registry study that allows us to collect more and more validation data and work directly with patients and oncologists to really refine the assay and collect more evidence for it. So with that, I'll pass it off to Dennis. We can really go through what that looks like, how we can actually measure these samples in our lab.

Brad Power 25:20

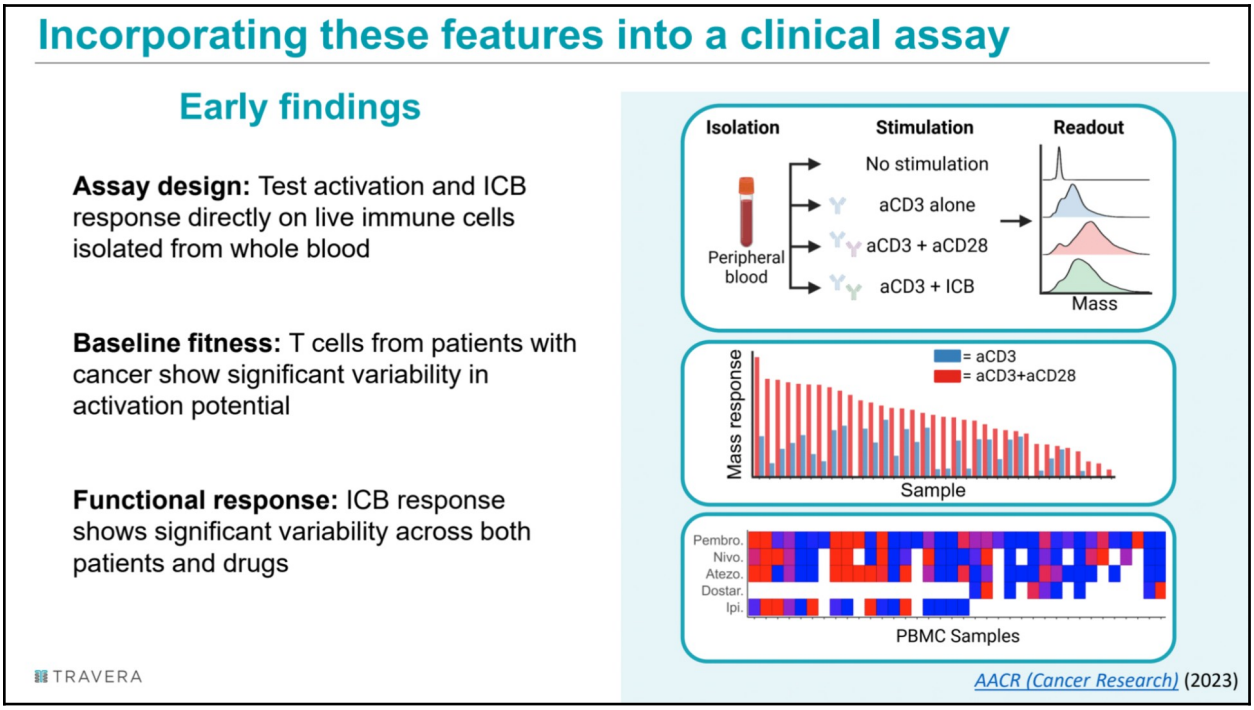
“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]



Keytruda, or pembrolizumab, is like a $10 billion drug, as you pointed out. It's a huge thing for Merck, and so if you come up with a companion diagnostic that basically would say this patient is not going to respond to Keytruda, go find something else and don't spend whatever it is, $20,000 a dose, some exorbitant amount of money on Keytruda, because it's only 40% effective. And in this patient, it's even less. It's like 10% likely to be effective. Are you going to get pushback from Merck and what's going to happen when you start to have a companion diagnostic that starts doing what's best for patients but may not be best for the drug company?

