“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

Brad Power and Emily Kim
March 19, 2025

Meeting Summary

Your immune system is a formidable ally against cancer, yet it doesn’t always win the fight. You can increase your odds of beating your cancer by looking at the hidden intricacies of your immune system and personalizing cancer treatments using new technologies.

Simo Arredouani, PhD, Vice President of Immunology and Strategic Partnerships at Omniscope, is uniquely qualified to describe how new immune system diagnostic technologies can transform your cancer care. Omniscope has combined proprietary laboratory technology that can monitor your immune system and predict your treatment response, applying AI to the world's largest immune system database. They look at protein complexes found on the surface of your white blood cells (T lymphocytes) that play a crucial role in your adaptive immune system, are specific to your cancer, and can be used to develop personalized therapies for you.

Why would you want to be able to analyze your immune system?

- **Predict your immune system response**: Know if a treatment, especially an immunotherapy, will work before you start.
- **Monitor treatment effectiveness**: Track your progress in real-time and adjust your strategy as needed.
- **Early detection**: Catch any signs of disease progression – changes in your immune repertoire can help identify potential health issues before they become serious and move you from a reactive to a proactive approach to your health.
- **Uncover hidden patterns**: Understand how your immune system works and understand your immune system diversity.
- **Deliver personalized care**: Tailor therapies to your unique needs.
- **Health monitoring**: Understand the state and fitness of your immune system – provide insights into your overall health and potential vulnerabilities; determine treatment efficacy much faster than current methods, potentially saving $15,000 per month by stopping ineffective treatments earlier. Use blood tests as a non-invasive alternative to tumor biopsies.
- **Treatment personalization**: Help predict your likelihood of responding to immunotherapies, potential adverse events, minimal residual disease (recurrence), and treatment efficacy – potentially saving you time, money, and unnecessary treatments
- **Athletic performance**: Help you understand your physical readiness and recovery needs from exercise.
- **Research**: Contribute to scientific understanding of immune system dynamics and individual variations. Contribute to personalized cancer vaccine and targeted cell therapy development, making “cold” tumors more responsive to immunotherapy.

What are the latest advancements in immunotherapy response testing?

- **Blood test advancements**: Using blood draws instead of your tumor tissue enables less invasive monitoring of your cancer, which is particularly useful for hard-to-access tumors like brain metastases.
- **High-resolution immune system analysis**: Detailed sequencing of white blood cells (T cell and B cell receptors) and using AI and machine learning can identify response patterns and identify unique antigens for potential vaccine or cell therapy development.
- **Early response and adverse event prediction**: Identifying immune system (T cell receptor) signatures that correlate with immunotherapy response, potentially predicting response within 2-3 months of treatment start and helping you decide whether to continue or switch treatments; tracking your immune repertoire changes before and after treatment can identify potential side effects and adverse events early and personalize your treatment.

What are the key challenges in applying immune system analysis to rare cancer types with low mutational burden?

- **Limited existing data**: Rare cancers have fewer samples, which makes it harder to develop reliable AI models and predictive signatures.
- **Slower treatment development**: Creating targeted therapies like TCR-T cell treatments requires extensive validation and may take longer for rare cancer types for target antigen identification and validation.

How can you access Omniscope's groundbreaking technology for your personal healthcare journey?

- Pursue their new comprehensive immune system health report for research on professional athletes, currently $2,000-$5,000 for one-year access and requires traveling to Barcelona for blood sample
- Ask your oncologist whether non-standard cancer treatment response prediction would be useful for you.

How can you learn more?

- Go to Omniscope's website and create a free account to view their sample data, research, and videos.
- See our discussion with Keith Wharton "Bringing Novel Immune System Tests from Research to Clinical Use" [#28]
- See our discussion with Heather Tomlinson “How MSI and Other Tests Can Guide Immunotherapies for Cancer Treatment” [#43]
- Contact Simo Arredouani at simo@omniscope.ai for the most current logistics and prices for accessing their consumer-facing immune health services.

medical treatment, product, or course of action. You should always consult a doctor about your specific situation before pursuing any health care program, treatment, product or other course of action that might affect your health.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

Meeting Notes

KEYWORDS

Cancer immunology, T cell receptors, B cell receptors, Omniscope, single cell genomics, AI models, immune system, cancer therapy, TCR sequences, minimal residual disease, autoimmune disease, vaccine development, bone marrow transplant, immune health, FC Barcelona.

SPEAKERS

Simo Arredouani (75%), Brad Power (9%), Nina Senna (7%), Richard Anders (3%), Rick Davis (2%), Cindy Ness (2%), Alane Watkins (1%), Sandra Balladares (1%)

CHAT CONTRIBUTORS

Alane Watkins, Nina Senna, Koryn DelPrince, Rick Davis, Helen, Sandra Balladares, David Plunkett

SUMMARY

Simo Arredouani, a cancer immunologist, discussed Omniscope's technology, which processes 1 million cells per sample, 100 times more than competitors. This technology aids in diagnostics and therapeutics, including T cell and B cell therapies. It can detect minimal residual disease, autoimmune diseases, and viral infections. Arredouani highlighted a collaboration with FC Barcelona to track athletes' immune health. The technology can predict treatment responses, potentially saving time and money. Omniscope's early access program for immune health assessments costs around $2,000-$5,000. The goal is to stratify patients and improve cancer treatment efficacy.

OUTLINE

Introductions, Simo Arredouani's Background, and Omniscope Overview

- Our purpose was to discuss cancer immunology with Simo Arredouani, a cancer immunologist and PhD in immunology from Harvard Medical School.
- Simo introduced himself and explained his background in cancer immunology and immunotherapy, including his work at Genius Bio and Tele Therapeutics.
- Simo introduced Omniscope, a tech-bio company based in Barcelona, and mentioned key team members like Vijay (CEO), Lynette (Chief Growth Officer), Holger (Scientist), and Matt (Chief Information Officer), and Nina.
- The immune system is important in fighting cancer, and T cells and B cells have a role in immunity.
- Omniscope's technology processes 100 times more cells than competitors, allowing for detailed analysis of TCR and BCR sequences.

Omniscope's Technology and Applications

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

- Omniscope's technology can be used for diagnostics, therapeutics, target discovery, and licensing TCR sequences for T cell therapy.
- Examples of how the technology can detect minimal residual disease in various cancers and decipher the autoimmune nature of diseases like small fiber neuropathy.
- The ability to detect viral infections and monitor immune responses to antiviral treatments using Omniscope's high-resolution detection.
- The technology can classify different cancers based on T cell and B cell signatures and rank patients on an immunological scale.

Case Studies and Collaborations

- Simo shares a study on brain metastasis, showing the high overlap between tumor, cerebrospinal fluid, and blood samples, making blood testing a reliable alternative.
- He discusses the use of Omniscope's technology in cancer vaccines, which can track the evolution of the immune response with high accuracy.
- Simo describes a collaboration with Immacor, which has an FDA-approved TCR bispecific for advanced melanoma, and how Omniscope helped identify mechanisms of action and adverse events.
- He explains how the technology can predict adverse events in immunotherapy and identify drug efficacy early in treatment.

T Cell and B Cell Repertoires

- Richard Anders asked about the diversity of T cell receptors and how Omniscope deals with HLA types. Simo explained the importance of HLA alleles and the challenges of predicting TCR sequences without considering HLA.
- Richard also inquires about the isotypes of TCRs and antibodies, and Simo clarifies that they focus on alpha-beta TCRs.
- Brad and Simo discuss the importance of understanding HLA for bone marrow transplants and the potential for Omniscope's technology to track immune rejection and GVHD.

Rare Cancers and Therapeutic Applications

- Alane Watkins asks about the application of Omniscope's technology to rare cancers like thymoma, which have few mutations. Simo explains that while vaccines may not be viable, TCR T cell therapies can be developed using Omniscope's technology.
- Helen asks about monitoring the efficacy of Avastin for rare ovarian cancer. Nina explains that while they have experience with similar monoclonal antibodies, they would need to conduct a clinical trial to develop a signature for predicting response.
- Simo adds that they are working on expanding their technology to other cancer types and therapies.

Consumer Access and Future Directions

- Cindy Ness asks about the practical application of Omniscope's technology for patients. Simo explains that while it is not yet available as a standard clinical tool, they are working towards regulatory approval and collaboration with hospitals.
- Simo mentions a product for assessing immune health in the general population and a collaboration with FC Barcelona to track the immune health of professional athletes.

- Nina adds that they have launched an early access program for consumers to explore their immune health, with plans to expand this service.

Q&A Session: Cold Tumors and Research Applications

- Rick Davis asks about the potential of Omniscope's technology to turn cold tumors into hot tumors. Simo explains that while they can identify T cells that recognize tumor antigens, they cannot currently turn a cold tumor into a hot tumor.
- Simo discusses the broader applications of their technology in transplantation, autoimmunity, and immunodeficiency, and their mission to help patients and advance scientific discovery.
- Brad Power wraps up the meeting, thanking Simo and the audience for their participation and questions.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

TRANSCRIPT

Brad Power
This is the Cancer Patient Lab. We're honored to have Simo Arredouani with us today, who is a friend of mine working with Omniscope. We have a couple of other Omniscope representatives present, Nina and Vijay. I met Vijay and Holger Heyn at JPM in San Francisco. I think we stood in the middle of a hotel lobby. If you've ever been to JPM, it’s this crazy “madhouse” of people, but that's where we met. I got to know them through a friend of mine, Damian Balsan, who's an investor in Omniscope.

