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Hi, and welcome to FYI, the four-year innovation podcast.
We are extremely excited today because we have Dr. Patrick Hu and we met recently at the Moffitt Cancer Center where he is the president and CEO.
Dr. Hu's career has been really incredible.
His current role is really exciting and one we'll definitely dig more into and really trying to leverage the community and create a real biotech community within the Tampa area.
We'll definitely talk a little bit about that.
It's also one of the things that Arc is working on as well and we have a couple of initiatives that maybe we'll share throughout the podcast, but important to note also that Moffitt Cancer Center is one of the nation's leading cancer hospitals.
It's also the only National Cancer Institute designated comprehensive cancer center based in Florida.
Dr. Hu, before that was as many of you probably have heard of and know it fluctuates, but usually the number one cancer center, which is the University of Texas, MD Anderson Cancer Center, and he was there for about 17 years.
Dr. Hu is internationally recognized.
He's a tumor immunologist, which we'll get more into and give some definitions there.
And he really led some of the pioneering research and clinical efforts to really better understand the interactions between tumors and the immune system and helped launch really the field of gene modified T cells.
So we're really excited to talk more about that.
Tons of research that Dr. Hu has done on many things related to cell therapy and others like the first chimeric antigen receptor directed against cancer.
And a lot of Dr. Hu's work focuses on vaccines, adoptive T cell therapies and immune resistance.
So we're very excited to have you on as you can probably tell, and I'm just excited to dig in.
Well, thanks so much, Allie, for having me on today.
Yeah.

No, we're excited.
First, I should say, is there anything that I missed that you wanted to highlight about your background or anything like that?
I think you covered it all.
I was at the National Cancer Institute where I worked with Steve Rosenberg, then MD Anderson, and now really excited to be in the Tampa Bay region to be heading up Moffitt Cancer Center.
Awesome.
One of my favorite books is the Transform Cell.
So a good plug for Steve Rosenberg, but impressive career.
So let's kind of get into the meat of it.
So immunotherapies, as we know for anyone listening that maybe has heard the term before, we've talked about things previously like CAR T's or like TILS.
They've gotten some pretty significant traction and there's also been some sort of setbacks for the field, I think in recent years, but we recently did a podcast for anyone who's interested and wants to know sort of a little bit more from some of the clinical perspectives and something we've talked a lot about was with Dr. Wasim Kaseem.
He had incredible success.
He treats pediatric patients with really difficult to treat cancers like T-cell lymphoblastic leukemia and others.
So I think to set up this podcast, maybe let's start sort of at a very basic level.
So what is immunotherapy and sort of how it differs from traditional cancer treatments and maybe sort of some of the benefits when we think about it compared to sort of the traditional chemotherapy?
That's a great question.
Chemotherapies kill cancer cells directly.
Immunotherapies stimulate the body's immune system to then fight the cancer.
And one of the advantages of this is that the immune system can go on and continue to fight that cancer.
One of the most important cells that we focus on is the T-cell, which can do what I call the kiss of death with a cancer cell, can touch the cancer cell, release enzymes that poke holes in the cancer cell and cause death to the cancer cell.
And then immune cell goes on to another cancer cell and can just continue to kill large amounts of cancer.
Now, those immune cells can live in the body for a very long time, in fact, decades.
And that's why with immunotherapy, as opposed to many other cancer therapies, you can get long-term, durable responses.
That's what patients want.
They want to be around five years from now, 10 years from now, 20 years from now, see their kids grow up, walk their daughters down the aisle.
And that is what immunotherapies can do in some patients.
Now, there are some patients where immunotherapies don't work, and we're still working very hard to get this to work for more people.
That's a really, really helpful overview, I think.