Rob Kimmerling 26:05
That is a great observation. I think with Merck, you're probably right, that would be their takeaway. But I think that question, even for oncologists, is often a hard one, because if we have a test that says a patient won't respond to pembro, that's not necessarily useful, because that data would have to be bulletproof to prevent an oncologist from using that as sort of a tool they have to treat. So for us, we very much think about the forward looking version of this assay is not just the same whether or not a patient will respond to pembro, for example, it's among a panel of different choices of checkpoint blockade drugs which is most functionally effective for that patient.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]



That's why I'm bringing this this slide back up here is another piece we found from a lot of our early data, is that when you test a patient's blood, what very often happens is they'll have a really strong response to one checkpoint blockade drug, but not to a different checkpoint blockade drug. So moving beyond this idea of whether or not a patient might respond to pembro, there's a question of whether or not a patient would be better served by going on IPI and nivo, for example, which is a combination of two slightly different drugs. We view the real clinical value of being able to separate those decision-making points, rather than just purely a prognostic readout of will a patient respond to pembro, which we would completely agree with you, as limitations and sort of how well it can serve patients.

Brad Power 27:27
To play that a bit further, for staying with melanoma, other than immune checkpoint blockade, what are some of the other treatment options that might be on the menu of that patient? So if they are considering a number of options, what else might be on the list, and then, therefore, might move up the queue based on your test?

Rob Kimmerling 27:46
So often, what will happen for melanoma? There are some systemic therapies that are kind of linked to the genomic readout of the tumor. So these are more of the just targeted therapies. There's also for later stage patients, tumor infiltrating lymphocytes as a therapy option for melanomas, this is effectively different than checkpoint blockade. This is where a patient's immune cells are actually removed directly from their tumor. They're grown outside of the body, and they're put back in to go back and sort of fight what's left. And that question as in terms of how things change in order of priority, I think is one that is really interesting when thinking about

this kind of test, because one thing we've gotten a lot of feedback on is often what will happen is a patient will receive these kinds of checkpoint drugs, which are doing quite a bit of damage to the immune system, sort of by design, they're sort of turning the immune cells on and having them Get to a really, really active state, but that might not be best serving the patient that eventually wants to have till therapy. And so there's kind of a decision point to be made as to whether or not these infiltrating lymphocytes are healthier if the patient doesn't receive a very long course of these checkpoint blockade drugs, that might not be very effective. So I think that's something we still need more data on to see how we do that ordering. But there's a pretty clear set of clinical questions that can be in addition.

Dennis Watson 29:07
I would just add one of the conversations we had with a breast cancer oncologist, for example, similar to the comment Rob was making a moment ago. If your test says that the patient's immune system is not fit enough to likely respond to pembrolizumab, I'm not going to not give it. I'm going to add something to it, like Rob said, I'm going to give them a CTLA4, or a LAG-3, one of these other drugs that might help recover that immune response to give us a higher likelihood that the patient's going to respond. And those are drugs that we can also test on this platform, those other classes of drugs outside of just the PDL once. So you know, there's some other added value that we can bring there too.