Standard disclaimers before we get started: first of all, this is for information purposes only. This is not medical advice. We try to arm our patients with information they can take to their medical team. Second, this will all be made public. If you're concerned about your image, your name, or anything you say being made public, you can hide your video, change your name, and not say anything. Finally, we are a nonprofit 501c3, and we exist on the kindness of volunteers who help run the operation and rely on donations. If you're inspired to donate, you can do that easily on our website, cancerpatientlab.org.

Simo Arredouani 2:04
Thank you so much for the opportunity to talk to your audience. Usually, we talk to immunologists, where we speak a different kind of language. I will try to simplify for better understanding. We will also have a Q&A at the end.

I'm a cancer immunologist. I have a PhD in immunology; I trained in cancer immunology and immunotherapy at Harvard Medical School. I used to head a lab at the Beth Israel Deaconess Medical Center. People in the Boston area may recognize the hospital. I then left for “the dark side” in Cambridge, where I first started at Agenus, an immuno-oncology company doing vaccines, checkpoint inhibitors, and cell therapies. I then settled for five years at Intellia therapeutics, where I was doing a lot of cell therapies. I'm sure you heard about cell therapies,

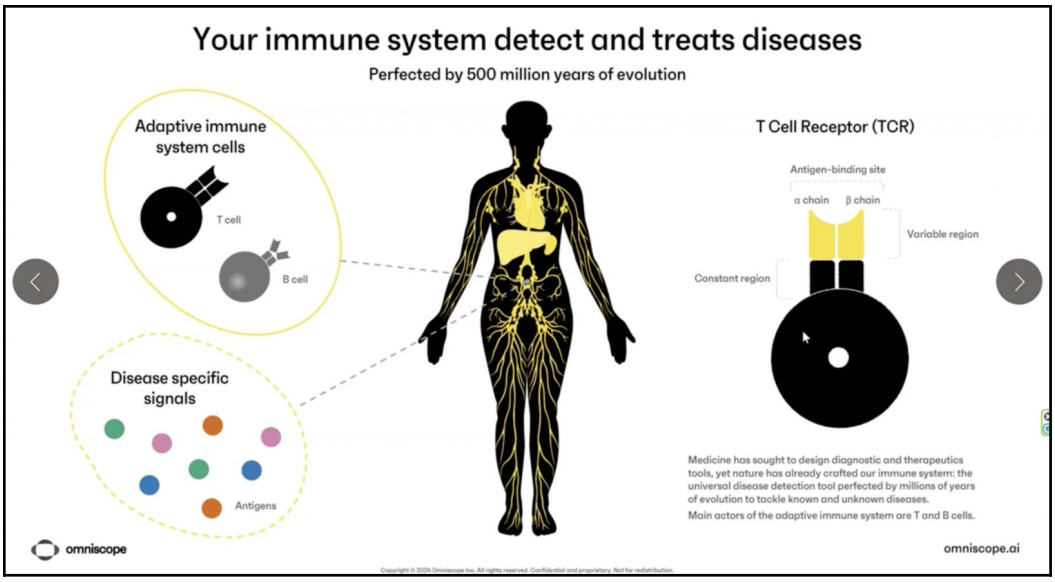
because, now, they are very fashionable. These therapies involve CAR T cells, CAR-NK cells, and T cell receptors (TCRs).

It was during that job that I had a lot of exposure with TCRs. There, I used some of the technologies that looked into TCRs, identified sequences, completed all of the TCR work, and developed therapies. We were fortunate enough to take a product to phase one. That was a very satisfying achievement.

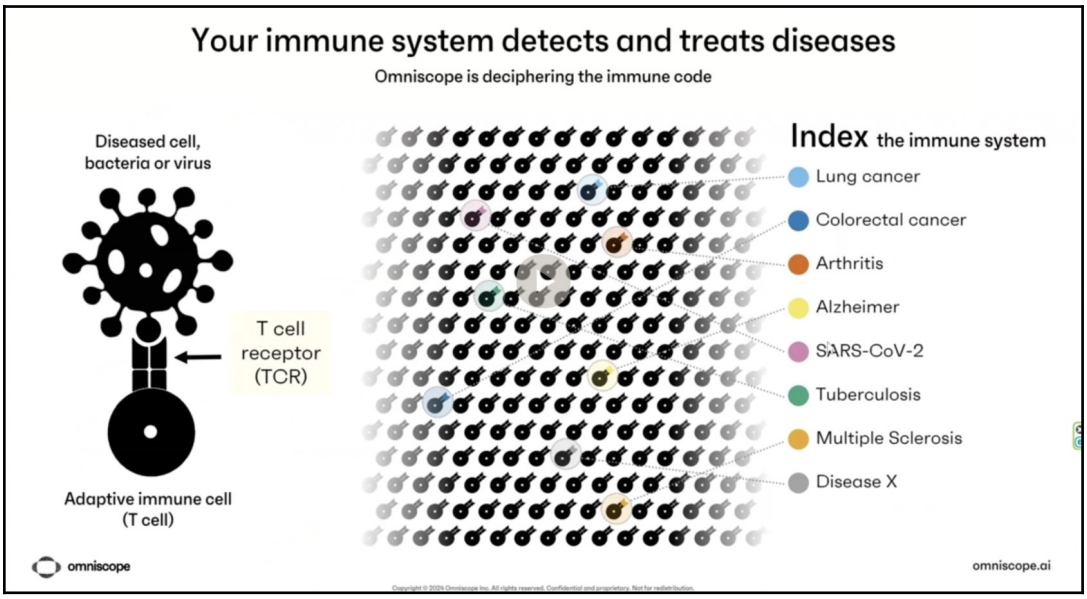
I recently joined Omniscope, which I'm going to introduce today. Omniscope is a tech-bio company based in Barcelona. In the audience, we have two of the co-founders. We have Vijay and Lynette. Vijay is the CEO; Lynette the chief growth officer. Holger is a scientist who is very well-known in the field of single cell genomics. His lab is in Barcelona, right next to where Omniscope is located. Matt is our chief information officer who takes care of all informatics and the very important artificial intelligence part of the company.

As you know, the immune system is extremely important in fighting against cancer. I’m certain that people who did not believe in the immune system’s importance before 2010 are now convinced that you can actually harness the power of immunity against cancer. We have a bunch of antibodies and cell therapies that work. We have some cytokines. We have the vaccine. We have a TCR bispecific. We have a couple bispecifics. There is no doubt that the immune system is important.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

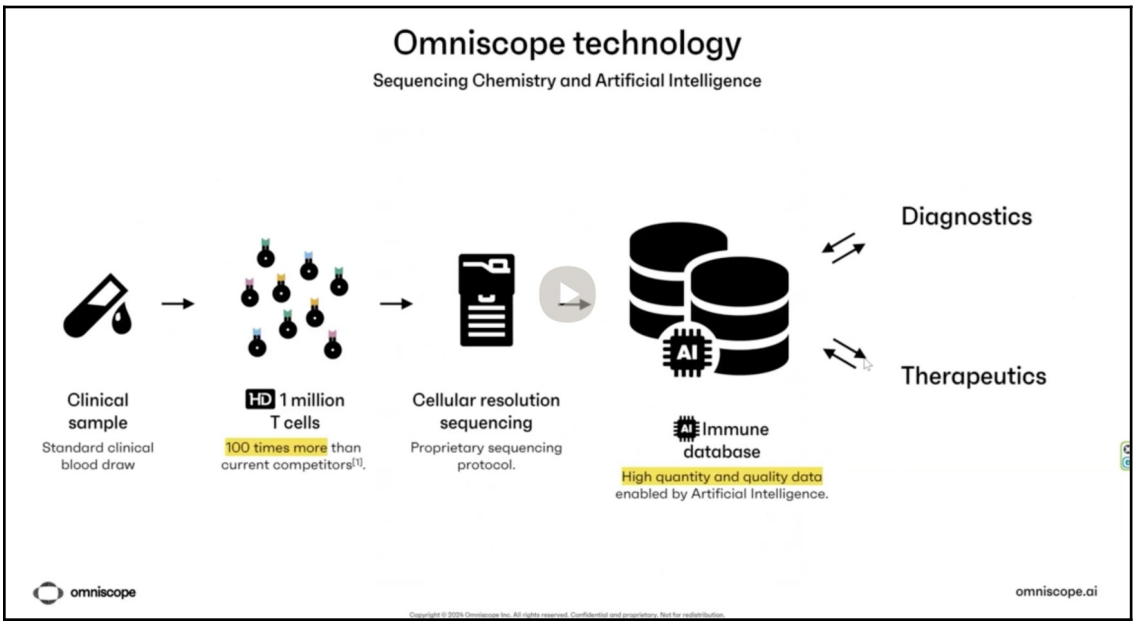


The fight against cancer is driven mostly by T cells; there is also a role for B cells. A lot of my slides will be about T cells today, but we treat T cells and B cells equally as we have products for both cell types. T cells are endowed with a receptor called T cell receptor (TCR), as you can see on the diagram, which is a dimer receptor composed of two proteins that align, find the tumor, recognize it in a specific way, and trigger activation of the cell to attack the tumor.