So thanks for that.
And I think for me, and probably for a lot of other listeners, you mentioned you were at the NCI.
To me, that was sort of the birth of immunotherapy.
I mentioned the book, The Transform Cell.
That was one of the ways I learned about it and sort of see it as the birth there.
So would love to know, you were sort of at the precipice when all of this was happening.
And so we now know sort of the benefits, the drawbacks.
The whole story has already unfolded, or I guess you can say the sort of interlude to the story.
I think there's going to be a lot more that we'll hear, but you were there really for the birth of this whole movement.
And what you say is so important because it's not that this targets your cancer cells specifically.
And as we know, if you don't do that, you're essentially wiping out your immune system and sort of starting this rebirth.
And so you're already sick with cancer, and then your immune system takes a huge hit.
And so I think immunotherapy has so much promise.
And so being at the precipice of when this all started is pretty incredible.
And we'd love to just hear about maybe some of your aha moments and really how you single-handedly
shaped the field and the landscape for immunotherapy, or what we know of today as immunotherapy.
Well, it was a really fun time.
I worked with Steve for 14 years, starting in the early 90s, and it was a really fun time to study the body's immune system against cancer.
That time it was a fairly novel concept, and most of the cancer treatment world did not believe that the immune system was important in treating cancer.
It was a funny thing.
We would go to conferences.
We would always be on the last day.
Our posters would always be in the smallest quarters in the furthest corners of the room.
But there was a group of people, I would say a couple hundred, around the country and around the world that really believed in this approach.
And so we got to be quite a tight community.
We saw some things that really made us believe that this could work.
For example, when we started growing immune cells from the cancer, a reasoning that the cancer had immune cells that were trying to kill the cancer, but obviously not doing a good enough job because the cancers were growing, we learned to take those immune cells out of the body, out of the cancer, grow them to billions, and then give them back to the patient in a process we call tumor infiltrating lymphocyte therapy.
And in our first few patients, when we saw large amounts of cancer shrink and go away, then we knew we were onto something that the immune system was very special and could shrink large amounts of cancer.

It was very exciting for us to see those first responses in patients to novel T cell based therapies.
That makes a lot of sense.
I think that's a really good precursor for when we talk about the advancements in immunotherapy.
So that was when you were at the back of the pack, no one was listening, no one cared.
You were accepted at the conferences, but you were the stepchild, which you were completely at the back of the conference.
That's not the case anymore.
I've been to plenty of conferences in the last couple of years where immunotherapy is just so prominently showcased as it should be.
Maybe now we can take a moment just to talk about some of the exciting advancements that are going on even within your own lab and your own clinical work.
Great.
Yeah.
So I think there are a couple of ways that we can stimulate the body's immune system.
One is taking the breaks off of the immune cells that are already in the body.
We call that immune checkpoint blockade.
The most common drug is anti-PD1.
There are a lot of different brands of that.
But it's taking the breaks off the immune cells that are in the body.
And with that, we can get long-term durable responses in some patients with what we call immunogenic tumors or tumors that are already trying to stimulate the immune system, such as melanoma, kidney cancer, bladder cancer, and some lung cancers.
The other big area is T-cell therapy, where we take immune cells either from the tumor like we talked about tumor infiltrating lymphocytes, or we take them from the blood and put genes in them to allow them to recognize the cancer.
And we're seeing great responses there as well.
With T-cell therapy, we're seeing that in melanoma.
And I think probably this year sometime we'll have the first FDA-approved agents for melanoma with T-cell therapy.
And then with the blood and taking the CAR-T receptors into putting those into blood cells, we're able to really attack blood cancers such as leukemias, lymphomas, and myeloma.
And with that, that was also something that we helped to innovate back in the National Cancer Institute in the early 90s called CAR-T.
We take immune cells, T-cells from the blood, put a receptor gene in them that allows those T-cells to recognize cancers, and then we give that back to patients.
And so that so far has been most effective in the blood cancers, but we're working very hard in the lab to try to get those to work against solid cancers, breast cancer, colon cancer, and other cancers as well.
And is that one specifically the TIL program?
Is that a partnership with Iovans, or is that a separate entity with Moffitt?
That's one of the programs.
Iovans is one of the companies.