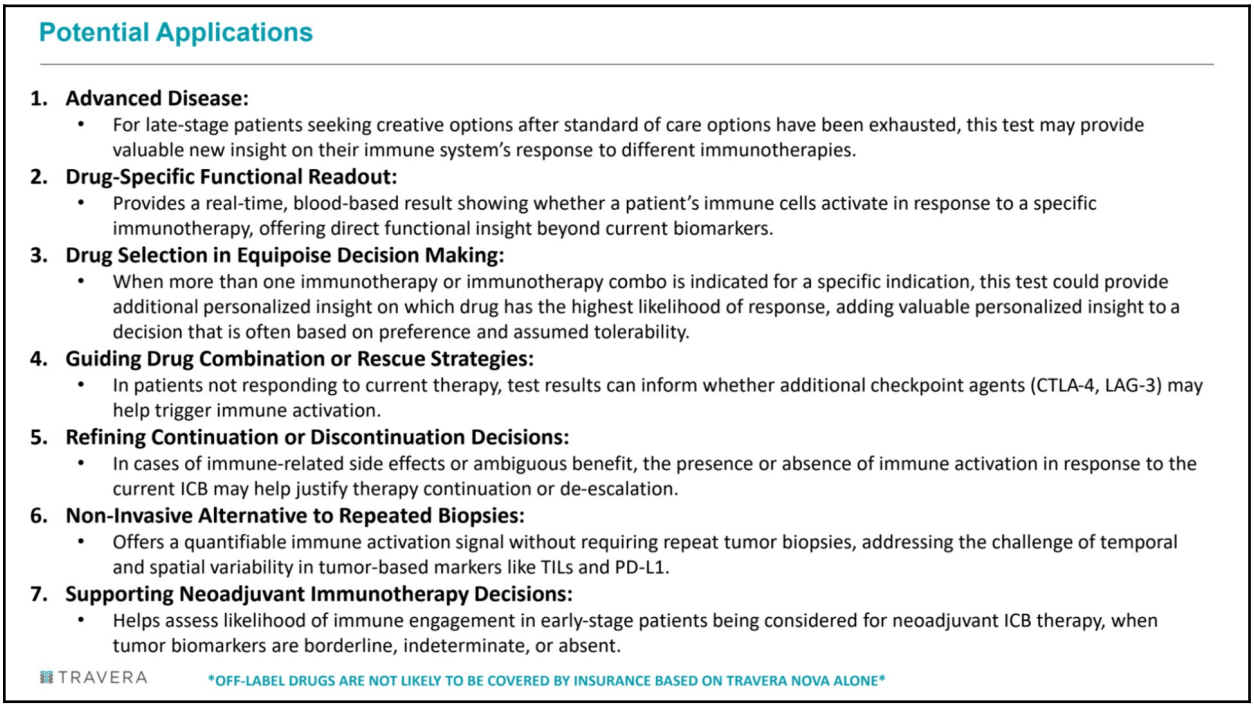
Brad Power 29:57
Can you test drug combinations? Along the lines of what you're saying, if Keytruda or pembrolizumab as a single doesn't work, let's say we think we're going to do a drug combination with something else, a targeted therapy. Can you test a targeted therapy plus, or can you make inferences about targeted therapy plus pembrolizumab?

Rob Kimmerling 30:22
So for us, we've had some interesting cases where we could run both versions of our assay. We can run both the tumor testing as well as the immune cell testing, and I think those are right now. Those are still run as kind of independent testing profiles where we're looking at the tumor cell response to the targeted therapy and then the immune cell response to the checkpoint blockade drugs. So those combinations are a bit difficult to do in the same assay, but interpreting them are still at the single therapy level quite helpful to have both of those assays from Enviro,

Dennis Watson 30:52
That would require cancer cells, though, from a fresh biopsy or malignant fluid collection. We're not able to do the typical cancer drugs, targeted, inhibitors, cytotoxic, etc., from a blood draw. We still do require live cancer cells for those, and we can't get enough live cancer cells from a liquid biopsy at this time.

Rob, why don't you jump down to my slide? I think I'll hit on one or two things here that might address some of the questions that are coming in. But then we'll go back to the questions that are in the chat as well.

This is what the report looks like. If you're familiar with our old reports, it's a very similar layout. We sort of, we sort of stack rank the drugs that we analyze. We score them from zero to 100 and essentially, anything above a 50 is, is, you know, showing a significant response in those cells that we analyzed, and anything below a 50 is not showing a significant response in the cells that we analyzed this list of drugs, it's what we currently have available. Relatlimab is the LAG-3 will be added, and that's probably going to be available in a handful of weeks. I don't want to hold Rob too closely to a timeline, but that one is in process of being validated. And then there's some other, some other newer checkpoint drugs that we're planning to add to the platform as well. So I'd say by the end of the year, this list might expand to, you know, seven or eight drugs in total, something in that general scope, but essentially right now, looking at, you know, the most common immunotherapies, these are the drugs we're actively running. Rob, if you want to go to the next slide, these are some of the potential applications.