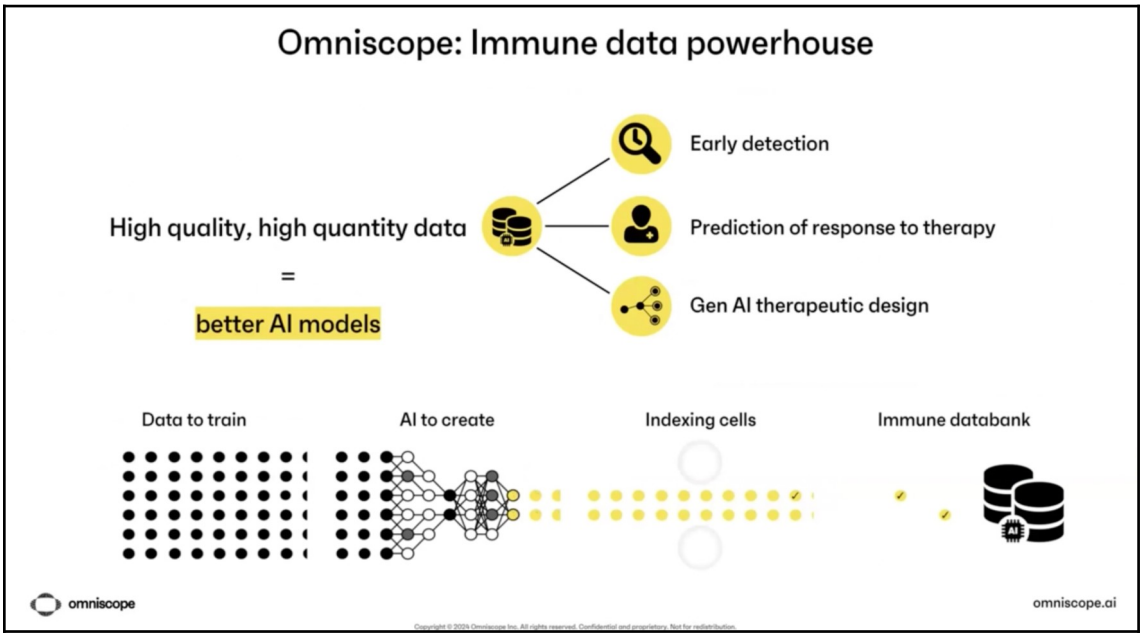


Our T cell repertoire is extremely broad and diverse. Our immunity is built to recognize everything that comes in, such as viruses or bacteria. They are also designed to recognize cancers, because cancers are unusual tissues, but they also recognize our antigens, and that's why some of us have autoimmune disease. How do you really profile all this diversity and make sense of it? How do you take advantage of it in the fields of oncology, autoimmune disease, or infectious disease? That's where Omniscope comes in.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

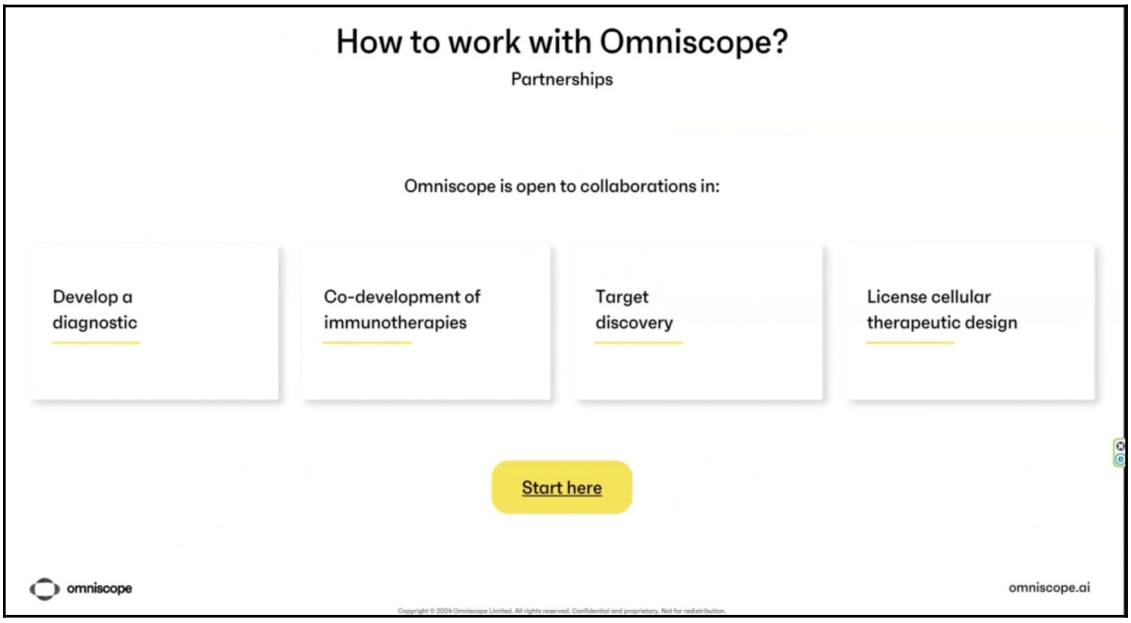


Omniscope has a technology that allows processing an unprecedented number of cells. I have personal experience using similar technology; Omniscope is actually processing 100 times more cells than the next competitor, with 1 million cells being processed per sample of blood or other tissues. The cells are then sequenced. The TCR is sequenced in T cells, BCR in B cells. We get readouts from each one of those 1 million cells. Then it goes into the informatics and AI pipelines for data refinements and analysis, which involves statistics, modeling, homology studies, and so on. That allows us to use these readouts into two large brackets: diagnostics and therapeutics.

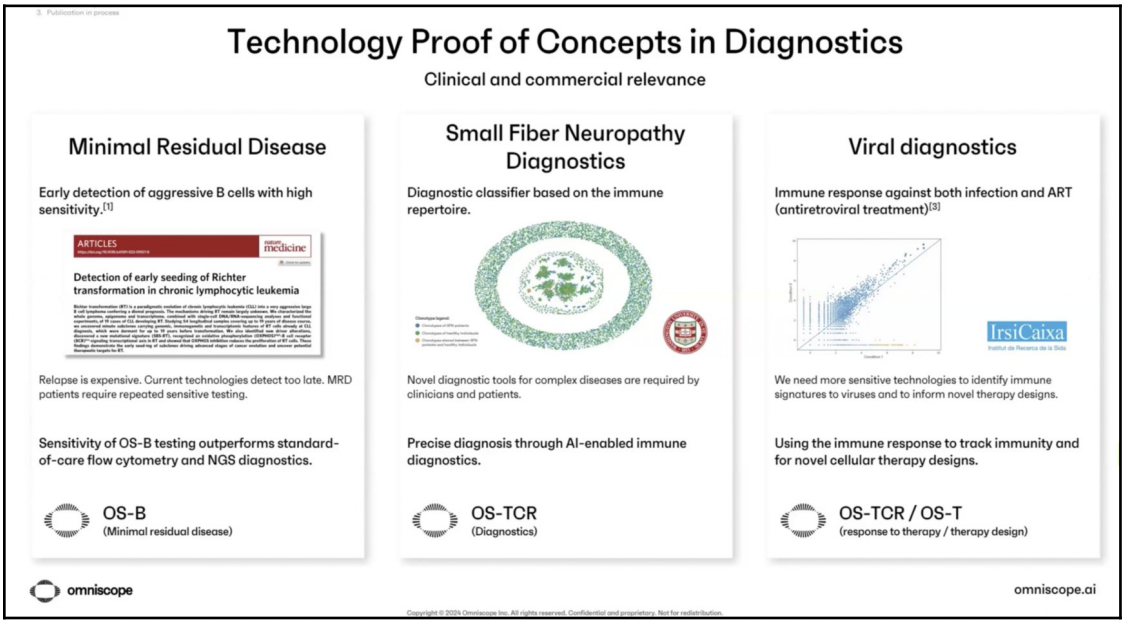


“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

The beauty of Omniscope is that they generate a lot of data from each sample; more data means better AI refinement, which means increased reliability of Redux, and that happens really fast.



We can use Omniscope in a multitude of applications. We can use it in diagnostics and the co-development of immunotherapies with collaborators. We can use it for target discovery. We can also license our TCR sequences for T cell therapy specifically, and we can do similarly on the antibody side, for antibody development.

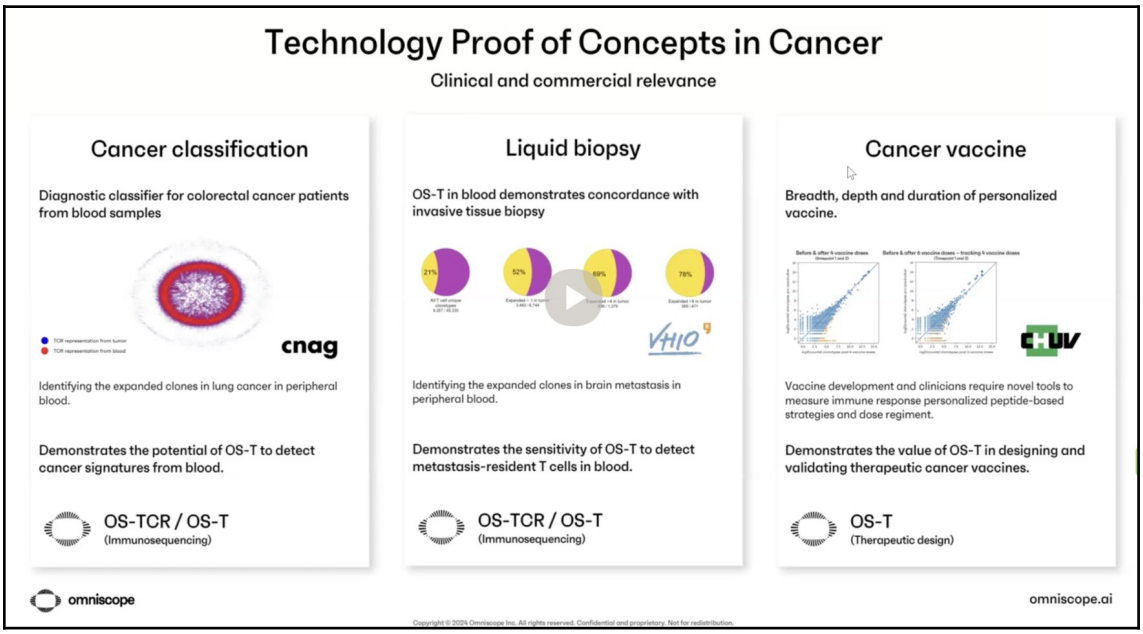


“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

I think that, for the audience, the main question is, “What can we do with Omniscope as a cancer patient?” I will just show you a few examples where we have been able to establish proof of concept. We can actually use it to detect minimal residual disease. I will leave you all the publications I'm going to refer to if you want to learn more.