Probably, we never know how these things go.
We may have the first FDA-approved TIL product, and we did work a lot with Iovans.
We're also working a lot with Turnstone Biologics right now to try to get the next generation TIL product, where we're sequencing the tumors and trying to get much more specific T-cells out of the tumor to improve response rates yet further.
Are you guys also working on gene-added TILs?
Yes.
In my lab, we're using a lot of CRISPR.
It's incredible.
The CRISPR technology is a lot of fun.
CRISPR is a way to edit genes within a cell.
All of our cells have the same number of genes.
We have about 20,000 genes.
And with CRISPR, you can take out a gene, you can overexpress a gene, you can change a gene.
And so what we've done so far is to take out genes.
And we've used libraries to figure out which genes we can take out of a T-cell and have the T-cell work like a super soldier.
And one of those aspects, we've taken out a metabolism gene.
And now the T-cell acts much more like a cancer and just explosively proliferates upon contact with the cancer.
So we're really excited by these approaches.
And I think with T-cell therapy, we're just getting started because there's so many different kinds of ways you can use technologies like CRISPR to modify T-cells for T-cell therapy.
Yeah.
And I think we've been highlighting some of the incredible things that have happened within the field from going from things that people were maybe not as excited about when you started here with the NCI to now this is a whole field and it's impacted by so many other fields.
So I always say when we talk about gene editing,
I think a lot of people assume that that's in a silo and immunotherapy is in a silo,
but it's really great to see.
And we talk about this a lot in the context of ARC,
the convergences between and among these technologies.
So CRISPR is great for gene editing.
It can also be done within an immunotherapy context.
And then we may see even better results for patients,
which is ultimately always the goal.
So I think the work you're doing in this area is just incredible.
Thanks.
It's really all of these fields converge.
So I think as we learn to treat cancer better,
these technologies are also used.

For example, now you can potentially cure sickle cell anemia
using the same kinds of technologies.
Right.
And that could be the first gene edited product to come to market.
So there's a lot of great catalysts with the regulatory pathway for this year
in terms of what's been submitted.
So we'll find out some interesting catalysts for that.
But I think that leads us to an interesting question,
which is we're working on all this amazing stuff.
We need to get it approved by the FDA
in order to have patients taken in a commercial setting.
So I think there's a question of what we do
in terms of the regulatory framework, right?
It does need to change in some ways
because there are new treatments and new modalities
that are coming to the FDA
that they've never seen anything like it before.
So we want to get these cell therapies over the line.
We want to get them accepted.
We want to bring them into commercialization.
I know we talked a little bit about this,
but you were working with Iovans on their till manufacturing.
The company has submitted their BLA
or their Biologics Licensing application to the FDA.
It takes a long time.
They're lengthy processes.
And maybe this is a big question that we'll find out what happens
and how we need to change ourselves
in order to better get these things accepted
and keep the safety as the most important for patients.
But it's been a challenging process for the company.
They're just new complicated medicines.
They bring new hopes for treating challenging cancers,
but they do also pose these interesting regulatory problems.
So you've started from the beginning in this process.
And so I'd be curious to hear from you
what your views are on some of these challenges
and how you think the cell therapies will evolve in the future
from this regulatory pathway perspective.
Yeah, it's a great question.
And first I want to preface it by saying,
I know a lot of the people personally
that work at the Food and Drug Administration,

these people are service-oriented people.
They want to see great drugs go to people.
And I think a lot of people blame them for inefficiencies.
But I can tell you, it's not an easy process,
especially when you're the first product of a kind.
And I think that's what the challenges have been so far
with TIL therapy.
If you'll think about the CAR T's that have been approved,
they were against a very specific target.
The first CAR T was against a target called CD19.
And so we knew exactly what those lymphocytes
were going to recognize.
A TIL cell coming from the tumor and growing that up,
that can recognize thousands.
There's probably thousands of different kinds of T cells
in that TIL product.
So it makes it much more challenging to regulate
and to understand.
You're just not going to know what all the specificities are
that TIL recognizes.
So we need to find different ways to ascertain
and make sure that TIL product is solid.
And so I think that's what some of the challenges are,
because this is the first product of its kind.
But I think once we get through this,
the subsequent products, hopefully,
will be much easier to regulate.
But we do have to continue as a field
to streamline regulatory issues and to make sure
in that time frame between the laboratory idea
to the clinical trial to the FDA approval,
because it's when you get to that FDA approval,
that's when you can explosively cure more people.
I remember with the anti-PD-1s, now an Evolumab,
Pembrolizumab, those are the first two.
We could only treat and cure very few patients
when we had trials that had very limited numbers.
But as soon as that got FDA approved,
we were able to treat just thousands of people
and cure a lot more people.
So that's why we have to, as a society,
continue to shrink that time between the lab idea,
the clinical trial, and the FDA approval