I say potential because some of this we have, you know, sort of clear data on some of this is what coalition clinicians and collaborators have come to us and said, “This is where I see utility for this test today, and as the data develops, these things could evolve, expand and change, etc.” But I'll just skim through them real quick and describe them.

The first is advanced disease. Anytime a late stage patient is just looking for creative options beyond standard of care. We might be providing valuable new insight on their immune systems response to different immunotherapies. We could give some additional insight there on something that may or may not have been a consideration previously, drug specific functional readouts like Rob really spoke to in his presentation, when when you know it's providing a real

time blood based result to show whether or not a patient's a single patient's truly personalized response is mounting a response in reference to one of these specific drugs. So that's a pretty unique data point that otherwise doesn't exist outside of this test drug selection and equipoise decision-making. What I mean by equipoise decision-making, if those are a new concept to you, is there are roughly 40 different indications across different tumor types, where second line recurrent colon cancer has three or four different immunotherapy options approved. There's not really any clear data driving right now the decision to choose one of those drugs over another. They are all sort of equivalently listed. It often comes up to just the doctor's prior experience and preference and which drug they choose there.

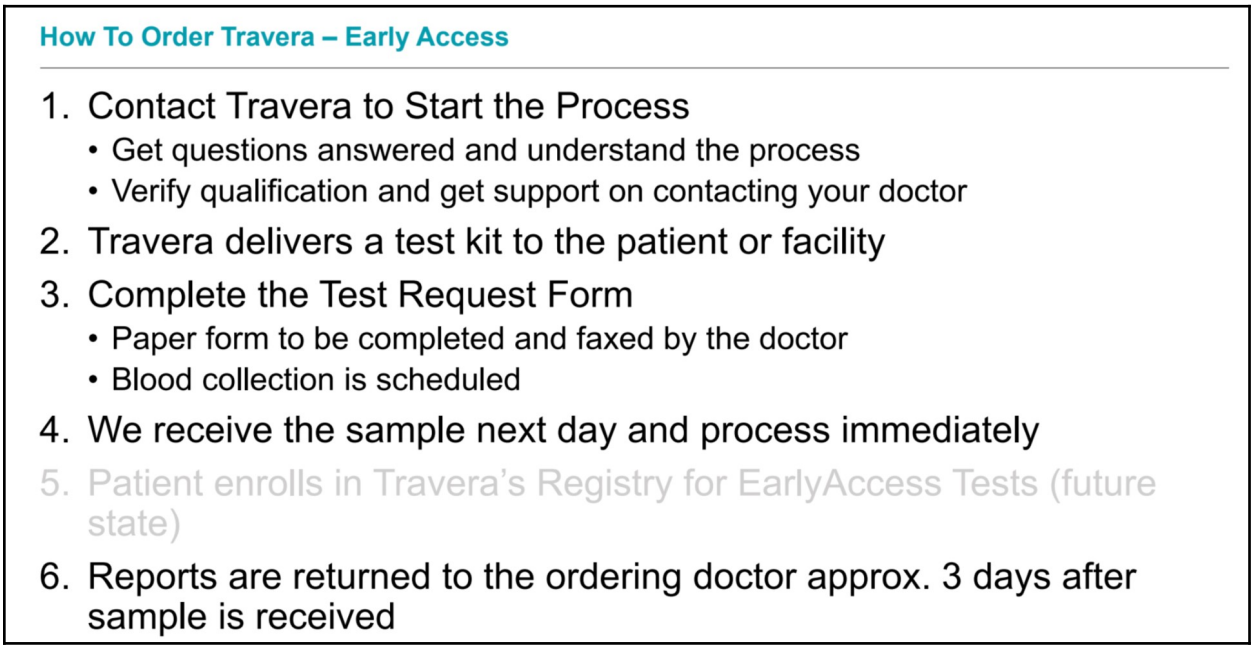
This adds an additional personalized data point, measuring your cells against those drugs that might help make that decision between nivo and pembro, or pembro and dostar, or whatever the drug options might be guiding drug combination and rescue strategies like we already spoke to in patients that are not responding to current therapy. This might inform if there's a different checkpoint inhibitor, or if adding additional agents like a CTLA-4 or a LAG-3 might help to trigger some immune activation, refining continuation or discontinuation decisions. For a lot of patients, by the time they reach the threshold of beginning immunotherapy, there's a decision to make at some point of between tolerability, whether or not you know you're kind of getting an ambiguous benefit, how long do I stay on this and having some clarity from a really simple blood test that says, based on what we can see, you are or are not likely to respond to this drug, might change that threshold for how long you stay on or how quickly you discontinue, and it's just additional personalized information to help make that decision, rather than just yours in the doctor's gut, non invasive alternative to repeated biopsies.