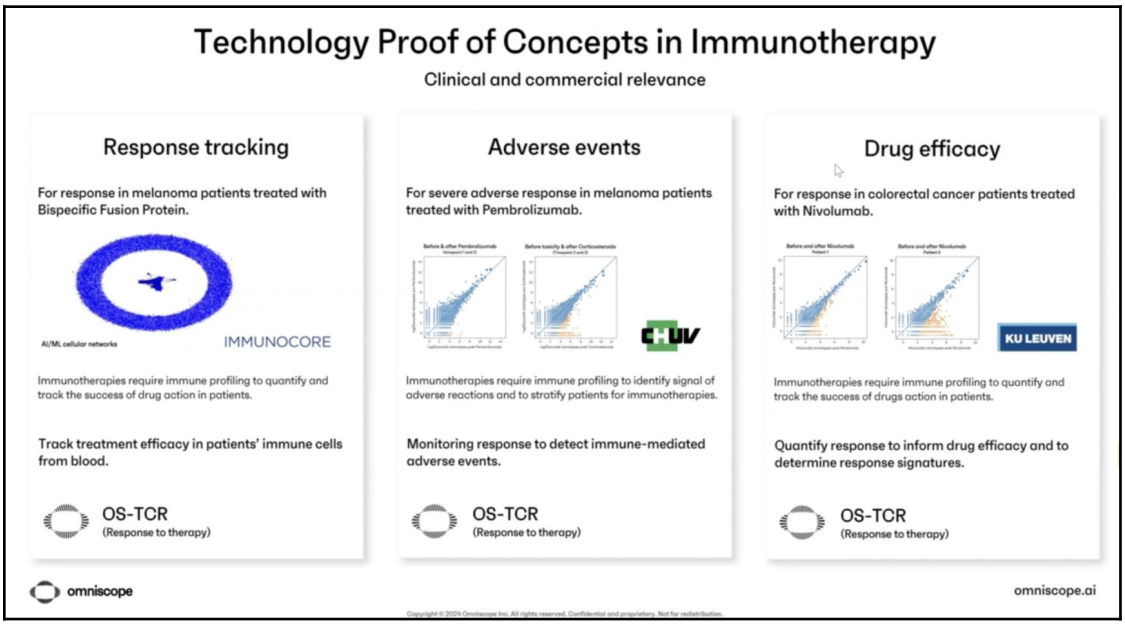
We can also decipher the autoimmune nature of disease. In this case, we looked at small fiber neuropathy, which is an autoimmune disease, but only 20% of the disease is autoimmune. It's really hard to diagnose. Using this technology, we can actually tell you, just by looking at the blood, whether the case that is presented to the doctor is actually autoimmune or not with quite a high accuracy.

In terms of viral diagnostics, just by looking at the blood, you can tell whether the patient has an ongoing viral infection, even if the symptoms have not yet shown up. Because of the higher resolution of detection, we are looking at 1 million cells per sample. But you can also look at how the immune system is changing if the patient is, for example, taking antiviral treatment, because that would also impact the repertoire of the immune system.



Simo Arredouani 10:37
We can also use it to classify cancers. Different cancers will impose different repertoire, or T cell or B cell signatures. By looking at those signatures, you can actually rank patients on an immunological scale. I like the liquid biopsy example in the middle. This is a study where my colleagues at Omniscope looked at brain metastasis. We had access to biopsy, cerebrospinal fluid (CSF), and blood. It was amazing how much overlap there is between the tumor, CSF, and the blood. In fact, the overlap is so strong that you could rely solely on blood testing to make very reliable conclusions, because it's not easy to get a biopsy from the brain and impractical to get the CSF from the patient, especially when you have to do it in a repetitive way. On the contrary, you can do it with blood very easily.

The panel on the right is “Cancer vaccine.” Our technology is probably the most straightforward in the vaccine space. Whether it's an infectious disease vaccine or cancer vaccine, because vaccines induce an immediate T and B cell response, the results are so straightforward. As you may know, vaccination triggers an immune response. The viral infection clears way, and then the immune response weighs down. Then you use a booster, and the immune response comes back again and weighs down; then you use another booster, and the response comes down. With our assay, we can, with very high accuracy, track that evolution or the dynamics of the repertoire, depending on phase of infection intensity and vaccine outcome or booster. We could easily determine whether the patient who is being vaccinated would respond to the vaccination or not. That's something we could do very early on during vaccination, instead of waiting for a long time to actually decide whether it has worked or not. For companies who develop vaccines, this could be a very important approach to save a lot of time and money.

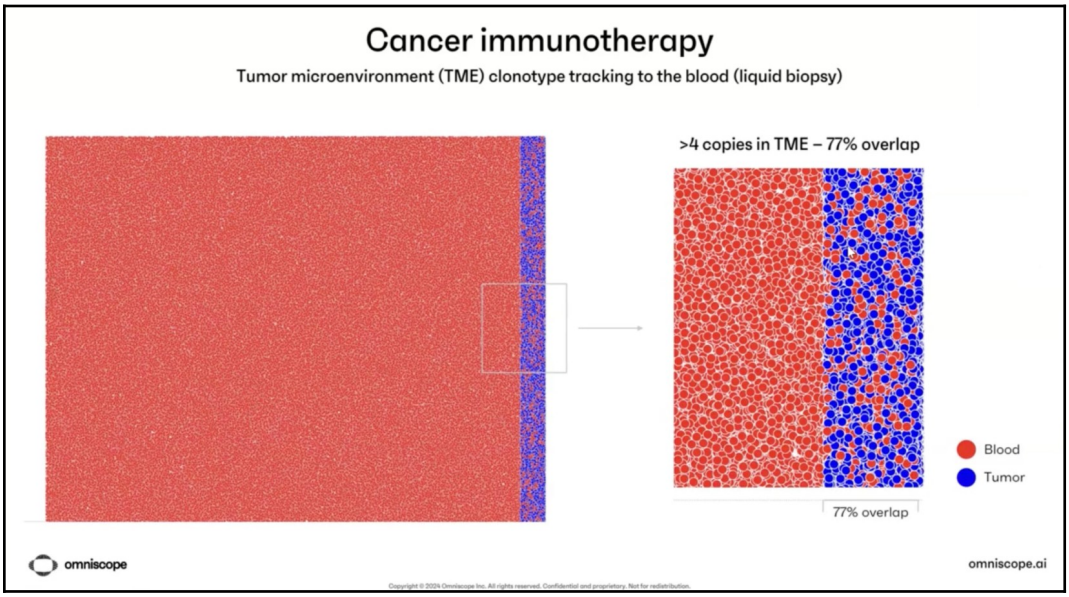


The panel on the left is a collaboration with IMMUNOCORE, which has an FDA approved bispecific using a TCR. This is the only bispecific antibody, part TCR. It's for advanced melanoma. It's targeting the gp120 antigen, specifically one small epitope. Although the drug is approved, IMMUNOCORE is still learning about the mechanism of action, because they have a wide pipeline of other incoming drugs of the same nature. We were able to actually help them identify some of the mechanisms of action, one of which is impacting phenotype of T cells, turning T cells into more anti-tumor phenotypes, and generating epitope spread, which means that, in addition to your target antigen, the immune system is now triggering a response to additional antigen, which magnifies the impact of your therapy. That was really interesting.

The technology could also be used to actually identify adverse events. For example, in immunotherapy in general, most patients would have some degree of adversity of the events, and just by looking at the dynamics of the T cell repertoire as well as examining pre-treatment

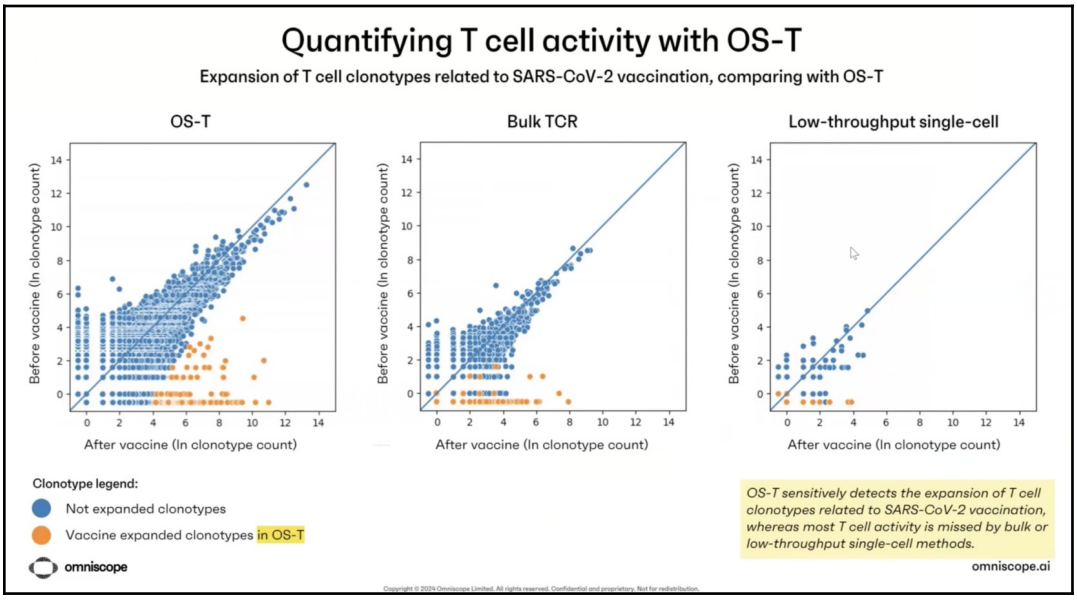
and post-treatment, you can already predict whether an adverse event is incoming or not. In this case, specifically, we have seen that with corticosteroids, the adverse events disappeared, and there was a big impact on immune repertoire. That means that there was a population of T cells that were driving that adversity.