for drugs that can really save lives.
Definitely. And while we're sort of on this complex topic,
we were talking about all the benefits,
and there certainly are.
But I think it's important to highlight
some of the challenges.
So one challenge, obviously, is regulatory approval.
And you mentioned accelerating the timeline.
So the timeline for context now is around $1 to $2 billion,
and probably it takes from ideation to commercialization
something like 10 years.
And that's obviously a huge challenge.
And ARC, we think those things are definitely improving
based on the convergence between artificial intelligence
next-generation sequencing.
And we think CRISPR is helping,
both from pre-clinical screen perspective,
but we also think it could command premium pricing
because it's potentially curative.
Some of these cell therapies may also
command sub-premium pricing.
So I'd be curious to know, I mean,
one of the things that would help sort of the pricing debate,
but also maybe even accelerate these approvals
is these cost declines.
And how do we lower the cost of these medicines
so that hopefully we lower some of the premium pricing
and we're able to get the money back to the investors,
but also encourage and incentivize pharmaceutical companies
to continue working on these potentially curative therapies.
So at ARC, we love following cost declines.
So we typically talk about Wright's law.
I mean, Wright's law for anyone who doesn't know
is a forecasting tool and it focuses on cost declines
and follows the rule that for every cumulative doubling
of units produced, costs will fall by a constant percentage.
So obviously no math needed here, no specific calculations,
but how quickly do you think costs for cell therapy
or other important drugs could decline
so that these therapies could be more democratized?
But again, while pharma and investors
can still be incentivized to produce them.
It's a great question.

We absolutely need to make these more scalable.
And I really think that we can do this rather rapidly.
There's really two ways, I think.
One is to really get engineers involved, bioengineers,
and we're starting an engineering department
within Moffitt Cancer Center.
We have a wonderful chair, Greg Sawyer,
who's going to be initial leader of that.
And one of their goals is to scale a cell therapy.
There's a lot of manual processes
that could just be done robotically.
And so I think that is going to really help us scale.
The other way is why do we need to make 100 billion till cells?
It's possible if we crisper and make them
much more effective super soldiers,
we could treat with a few million.
And a few million would be a lot easier
than making a few billion.
And so I think those are the two ways.
We can engineer with, take the manual processes,
make them much more automatic.
I think one day we'll have just a box
that will put the cells in at one end of the box.
The other end of the box will get the cells back.
So engineering that process and then innovating
even more effective cells so that we can give fewer cells
and fewer cells that have been cultured
for smaller amounts of time.
So I think those are the ways that we're going to cut the cost.
I think rather rapidly for cell therapies
so that once these get approved
that they can be distributed to all the people who need them.
Yeah, I think those are all really, really good points.
I was reading an article.
It's a gene therapies algenzema,
but I was reading an article about a government in Brazil
and a bit of woman who sued
because she couldn't afford the medication
but her son desperately needed it and she actually won.
And they did a type of value-based care model.
I think this was in the Financial Times.
And the idea is that as long as you're benefiting
from the medication, people should get it,

farmers should be incentivized, investors should be incentivized,
and patients should have access to it.
So it's going to be a really interesting model
to see how we can employ and work with payers
and get some type of value-based framework
where everyone's values and incentives are aligned.
So I'm really excited to see sort of how this evolves.
But as you mentioned, the quicker we can get the cost to decline,
I think the easier it will be to implement
some of these pricing processes.
So really excited to see how that shakes up.
Yeah, absolutely.
In fact, Ali, even with what we have today
and all the therapies we have today,
if you just plug someone's zip code in,
they're going to have far variable outcomes.
Just their zip code.
Part of this is genetics, part of it is societal,
part of it's environmental.
But there's also a part of that is access to the care
and be able to be with physicians
that know about all of the cutting-edge possibilities
that are out there.
Exactly.
And I know we talked about this briefly,
but I love the idea of creating some type of resource guide
because I actually think there are so many resources for patients
that people just don't know about.
One such resource is clinicaltrials.gov,
which is a government-run resource,
and it has all the clinical trials that are available
at all of the centers, including obviously
your own at Moffitt Cancer Center and others.
And so there are a lot of these resources to help patients.
And so to get the word out there and to get access
when access seems difficult is definitely
something that everyone should try helping with.
Yep.
So sticking on the challenge side,
I don't want to be overly negative,
but of course, there's so much promise
with a lot of these therapies.
And we know about that, and we've highlighted some of them.