The one thing that we get from a lot of collaborators we talk to is the biomarkers they're working from are at a point in time from a biopsy procedure, in most cases, that was done at some point in the past. They all know that these immune signals can and often do change over time and in response to different circumstances, but the only way to really actively measure that is to re-biopsy, which is not always realistic.

Being able to get a simple blood test with a three-day turnaround time to give some indication as to whether or not there's a likelihood of a response here, could either justify that biopsy a little more fully, or may just provide enough information on its own to help make that decision, and then supporting neoadjuvant immunotherapy decisions, much like the example of what we rolled out In that melanoma cohort, you know, there's clear data to show that we can predict the likelihood of response for those patients in a neoadjuvant just in a neoadjuvant environment. But often when neoadjuvant decisions are being made, there's a decision to be made of is neoadjuvant the right choice for me, or should I go straight to surgery and adjuvant therapy? And if you have an indication that this immunotherapy is unlikely to provide you benefit, you might jump quicker to skipping a neoadjuvant approach and going directly to an adjuvant approach as an example. Again, these are not all questions that we have specifically, individually studied and validated. This is based on what is known of what the assay produces, feedback we've gotten from clinicians and collaborators of areas where they see applications and utility of the test kind of as it is today.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

I thought it was important to share all that now also important to understand in the context of everything that I just said that if this is an off-label drug situation, even if we show that you might be responsive to pembro in your in your circulating, systemic immune cells, but you otherwise don't have any clinical indications to get pembro. Our test is not going to be unlikely. I should say, to get that drug covered, you're going to probably need more but refining decisions and situations where you already know immunotherapy is an option, I think there's a great deal we can add there. And obviously, as our data grows, that situation might change. But today, this is very new. And so, you know, the off label drug thing is always one to just be aware of.



Dennis Watson 39:43
As many of you are familiar with the Early Access program we've had available with our tumor tissue testing. We are running this test through that same program, which means we will be offering it for a limited time in the East at absolutely no cost to patients that come to us through advocacy groups through different sources where they find us, and you can just reach out to me or us directly. We explain the process to you. We can support you and provide information to take to your doctor. This is the CLIA-approved test. It does require a doctor's order, but often I provide a draft email that a patient can send to their doctor to say, “Hey, I've learned about this test. I'm interested in it. What do you think?” We'll support you in any way we can. We will send you a test kit. Your doctor gets you the blood draw, it comes back to us 24 hours later with an overnight label that's on it. And then about three days after that, we would return those results to your doctor, like the ones that I showed earlier. We are opening a clinical IRB approved registry that Rob also briefly spoke to that's not actively open yet, but it's going to be coming really soon. Our real task in doing the test right now, at no cost, is that you share with us your experience. We can continue to build out our experience, expand our case experience, expand our real world data, all things that are valuable to us as we start to seek things like reimbursement.