Drug efficacy is an aspect where we are doing a lot of work because of the many FDA-approved checkpoint inhibitors. There's so many cancer patients who are actually taking those therapies. I'm talking about PD-1, PdL-1, CTLA-4, and to some extent, LAG3. You are being treated without knowing how you are going to respond. While half of the patients meet the eligibility criteria, when you look at the statistics, only 20 to 25% percent of those patients will actually respond. In the course of treatment with ICI, we are spending a lot of money–$15,000 per month, on average, here in the US–and have to wait for two years to know who responded and who didn't. With our technology, we can actually do that in the first two to three months, starting after the treatment began, because there is a certain TCR clonotype signature that correlates with the response. If you don't see that signature, it means that the patient is not going to respond. If this would be applied in the clinic, you would probably advise the oncologist to stop the treatment and put the patient on an alternative instead of wasting two years. That's my personal opinion.



Simo Arredouani 17:10
When we say that we are using blood as a surrogate for tumors or other tissues, where a pathologist would typically be in charge, the equivalency of blood to a tumor, the main tissue, is highlighted in this slide. What we see here is that the blood is in the red color and the tumor is in blue color. We are detecting the specific TCRs in the tumor from the patient and in his or her blood: this is matching blood to tumor. If we only zoom in on the TCR clonotypes, they are represented in at least four copies, where we see 77% overlap. This is a very astonishing number. This is a very high overlap, allowing you to use blood instead of even bothering to ask a pathologist or surgeon for a biopsy. Just from one tube of blood, you could get enough

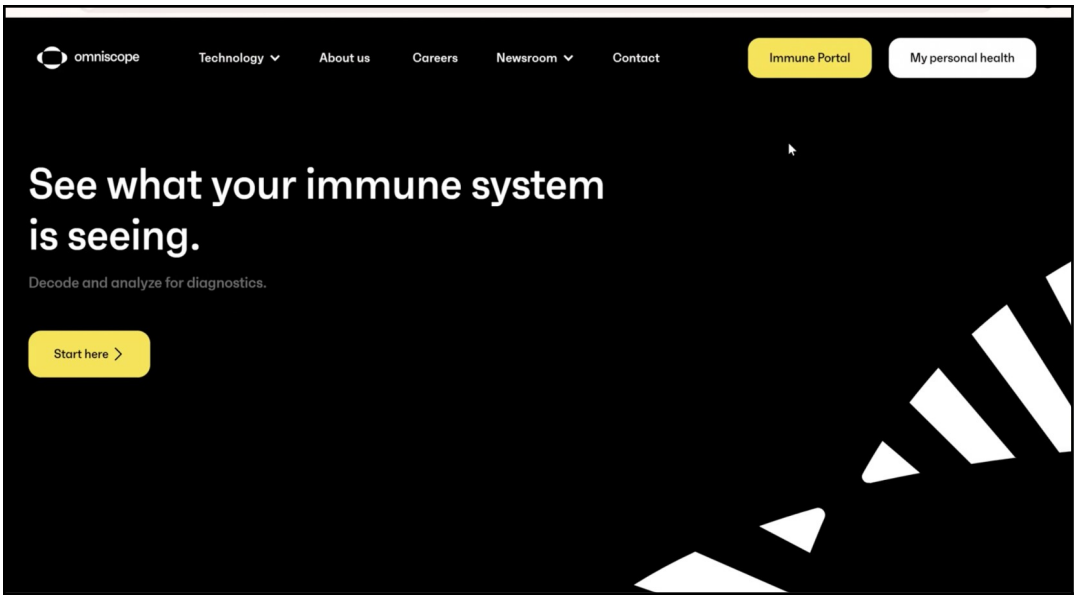
information that you would get from the tumor. This is as long as you are focused on TCR or BCR repertoire, because if your intention is to also profile the tumor environment, then you need to do a different assay, which we also provide.



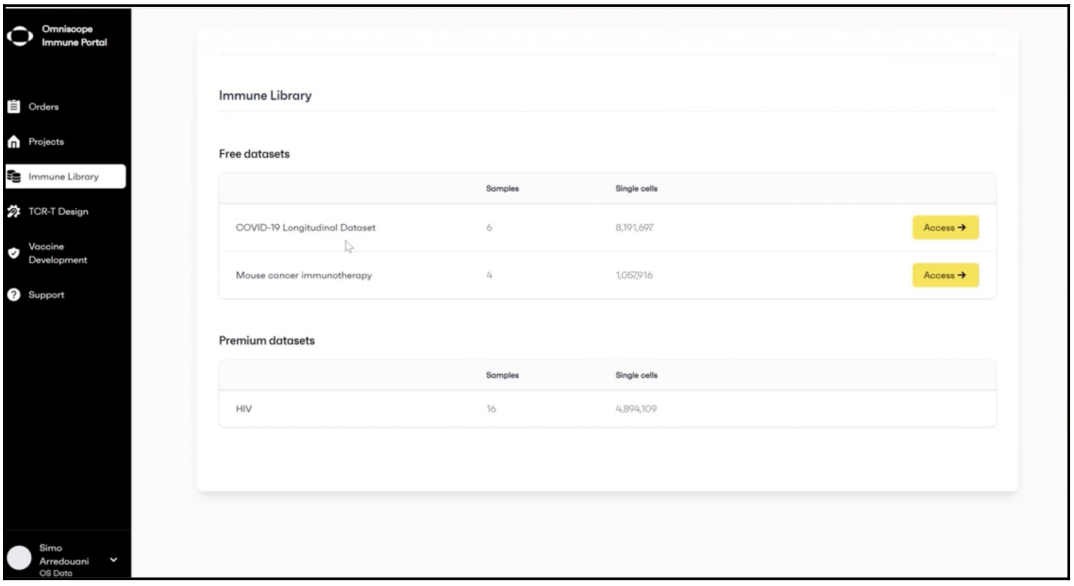
This slide is comparing our technology on the left. “OS” stands for omniscope; “T” stands for T cells or TCRs. This is the resolution of detection. The orange dots are the statistically significant TCR clonotypes that are triggered by the treatment. In the middle is a different detection technology, and on the right is another technology trying to detect the same thing. Our detection technology is evidently more sensitive–the detection is much higher.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

If we take 1 million cells in the lab and then make dilutions–we dilute it to 100,000 cells, 50,000 cells, 10,000 cells, or less–the more we dilute, the more signal we use. In essence, we are not detecting much when we dilute 5 or 10 times. The advantage of analyzing 1 million, which is unprecedented in our field, is really powerful.

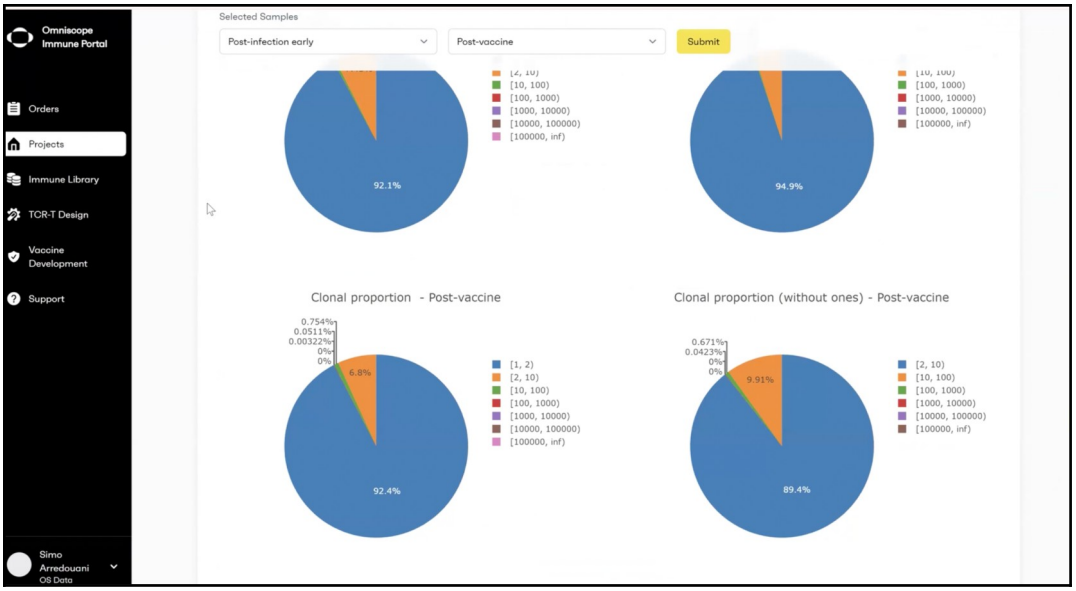


If you are really curious about Omniscope and want to learn more, I invite you to go to our website, omniscope.ai. We are an artificial intelligence company. If you click on “Immune Portal”, you can create an account free of charge. That account will allow you to browse the website.