But I want to stick to sort of like,
how do we make it even better?
So another challenge in immunotherapy
is just understanding why some patients respond
and others don't.
And so maybe it'd be helpful to hear a little bit about
how we're making headway on this.
Some of the modalities that may help our biomarkers
or something that I worked on the past
was using artificial intelligence
to try and find patients that were most likely to respond.
Because if you did, your costs would go down
because screening a ton of patients can be expensive.
And opening a ton of centers for your clinical trial,
if they don't have the right patients
that will respond and recruit quickly is also expensive.
But also having patients who respond
means that you can get that data to the FDA even sooner
and hopefully get to commercialization
a little bit sooner as well.
So just curious on how you guys are thinking
about which patients respond, which patients don't,
and how do we get these medicines to the patients
that will actually respond?
It's a really great question.
We have to continue to get better at this.
You're talking about getting the right drug
to the right patient at the right time.
And the question is, how do we do that?
These biomarkers can be quite complicated.
I treat advanced melanoma, a disease
that starts on the skin, goes throughout the body.
We used to have nothing but a couple of chemotherapies
that really didn't work very well.
And so that's what everybody got.
Now we have so many great drugs, targeted agents,
immune agents.
Sometimes in the clinic, I'm a little confused
as to which ones to use first, which ones to use second,
which ones to use third, and in what populations.
Because we still need to do a lot better with the biomarkers.
We have some hints.
So for example, if they have specific mutations,

if there's a BRAF mutation, for example,
in my melanoma patients, I know that targeted agents,
pills that cut off the circuitry that allow cancer cells
to proliferate, we can use those pills.
So some of it is looking at the mutations in the cancer.
Some of it is looking at the immune cell infiltrates
in the tumor.
But none of those are perfect yet.
And there's a lot of overlap between patients that respond
and don't respond.
There's one thing to say, there's a statistical difference
in the responders and non-responders.
And you can write a nice paper with that.
But for me in the clinic, you have to have huge separation
between the responders and non-responders in your biomarkers
in order for me to make a clinical decision.
For example, if there's a hint that this group will not
respond as well as another group, but yet some of the patients
in that group still respond really well,
I'm still going to try for that patient,
because they may be one of the ones that respond really well.
We need a huge separation of those two groups.
For me to have a clinically relevant biomarker.
And so we really lack those right now.
What we need to do though is put all of our data sets together.
There's so many ways to analyze the patients.
One is using what's called germline DNA,
and that's the DNA that you inherit from your mother
and your father.
So everybody probably has a different ability to respond
to different therapies based on their germline DNA.
The other is the tumor DNA,
the sequences of the DNA in the cancer
with a lot of mutations in some cancers
and other genetic abnormalities.
Then there's the immune components of how that works.
There's a lot of the environmental and behavioral
is a patient a smoker, for example, or they obese.
And then there's new techniques, most exciting
which is spatial analysis, where we can now do sequencing,
not just of the whole cancer,
but we can sequence and figure out,
are the immune cells next to the cancer cells?

Are they next to blood vessels?
Are macrophages next to the T cells?
And we can define these spatial neighborhoods.
And I think this is a lot of data,
but if we can put all of that data together,
my hope is we can really figure out who responds,
who doesn't respond to different therapies.
And then in the clinic on that precisely,
let's give this drug, this combination of drug,
to this patient.
We're getting there.
And that's a lot of data.
So we're going to have to use AI,
artificial intelligence and other ways to put it all together
because there's just too much data.
I used to be able to put all my data
on a handwritten spreadsheet, Ali,
but now it's, there was so much data
that we're really going to need machine learning
to go through that and help us distinguish
clinically relevant biomarkers
that will allow us to determine
which drug to give the patient at the right time.
So as you mentioned, one of the challenges,
not only with melanoma, not only with immunotherapy,
but I think playing society is we have so much data
and data is like gold.
Data is so valuable, but I think one of our challenges now is,
okay, what do we actually do with that data?
And how do we clean the data?
And how do we analyze this data?
So even the idea that we only had a spreadsheet
or that you only had a spreadsheet
of your patient's data previously is so interesting
because you were almost working blind before,
whereas now you're almost oversaturated
and there's so much noise within the data
that it would be great to get it to a place
where we're definitely getting actionable insights
from a lot of the data that we see now,
but it would be great to even get further insights.
And on my tour of Moffitt
that you generously invited me to do,