“A New Blood-based Test which Predicts Your Response to Immune Checkpoint Inhibitors” (Rob Kimmerling and Dennis Watson) [#153]

Brad Power 41:34
Who is this ideally for? Obviously, you've done it in melanoma. So if I were a melanoma patient considering getting an immune checkpoint blockade, that's an obvious use case. How would you generically describe if I'm a patient saying, “Well, you've got a free test, all I have to do is go in and get a blood draw.” That's a pretty attractive offer. Might give me information, might give me useful information, but I'm not going to do it to anybody. Who would be the ideal candidate?

Rob Kimmerling 42:12
Melanoma is a good example, because there is a clinical question that has essentially a coin toss right now, where there is equally good data for a patient receiving pembro as a single therapy versus ipi and nivo as a combination, for example, in a neoadjuvant setting. So I think ideally that kind of clinical equipoise question is a really good fit for this kind of test where essentially an oncologist is in a position where they could give one two or three different regimens, but data supports giving any of those three, so additional information about a unique patient's immune response to those drugs could be really valuable. So I think melanoma is a really good example of that. There are a couple other indications, as well as another one, where there's clinical equipoise, and this kind of information could be immediately helpful for oncologists.

Dennis Watson 43:02
The question that Rob just described Brad is true in all MSI, high solid tumors. It's true in colon cancer. It's true in rectal, esophageal, gastric, renal, bladder, there's, there's a lot of applications where there is an equipoise decision like that to be made. So our earlier data included a lot of different tumor types, but as Rob described, was just kind of muddy, which is why we went on to do that melanoma specific trial, because it was just a really clean cohort where patients were only receiving checkpoint inhibitors and not other stuff. But because this is looking at the systemic immune cells and not the tumor specific immune cells, we really do have every reason to believe at this point that this is a kind of pan cancer test, but that is something we're going to continue to investigate and understand as it moves forward.

Brad Power 44:10
Patients are interested in improving their immune status, often with natural over-the-counter stuff, integrative medicine stuff. Would your baseline T cell fitness assay be something that could be used for that setting as a potential application? I could imagine, like, “Do I have a healthy immune system? What do you think, Travera?” Then I could try supplements, or I could try exercise, or I could try meditation over a period of time. I could go to an Ayurvedic clinic, and I come back and I say, “Did my immune system get boosted?” I walk in the woods, whatever. Could I be getting blood draws every week, let's say, and I'm trying various experiments on myself in various supposedly immune boosting activities. I'm taking curcumin, whatever it might be. Might that be a use case?

Dennis Watson 45:01

Yeah, I think that it absolutely makes sense, and one of the values of this being a blood test rather than a biopsy is that there are things you can do to change your immune system and your immune response over time, and being able to go back and just get one more blood draw to measure if that has changed, could be a really valuable application of this. And in fact, we even see potential applications into things like autoimmune disease and transplant, and a lot of other areas that don't use checkpoint inhibitors.

Rob Kimmerling 45:46
The value of the blood draw is, to your point, is doing the longitudinal collection, so taking a blood draw, looking at the state of the cells, and then after a week, a month, whatever it might be, doing that same measurement again, and see there's a difference in the functional readout we're getting from the cells. We're still in the early days of understanding what those physical measurements mean for just baseline fitness. It's a big reason why we're excited about the registry study, because in addition to the physical measurements of these cells, we're also collecting molecular profiling, so things like gene expression, looking at the phenotype of these cells with flow cytometry and long term, what we're really trying to do is build the data that shows what that longitudinal profile of a patient's immune system really means biologically. And I think with that in mind, it could be a really powerful tool for helping people guide their own interventions to kind of recraft that immune system in the right direction for sure.

Brad Power 46:55
Question from Rick Davis in the chat: Can the Travera technology be applied to understand why certain tumor types are cold? Can we re-engineer T cells to penetrate cold tumors?