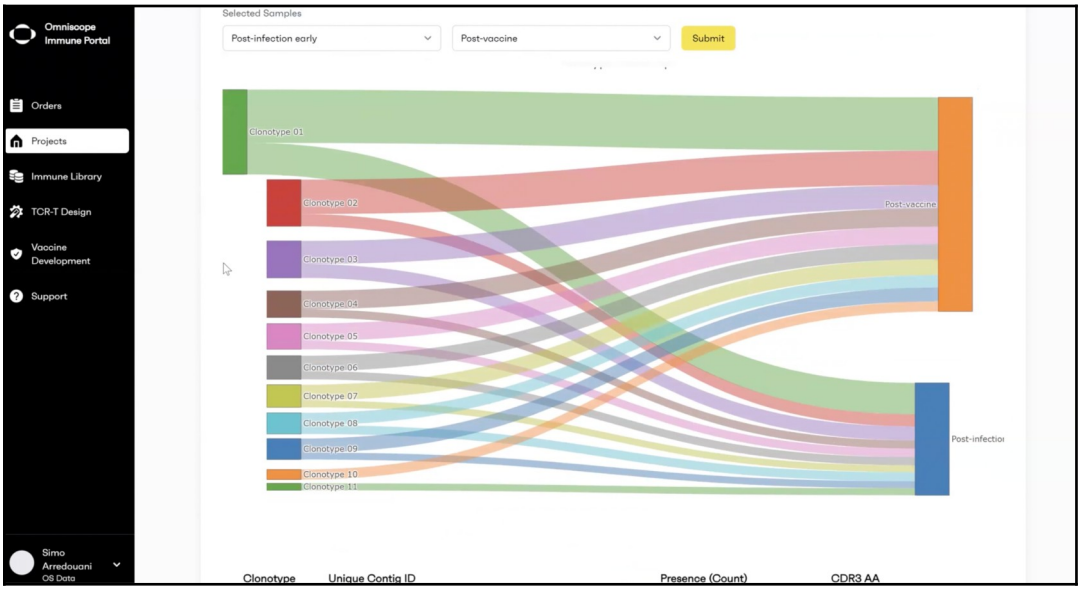


When you log in, you will be able to check a couple studies that we put out there for the public, just to get a sense of what's going on. This study, for example, is about a cohort of patients that

got COVID-19 and had the vaccine and the booster. We analyze the data from so many different angles using modeling and statistics.

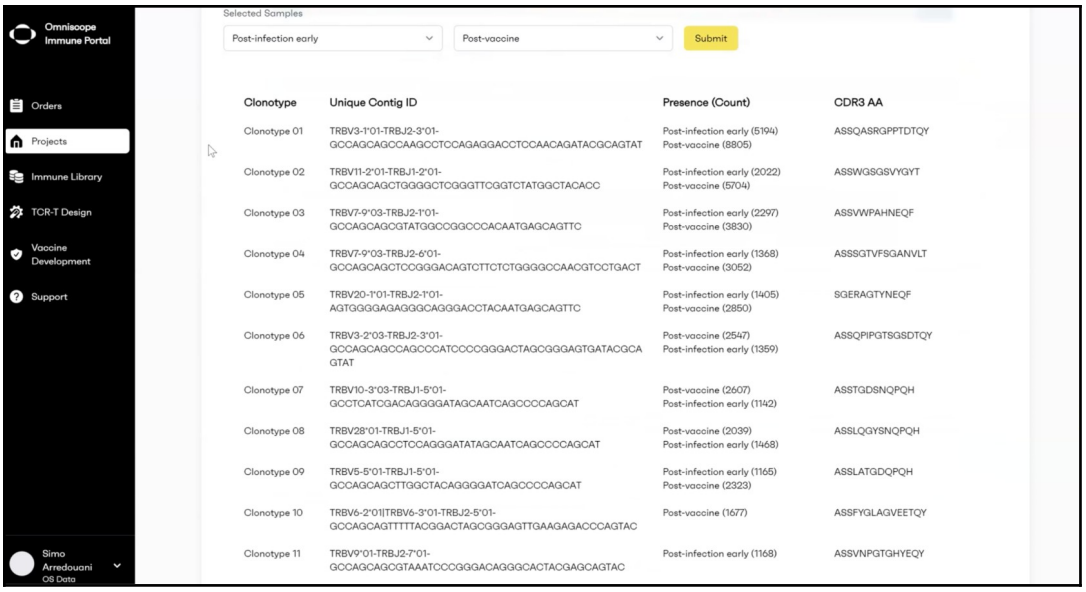


We have very high resolution plots. If you are in my field, you would appreciate every one of these plots, because each one is telling a different story. To have a view that is as comprehensive as possible is great.



You can actually play with the dynamics of the clonotypes. The thickness of the line tells you about the size of the T cell clone.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]



You also get the sequences. Everything is downloadable. You can reanalyze if you want.

Just by touching the dots, which are actually populations of T cells, it already tells you the number of cells post-vaccine and post-infection. For example, this one is almost 9000 cells which have the same TCR. This is what a clonotype is.

Please take a few minutes to visit the website, create an account, and play with some of the data.

Simo Arredouani 22:49
Once you are in the website, there is an entire section with videos. Videos are made by my colleagues and some of our collaborators in a way that could be understood by any audience.

You don't really need to be an immunologist or an AI person to understand. There is a publication section. We have peer reviewed papers. They are all publicly available, and we have scientific posters and high resolution PDFs that you can also browse. We have application notes where we describe the applicability of our technology in different spaces and different diseases.

Simo Arredouani 23:43
Brad, I think I went beyond your instruction in terms of 15 minutes. For that, I'm sorry; we have a lot of material. I tried to be as selective as possible.

Brad Power 24:00
You mentioned T cells and B cells, and I'm knowledgeable enough about the immune system to know that there's another kind of lymphocyte called NK cells. Why do you do T and B and not NK?

Simo Arredouani 24:34
T cells express the TCR receptor and B cells express the BCR receptor. That is what is driving the diversity of our immune system. With T cells, for example, our genome could easily produce 10 to 15/18 different combinations. The beauty of our technology is that it’s able to detect any of those combinations. To answer your question, NK cells do not have receptor diversity. They have some receptors that are extremely important in cytotoxicity, because they are “killers.” After all, that's what nature made them for. They have lots of receptors that actually produce our tissues from immune damage. They are inhibitory. But they don't have that diverse class of receptors like TCRs and BCRs do.

Brad Power 25:49
I understand that you can predict, or you can observe, response to an immunotherapy that's been started, like an immune checkpoint inhibitor. But do you have the ability to predict response before someone starts their treatment?

Simo Arredouani 26:12
For us to be able to do that, we need to have an idea of what happens to the repertoire when the treatment starts. We are gathering as many samples as we can, pre- and post-treatment. Once we can identify a repetitive trend that is actually changing every time you use the same therapy, we can then use it pre-treatment without taking a post-treatment sample. As I mentioned earlier, AI, machine learning, and algorithms are getting better with data, and we are feeding our AIs on a daily basis to improve them. The more samples we process, the more cancers we can take samples from and different therapies we can try. In addition, we can achieve higher precision in terms of the trends, patterns, and the repertoire dynamics, which we could associate with a certain parameter (for example, PD1 blockade).

Brad Power 27:25
Richard Anders, who is listed as Mass Medical Angels, has a question.

Richard Anders 27:45

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

B cell repertoire is kind of predictable, but T cell repertoire is going to vary tremendously by HLA type. I gather that you're looking at T cell and B cell repertoires when you do this. How do you deal with the vast diversity of HLA types? Or do you sort of figure it out using AI or something of the sort?

Simo Arredouani 28:23
Great question, and I have to actually take maybe a couple of minutes to answer in some level of detail. It's true that T cell receptors are HLA restricted. The TCRs we have in our bodies were dictated during thymic education, where the HLA alleles–each one of us has up to 12 different alleles, because we have class one and class two–is going to dictate what TCRs we get. That does not mean that we cannot make prognostic or diagnostic decisions based only on TCR. If we ignore HLA, we can do that. I will answer your question with a deeper answer: the HLA allele is extremely important if you want to know what your TCR sequence is seeing. If you want to know the antigen, you have to plug in the HLA allele so that you can then predict. We are working on that, and it’s not an easy task, because dealing with just the TCR alone is much easier than dealing with the TCR, the peptide in the middle, and the HLA. Part of that would require understanding the 3D structures of the TCR peptide MHC. There are different tools and prediction models that do that, and we are currently plugging that into our platforms.

Richard Anders 30:12
Just to clarify, I think isotype applies more to antibodies than TCR, but it seems you're sort of looking more at the isotopic level of the TCR receptor than you are of the actual receptor and what it hits.

Simo Arredouani 30:33
We actually do both. Isotype is for antibodies. Antibodies come in different isotypes, right? TCRs come in chains. There is alpha beta and gamma delta. We only do alpha beta right now, because that's where T cells most frequently occur.

Richard Anders 30:59
You're looking at broad stroke characteristics of the T cell receptor that are far less variable than the actual, granular T cell receptor.

Simo Arredouani 31:11
We are looking at the granularity, because what we are sequencing is the CDR3 domain, which is the diversity. Every sequence we get is the very diversity of that TCR. We don't measure the whole TCR, because most of the TCR is common sequences that we don't need to sequence–they are always the same. What changes in the TCR and the BCR is the variability region, which is what we capture and measure. Everything we measure is 100% diversity.

Simo Arredouani 31:53
At the level of DNA, there are little pieces of genes that make the TCR diversity domains: V, D, and G. That's what we capture together through PCR, sequencing, etc. Our AI is going to put them together and make sense of it. We do that for alpha as well as in beta.

Brad Power 32:20
I'm looking forward to writing up the notes and defining all the terms you were just throwing around, such as HLA.