one thing that struck me is how data driven
you guys are.
So I just kind of wanted to highlight that for a second.
So you have obviously extensive departments
and one of the things that really I thought was interesting
was you guys have a specific math oncology department
which essentially takes whatever data you can have
and you try to predict a patient's potential trajectory
which I thought was pretty fascinating
and some of the data coming out of it looked really great
and I actually want to circle back with the team
and maybe something we can focus on in a later podcast,
but just amazing how we can actually utilize that data
in a really productive way.
I know you also have NALMEL, AI, LLM department.
If there's anything you kind of want to add here,
I just think the way that you guys are differentiating
yourselves and really focusing on the data
and separating it from the noise
and getting actionable patient insights.
And I think one of the math oncology department examples
that we heard was specifically about like,
is this patient's best drug going to be the one
that we're choosing for that patient
and how will they respond to it?
So I think the more we can do for that,
the better for patient outcomes.
So we'd love to hear just a little bit about
how you guys utilize math and data aggregation and LLMs
and it's pretty impressive how you guys
incorporate all of this into sort of your clinical
and bench research.
Oh, thank you. It's a great point.
I like the word that you use.
There's a lot of noise in the data.
I think everyone says,
I'll just use AI on your data.
Well, there's a lot of noise
in the current data sets out there.
We really need to cleanly know who are the responders,
who are the non-responders
and what's their molecular situation.
And so we have to put it all together and have clean data.

So that's really where we start with our data sets
and make sure that we can have as clean data as possible.
Once you have that,
then you can apply AI, math oncology and other things.
The math oncology group is a group of mathematicians
that are helping to use math
to solve cancer treatment problems.
One of their approaches is to use evolutionary biology.
So just as the dinosaurs went extinct,
we're trying to make the cancers in the body extinct.
And so we track how the cancers shrink
and there are formulas that tell us
that when the cancer has maximally shrunk,
then we should maybe lay off of the drug
and let the sensitive cells outgrow the therapy resistant cells.
And when we do that,
we can then, if the tumor starts to grow,
then we can add the therapy again.
And we can just do that and continue doing that
until the cancers are extinct.
And that allows us,
using mathematical formulas to use less drug,
have less toxicity and have more effectiveness.
Just based on that principle that when you take the drug away,
oftentimes the cells that are sensitive to the drug
outgrow the resistant cells.
So it decreases resistance.
We're doing studies in prostate cancer, for example, with that.
But that's having mathematicians
work with our cancer biologists and clinicians.
We're also using AI to analyze the x-rays.
And there's a lot of information we have in x-rays and CTs
that we're not using right now.
We usually just measure the size of the cancer,
but there's a lot of other information in that.
And that's called radio mix.
And we're using our machine learning techniques
to understand that so we can predict how a patient's going to do.
So we can design their radiation and modify their radiation.
While they're getting it,
there you have a six week course of radiation.
We help to use the AI and the radio mix in the first three weeks
to model out how we dose the next three weeks.

And so those are ways that we're trying to use AI,
machine learning, and math oncology to treat patients.
That's really helpful.
And I think it will help with sort of a lot of the
find the right patient at the right time at the right place
who is most likely to respond.
One of the other challenges that I think is worth mentioning here too
is that I think immunotherapy has had a bit of a challenging year.
And I think that's from the persistence perspective.
So an example, I know we're talking a lot about T cells,
but there are other immune cells that can be used,
for example, like NK cells.
And so I think some issues that we've seen are,
I think a lot of people got excited.
Could this be a one dose thing?
Could we just dose a patient and then they're cured
and they don't have to worry about,
we find the word cured sometimes hard to say,
but could they be in remission?
And then they can go about their lives
and hopefully not have their health plaguing them.
But I think the challenge of persistence
has been one that we've heard a lot about this year.
I think it's hurt the field in some ways,
but there's also innovation solves problems,
as Kathy always likes to say.
And so I think there will be new innovative approaches
that will come out of this to solve this challenge as well.
But just curious, I don't know if you're working as much
with NK cells, but within the realm of persistency
of the therapy, how are you thinking about that
and maybe tackling some of those challenges?
It's a good question.
With targeted therapies and chemotherapy,
as soon as those therapies are out of the body,
they're not working anymore.
The advantage of immunotherapy is these activated immune cells,
T cells and other cells can live in the body for decades.
And once you activate them,
you can get long-term durable responses.
That's if the T cells persist.
So we've done most of our work with T cells,
and we know they can persist for decades.