Rob Kimmerling 47:08
There are two different ways of looking at the concept of “cold”. I think one way it's often looked at is whether or not, by pathology, if there are T cells that are sort of physically co-mingling with the tumor. And for us, that's not really something we're reading out because we're looking at blood. We're looking at peripheral cells that are not really involved in the tumor. And so I don't think there's much we can really comment on in terms of that type of tumor hotness, in terms of how they're infiltrating in but another way to think about whether or not immune system is hot or cold is how functionally responsive that patient's cells might be, just generally, and that's something we can potentially pick up with just the blood draw, which is at a sort of baseline level, is this patient's immune system capable of mounting a pretty aggressive response to a threat? And so I think that piece we can get at with the blood test, but not necessarily more of these pathological folks and pieces.

Allen Morris 48:09
I'm just curious about your technology. You explained it, but I'm going to try to regurgitate and you tell me where I'm getting things wrong. So you have this crazy measuring device that can wait, that can do metrics on cells, such as density and size and all that, and that's what you're using to tell whether or not the cell has been activated. Okay, so it's an activation test, then what you do is you take the person's blood and do you isolate their T cells, or are you just running all

of their immune cells, which include all the lymphocytes, all the B cells, all the bad T cells, like the T regulators. Are you running them all through this diving board?

Rob Kimmerling 49:06
When we're running the test, we do all of the activation in the presence of all of those cells, so it includes the monocytes of all the T cell types. When we run the actual readout, right before we run the readout, we purify the T cells. So effectively, what we're doing is we're trying to capture the effect of all those background cells, but using T cells, we got a clean endpoint.

Allen Morris 49:25
Specifically, are you segregating out the CD3, CD8, potentially as the marker of or signature or cytotoxic T lymphocytes from all of the T-reg, which are the generic word for the bad T cells. Are you segregating that out?

Rob Kimmerling 49:46
We're doing a pan T cell. So this is just CD3 isolation. So that will include CD4, CD8, the T regs.

Allen Morris 49:55
May I suggest that if you were to isolate CD3, CD8 cells in particular, your area under the curve might improve. Does that make any sense?

Rob Kimmerling 50:11
We have another cohort of that same melanoma group of patients. For that cohort, we're going to be performing single cell RNA sequencing for all the cells that we're measuring in our device and to get answers to those exact questions: Are there subsets of T cells that are more informative to this readout that we should be purified?

Allen Morris 50:35
You have this measuring device, you're passing the person's peripheral blood trying to look at subsets of lymphocytes, maybe even T cells. T cells, in general, the test you're doing is baseline, you're activating their T cells with some sort of activating agent, and then you're doing a test activating their T cells with Keytruda or some immune checkpoint inhibitor. Is that what you're doing, you're doing the best baseline activation. This person's cell size and density and all that is increasing with a generic activator. That's their baseline T cell response. And when we add Keytruda, it's even higher. Is that basically the differential you're looking at?

Rob Kimmerling 51:27
That's exactly right. Typically, a T cell requires two signals to become activated. The first is antigen, so it has to use its T cell receptor to find a target, and then the second signal is Co-stimulation. And so what we're doing is we are providing signal one, we're giving anti CD3, which essentially just activates the T cell receptor, but all of the Co-stimulation is coming from the background population of cells that the T cells are experiencing. And so the kind of working theory is that by adding in a checkpoint blockade drug like pembro, that background signaling starts to get tilted more and more towards co-stimulation and away from suppressive signaling.

And so if that's working, we expect the activation to be a bit stronger. So you're absolutely right in terms of what the structure of the assay looks like.

Richard Anders 52:27
I had a couple of comments about how the product would be used clinically. But the standard question always is, “How do you avoid overfitting data?” You have a really limited dataset, and an endless number of parameters. What are you going to do to turn that into a test that there's confidence is really actionable?