Simo Arredouani 32:44
Brad, just give me a few seconds to define what HLA is: HLA stands for human leukocyte antigen. It's what makes every one of us unique. That's why I cannot just “get your kidney,” Brad, because my immune system is gonna reject it. If I get your kidney, I will have to put myself on immune suppression, because otherwise my body is gonna reject it. The language that tells the immune system what is foreign is the HLA. We all have different HLA, and humanity has more than 5500 different HLAs just in the class one alone. Every one of us is extremely molecularly unique when it comes to HLA and when it comes to TCRs and BCRs, and having a technology that captures all of this is just mind blowing.

Richard Anders 33:54
For bone broth transplants, that's one of the things that you need to do: you need to match people, because from a non-match donor, you're going to have an immune reaction.

Simo Arredouani 34:06
Absolutely. When someone gets a bone marrow transplant, unless it's from an identical twin, that bone marrow will never be identical. We do HLA matching, but not every HLA is a match, because it's not an identical twin. That means there is always a risk of immune rejection or an attack by the graft to the body. It's called GVHD, and we can actually measure the response. This technology, after the bone marrow is grafted or a human stem cell transplantation is performed, can track the expansion of the donor T cells.With some level of accuracy, we can also imply what antigens they are seeing. That's very important in bone marrow medicine, because if you can understand rejection early, then the Hematologist/oncologist can actually take some measures of precaution with the patient and keep an eye on them.

Brad Power 35:24
I'll just mention that I heard the term HLA because I got CAR T, and one of the entrance criteria was I had to have an HLA type of one sort or another. I think 50% of people have this kind of HLA and the other 50% have that kind of HLA. If I didn't have the right kind of HLA, then I was not going to be a candidate for CAR T.

Alane, you have your next step with a question.

Alane Watkins 35:58
Thank you. I was wondering if you've got much experience with a rare cancer called thymoma. It's a cancer of the thymus gland that implicates the B and T cells. If somebody has an autoimmune based cancer, does this technology get them to a vaccine that works? For example, in thymoma, there's very few mutations associated with it. Cancer vaccines are not always a viable option for patients with that cancer. I was wondering if you could speak about

that. If there's already a dysfunction in the immune system–in fact, that is the cancer, like in thymoma–how does this technology work for that?

Simo Arredouani 36:43
When there is an opportunity to develop a vaccine, we can actually be extremely helpful. When you say that thymoma doesn't have many mutations, that does not mean that it's not immunogenic. You can still find thymoma specific antigens for which you can make a vaccine. But what we can also do in addition to that, is get T cells from a patient with thymoma. If we can associate those T cells to the tumor with some precision–it will always take some laboratory validation–we can then use our TCR sequences to develop a TCR T cell therapy for that patient.

The reason why we started doing TCR T cell therapies, for example, is because not everyone responds well to vaccination. Most patients with cancer who tried vaccination found that it didn't work, and we only have one vaccine on the market: PROVENGE, for prostate cancer. Coming from a prostate cancer background, when PROVENGE was approved, I didn’t think it was a good vaccine. In reality, it's not a powerful vaccine. Because we cannot elicit a very good immunization response, we can actually make billions of those cells in the lab. That's what the concept of cell therapy is. You are going to make billions or hundreds of millions in the CAR T cell space in hopes of overwhelming the tumor.

So, yes: we can help with vaccine development, as well as with TCR T cell development, because we can also extract antibodies.

Brad Power 38:55
Helen has a related question. It's about Avastin: it's MRD or minimal residual disease monitoring, which differs from other treatments like immunotherapy. Obviously, you can track the immune system and how it's responding to an immunotherapy, but how can you also track something like Avastin? Is there a way for you to measure whether the Avastin is working for her rare ovarian cancer?

Simo Arredouani 39:34
Is the question about looking at residual tumor cells?

Nina Senna 39:43
I think it’s more about tracking efficacy in real time, longitudinally, and I've done some research–the drug mentioned is a monoclonal antibody, which we have experience with. So, yes, it’s super possible.

Simo Arredouani 40:01
Nina, I'm not aware of the studies that you just mentioned, so if you want to briefly give us an answer, go ahead.

Nina Senna 40:11

I'll do it as quickly as possible. The Avastin therapy, described as a monoclonal antibody, is something we have experience with. What the question poses is true: yes, we could, in theory, make a clinical trial for efficacy of the drug using only blood samples. As Simo mentioned earlier, as long as we build that database where we see enough positive and negative responders, we can then find that signature of response and use it for predicting before a patient is given that drug, therefore ensuring that the drug is allocated to the correct patient with its maximum impact possible.

It would be a longitudinal sampling after the trial for us to measure efficacy. Once we find the signature and we have that classified, and the model is trained, it can then be theoretically applied to another patient to monitor them across the course of their therapy.

Simo Arredouani 41:32
Thank you, Nina.

Brad Power 41:33
I think the answer to Helen is “we don't do it today, but we could do it.”

Nina Senna 41:40
Yes, exactly. We require samples from that cancer.

Simo Arredouani 41:44
Just to add on, when we don't have enough data to tell you something with confidence, we don't pretend. We wait until we have enough samples processed and analyzed where we are confident with outcomes; statistics are very important in our conclusions and statements.

Sandra Balladares 42:10
Thank you, Simo, for the presentation. I'm a big fan of the immune repertoire, and I think that, one day, the immune repertoire could be used to determine the state of disease or health in an individual. What you just presented is super exciting. How do you calibrate for other factors that individuals may have that may switch that pattern of the immune repertoire?

Simo Arredouani 42:45
That's a very nice question. Our repertoire is shaped by our exposure to everything. For example, if we take your blood right after you had the flu, your repertoire is going to be skewed toward anti-flu repertoire. Similarly, if we take your blood after you got your flu shot, then we can see immediately that you have the vaccine, because what the vaccine is going to do is reduce the diversity of the immune repertoire and hone in on a few clonotypes, which are the anti-flu clonotypes.

When we analyze our data, we look at those things. If you take a sample from a supposedly healthy person, there is a certain expectation in terms of TCR repertoire diversity. There are entropy and diversity parameters that we measure; we can say, whether there are perturbations in the sample or not, we take those into account.

Brad Power 44:01
Thank you. Cindy Ness, you're up next.

Cindy Ness 44:07
Fascinating presentation. I'm thinking about how to bring this down to the level of therapeutics for the patient. Clearly, this is not coming out of the standard of care treatment space/institutions. What would this look like for someone who wanted to come to Omniscope? When you introduce this as a possible avenue of therapeutics that a patient should be considering before or after they start any treatment, what can I tell my patients? How would I describe Omniscope to them?

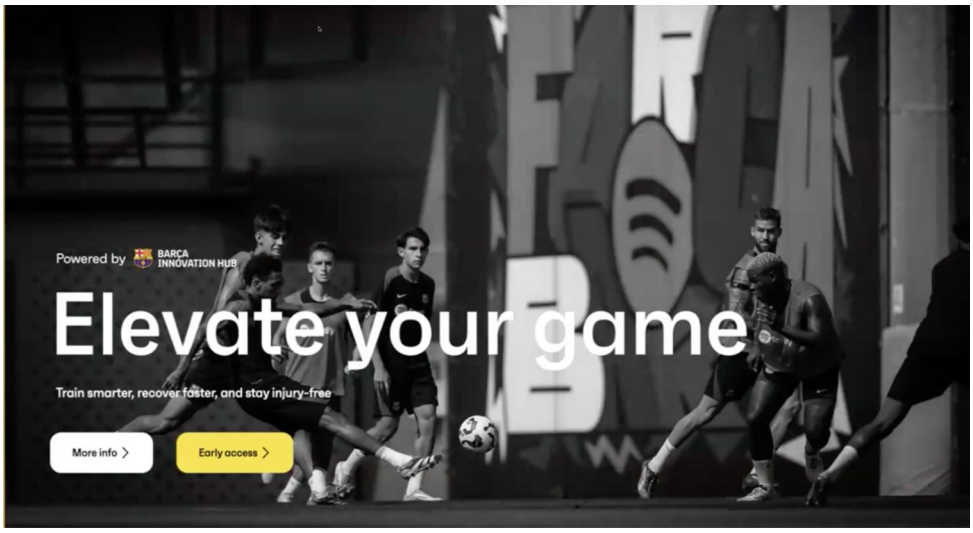
Simo Arredouani 44:55
In terms of Omniscope’s applicability to the clinic as a prognostic or diagnostic tool, we are not yet there, but that's the path we would like to take, as that's how we can help patients. That path has regulatory and insurance components. The oncology community also has to foster and adopt Omniscope.

Hopefully we'll get there, and when we do, then the patient is not actually required to do anything. It's the oncologist who is going to say, “Oh, I have this good treatment for you. But first let's send your blood and see whether you are a good candidate.” It will just become one of the measurements of eligibility. The same way we measure mutations, we measure PDL-1 expression, micro-satellite stability, and many other things that are now implemented. All of those assays had to go through much development and approvals to get there. In essence, we are on track, so hopefully we'll get to the end.

Cindy Ness 46:06
Is Omniscope available now? If I wanted to send a patient to you, what would you do with that person?

Simo Arredouani 46:17
That could be available only if it goes through your hospital and your oncologist. You are giving me the chance to mention another product we have for the general population who want to understand the strength of their immune system. We only process samples in one hospital in Barcelona, but our strategy is to expand it so that everyone can send the sample to us. Then, we submit a report with many details about the fitness of the person's immune system. I'm not talking about sick people–just the average person.

I would also like to mention that we are already using the technology to assess the health or immune health of professional athletes. We recently signed a big collaboration with the soccer team FC Barcelona. If it's not the best soccer team in the world, it's probably the second best or third best. We are extremely proud to be working with these guys. Our company is located right next to the stadium, so the collaboration entails us tracking the immune health of their athletes just using a sample of blood and nothing else.

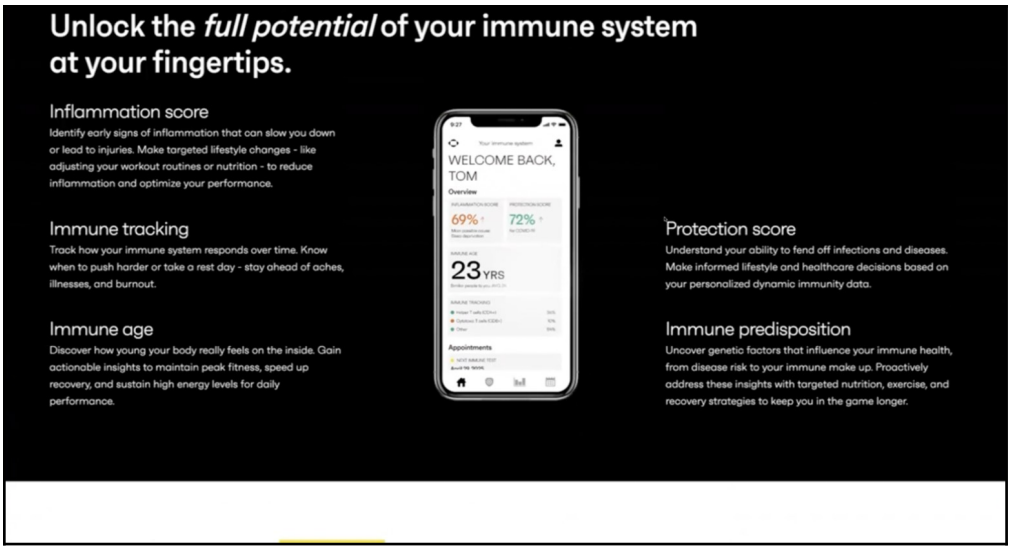


This is how the website looks. If you want to do it, you would have to go all the way to Barcelona to give a blood sample–not very practical! We will do our best to bring you to the US.

By understanding the dynamics of the immune system of the athlete, you can actually make some suggestions in terms of arrest, physical effort, taking some breaks, fitness to play games, etc.

Nina Senna 48:32
To complement the answer, this perfectly poses the tech for any patient use. If a patient is interested and wants to circumvent speaking to their hospital, clinician, or doctor to send us the blood, this is exactly the way that they would do it. We currently have it open, as Simo said, for athletes, but we do see this as our customer facing product where a patient themselves can take advantage of understanding their immune system.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]



We've launched with these five features, but more are on the way. We just launched this two weeks ago, so that's why it's so new. As he said, we launched it together with FC Barcelona, but the Early Access is open to anyone who would like to sign up.

At the end of the page, there's a form. It's open for everyone who wants to explore their health. Of course, this is Research Use Only. It hasn't gone through the correct approvals, but these are the first steps to getting there. To elaborate, the first steps are using it as a stratification tool, therapy stratification tool, or e a prediction of what is the best course for the patient. Thank you.

Brad Power 50:00
Alane is a Global Traveler, and she's looking for an excuse to go to Barcelona.

Alane Watkins 50:12
Already looking at flights!

Brad Power 50:13
What would the consumer accessible test cost?

Nina Senna 50:21
There's currently no set price because it's still early access. If you are interested, sign up on the form. I'll send you an email, and we can take it from there, because there's different features. The price ranges from 2000 to 5000 for early access one year.. Of course, you would have to go to Barcelona, but we could talk more via email.

Brad Power 50:49
Okay, Rick Davis is up next.

Rick Davis 50:52

Now I understand why FC Barcelona is having such a good season this year. I think I'm going to recommend it to Mikel Arteta. I'm interested in how this technology applies to cold tumors. Since Simo comes from a prostate cancer background, he probably understands the root of my question. By the way, Dr. Fong is on our advisory board, and he's a wonderful doctor: he’s not only smart, but very compassionate as well. What I'm wondering is whether this could be a shortcut, saving time and money for researchers who are trying to figure out how to make a cold tumor hot; whether they can make shortcuts, using your technology, and cut off a line of research quickly if they find that there's no response,

Simo Arredouani 52:05
Great question. There is actually a huge amount of effort in the pharma industry to find modalities that would allow you to turn a cold tumor into hot. Theoretically, there's a lot of options, like cytokines, but cytokines are toxic. You can do it with antibodies. You can do it with vaccination. Vaccines can turn your tumor from cold to hot. That's doable.

Our technology can do something in this space. We know that you don't need to have cancer to have tumor specific T cells in your body. I had the pleasure to get in hundreds, if not thousands of TCR sequences from healthy people who never saw cancer. Because of the diversity of our repertoire, we have TCRs for basically anything, including two tumor antigens, even when we don't have cancer. Our technology can actually go see those T cells in the healthy patient. In the prostate cancer patient, there will certainly be more T cells. The coldness of the tumor does not mean that you don't have T cells that see the tumor. It means that you don't have them in the tumor, but you have them elsewhere, and we can see that in the blood.

Our technology is not going to turn the tumor into a hot tumor. It can probably provide a new set of science to trigger some new research. But we don't have the ability to go from cold to hot, because that's an issue in a lot of solid cancers, not just prostate cancer.

Brad Power 54:17
We are approaching the hour. It seems we've run out of questions. I'd like to give Simo a chance to wrap up with any parting words of wisdom or any key message you want to leave with us.

Simo Arredouani 54:34
Thank you, Brad, for the invitation. Thank you for a very curious audience. I enjoyed the questions, and I'm trying to figure out some of the answers that were not really clear in my mind. I will go and do some research and develop myself further.

The mission of Omniscope is to get to the hospitals and help patients. We cannot take therapies that only see 20% response. It's too costly; in the US, we are bleeding with the cost of health care. Part of it is that we don't have tools to stratify patients. That's one of the areas where we are putting a lot of time and thinking to really get tools that can stratify patients. Predictive tools are also very important, and we're trying to expand our science to transplantation, auto-immunity, immunodeficiency, and bone marrow transplantation. We can actually get involved in

anything that is immune-related, or where T cells and the B cells play a primordial or important role.

We are helping science for discovery, for drug development, and for, ultimately, helping the patients.

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

CHAT CONVERSATION

00:34:38 Alane Watkins: Clarifying question: when he talks about million cells, is he referring to T cells or circulating tumor cells?
00:37:06 Nina Senna - Omniscope: Replying to "Clarifying question:..."

Hi Alane! And thank you for the question. We are able to capture 1M T cells per sample, this is what Dr Arredouani meant
00:41:30 Koryn DelPrince: I’ve been seeing time and time again people with “UBOs” (unidentified bright objects) on their MRIs. Someone seeking a diagnosis without an invasive biopsy (specifically with regards to something deep seated within the brain), where would they start if they wanted to use something like omniscope for diagnostics?
00:42:27 Rick Davis, AnCan Foundation: For research addressing cold tumors, can this technology cut time and costs? Are researchers adopting it?
00:46:24 Nina Senna - Omniscope: Here’s where you can read more on our published work: https://www.omniscope.ai/publications
00:48:32 Nina Senna - Omniscope: For those interested, our Application Notes are a quick read and aimed to not be too deep into specifics - poised more to offer explanations on the technology’s application in different areas. You can find them here: https://www.omniscope.ai/publications
00:50:31 Nina Senna - Omniscope: Super interesting question! We also see a high impact the technology can make in transplantation. Not only in matching donor/patients in a way that minimises toxicity, but also in monitoring and early-detection of toxicity. We are involved in a trial currently investigating this in kidney transplants. Here’s more info on this trial: https://tackleit.com.au/
00:51:34 Helen: This question may not make sense: Question re AVASTIN, a study in the UK was looking at the efficacy of Avastin on each patient by looking at a molecule called Tie2. I’m not a scientist and hardly understood the presentation. But where I receive Avastin, in France, other than the normal blood works, there isn’t a specific test to see if I am responding well to AVASTIN, if indeed it is working on my rare ovarian cancer. Is Omniscope able to assess Avastin’s success on a patient, in real time?
00:56:00 Helen: Thank you.
00:59:02 Nina Senna - Omniscope: Replying to "This question may no..."

Yes absolutely. Here’s a study where we did something similar, where we used our blood-based T cell test to track efficacy of a therapy. We were able to find a shared signature for positive response - from the pre-treatment sample! This proved that, with as little as 20 patients, our technology goes deep enough to unearth these signatures and hence predict - from initial sample - poor and positive responders to a cancer therapy. If you’d like to read further here’s the study I am mentioning😊 https://eu1.hubs.ly/H0crJM10
00:59:55 Alane Watkins: Is this available now to patients in out of pocket or clinical trial setting?
01:03:03 Alane Watkins: What is the cost of this immune test
01:03:22 Helen: Replying to "This question may no..."

“Unlock the Potential of Your Immune System” (Simo Arredouani, PhD) [#135]

Thank you
01:05:36 Nina Senna - Omniscope: Here’s the webpage I shared earlier where anyone interested can sign up: https://www.omniscope.ai/sports - if you’d like to have specific conversations after this, please feel free to reach out to me on nina@omniscope.ai
01:08:46 Alane Watkins: This was incredibly helpful…thank you!
01:09:02 David Plunkett: Reacted to "This was incredibly ..." with 👍
01:09:06 Sandra Balladares: Thank you very much for the presentation! I have to drop, looking forward to seeing you in the next meeting
01:09:20 Koryn DelPrince: Thank you!
01:09:28 Nina Senna - Omniscope: Reacted to "This was incredibly ..." with 🙏