Rob Kimmerling 52:53
The way we focus this initial cohort is because we were only around 20 patients or so, we've limited the analysis to just two parameters, so we're looking at the mass and the volume of these cells that we're actually measuring the readout for. And with those two parameters, we also ran cross validation for the data that I showed, just to leave a subset of those samples out, while kind of building this predictor for that model. So it's something that is a very fair point for us. Another caveat there is the AUC measurement, for example, is point eight. But because it's such a limited data set, the confidence interval on that is quite high. And so what we need to do next is kind of just build out that data set with more patients. Right now, it seems like with around 85 to 100 patients, that confidence interval will get small enough that we'll be pretty confident that we're performing above kind of the standard in the field right now, which is two mutation burdens. So that's kind of our target, and that's samples we have in the freezer that we're kind of actively working through, so hopefully that the day will hold up.

Dennis Watson 54:00
The good news is the academic collaborators that we've worked with are really excited about how unique our specific measurement is. So we've already gotten verbal commitments that we're working through the specifics on around 1500 additional specimens in a variety of different tumor types, and so we expect this data set to grow very rapidly.

Richard Anders 54:34
It's really exciting and would be clearly valuable, the details of sort of how you fit the data are kind of lost in the development process. There are two parameters you say, but you're looking at a lot of cell types, so all of a sudden there are more than two parameters. And you might have looked at five parameters, but throughout all but two, the test result now just uses two. So it's not quite the same as saying we only started with two, we ended with two, but we didn't, we started with a lot more parameters. But if you stick to a fixed formula at this point and then start looking at a lot more data with a fixed formula, then it'll clearly be a much more robust, statistically valid test.

Bill Paseman 55:29
You mentioned that there were 17 out of 21 responses which showed was promising. But I was wondering if you got a little bit more color on that. Were the particular cancers that this thing worked better for than others, and why is it that it didn't work? why didn't it work 100% of the time?

Rob Kimmerling 55:51
I think our goal is to get it to work 100% of the time. So those misses are really the core focus for any of these; the data we were showing is actually only in melanoma. So this is entirely a cohort of melanoma. So there are 21 patients who are all single malignancy. In terms of the misses, one thing we think is not being captured by blood is whether or not there is something for the immune system to target. So this is where that tumor mutation burden piece comes in, where we were able to improve the accuracy of prediction by also layering in the tumor mutation burden for these patients. And so I think as we get more data, we'll find other pieces that hopefully kind of rise that time to get the accuracy higher and higher. But that's absolutely the goal, is to find the sort of combination of biomarkers that makes us able to predict this for every patient, whether or not they'll respond.

Bill Paseman 56:42
Let me repeat what I heard you say. In essence, you're only measuring one thing, and as a result, since it's a complicated process, there's a couple of factors that'll go on to determine whether or not a drug is going to work, and you only measure the one. It seems like it's a pretty high order bit in terms of figuring out what the response is going to be, but you've got some other bits you need to figure in.

Dennis Watson 57:23
I’m happy to follow up with anybody that is interested in talking about this more, getting some questions answered, seeing if it works for them. For providers, clinicians, if you have patients you think might like to try this, or research ideas you have, we're really open to those kinds of conversations.

As I said, we are offering the test at no cost right now. It is CLIA-approved. We're happy to run those sorts of experiments, but the data is encouraging and early, so there's plenty we don't know, and we're going to continue to build out these cohorts of interest and validations, and grow this data, hopefully very deeply and very rapidly. What's nice about this versus our old other sort of cancer-cell-specific test is that we can do this from frozen blood specimens, frozen PBMCs, which for existing immunotherapy cohorts. That's why I mentioned we have commitments of about 1500 unique patient specimens. There's a whole lot of stuff in bio banks around the country that we're going to have an opportunity to test very quickly, that already have all the clinical outcomes tied to them. So that's something that's going to allow us to build this really fast, but those are the top levels.

Rob Kimmerling 59:27
Collecting evidence is really our biggest point, based on your questions. You're clear-eyed about what this is and where it needs to go to improve and get evidence. We need partnership to do that, and working directly with patients that are thoughtful about what this means is very helpful for us.