That's why some vaccines you only need to get
when you're young and you never have to get them again.
It's because the lymphocytes live for a very long time
and have what's called memory.
Now, there are other kinds of immune cells as well.
And there are also different kinds of cancers.
I think for your blood cancers like leukemia and lymphoma,
some of those cancers can be killed pretty readily,
and the immune cells may not need to be around
for a very long time.
Some of the lymphomas are like that, I think.
But with solid cancers,
cancers that kill 90% of cancer patients,
the breast cancers, the colon cancers,
liver cancer, lung cancers, those cancers,
I think we're going to need persistence of our immune cells.
For that, you're going to need long-lived immune cells,
T cells that live for a very long time.
Now, there is another kind of cell type
that you mentioned, natural killer cells.
They're a different kind of immune cell,
really interesting immune cell.
And there's some evidence in mouse models
that they can be helpful to kill cancer.
And I think that is a new field.
We still are waiting for the definitive data
that they're going to be helpful in cancer patients
in the long run.
But there's a lot of companies working on natural killer cells.
I focused most of my career on T cells,
because I think we know those cells can eliminate cancer
and can help in some situations have very long-term,
durable responses, essentially cures.
That makes total sense, yeah.
I think the idea and the promise of NK cells
was really exciting when we said,
okay, well, maybe there'll be less toxicity,
maybe there'll be less what we call T cell exhaustion.
But I think the durability is a pretty significant issue.
And I think we've seen that T cells
certainly have that element.
So that makes a lot of sense from a focused perspective.
So I think we've kind of gone through a lot of the challenges,

but I think now would be great
if you have any remarkable success stories
that you've seen with immunotherapy,
we know there are a lot of them.
Or in your clinical work or your day-to-day,
if you've seen any really inspiring stories,
we've highlighted two previously.
As I mentioned, we did a podcast with Dr. Wasim Kassim
in England who has treated several pediatric cases
of difficult-to-treat cancers.
And obviously the base edited CAR T cells for Alyssa,
the 12-year-old girl who's now in remission
was a pretty incredible story.
We also featured Tom Whitehead on the podcast previously,
who's the father of Emily Whitehead,
who was one of the first children to ever get CAR T.
So very brave family.
So we'd just love to hear if you can share any stories
that have sort of inspired you throughout your career.
Absolutely.
And that is really why we kept on going.
Even during the dark ages, we call it when no one believed us,
we had patients who were essentially cured
with long-term durable responses.
I'll tell you about one of them.
One was a kid who came using high school.
He woke up one morning, had a bleed in his brain
from melanoma that had gone there,
couldn't see out of one side because of that bleed,
and it was in the visual area of the brain.
So we cut that out, and then he had disease throughout.
We gave him one immunotherapy, didn't work.
So then we cut out a tumor, grew up the TIL cells
to large numbers, gave him billions of TIL cells,
and then his lung mats, everything went away.
And it's been 10 years now, and over 10 years, I think.
And then he came to see me in clinic a couple of months ago
with his baby.
And it was just a feeling that he had gone through high school,
gone through college, got a great job, got married,
now as a baby.
So, and that's why we do what we're doing.
And he was a football player in high school.

He actually wrote a book.
It's on Amazon called Changing the Game Plan
because after he knocked out his football career,
but he talked about all of his experiences
getting TIL cells.
Wow. I actually, I read a lot about this,
and I've never heard of that.
So I appreciate the book recommendation.
I'm going to read it.
Great.
And we have other stories that are wonderful and other
than I have a young father that was a father of four boys,
and we took his TIL cells and goose them up
to make them super soldiers by putting in a gene
to essentially make them resistant to the nasty tumor
microenvironment, gave those to him,
and that got rid of his cancer.
And he's been doing well for many years now,
and we become great friends,
and we got to throw out the first pitch
at one of the Tampa Bay Rays games together,
but it's truly great to see that.
Just a few of these cases and you just feel very fulfilled.
And the reason is is immunotherapy
can give these long-term durable responses.
It's essentially cures.
And so I become quite close to some of my patients over the years.
Yeah. That's awesome.
And being an oncologist, it's incredible to have sort of
these lifelong relationships with people
because the alternative is terrible.
So that's pretty incredible.
I got chills.
So I'm excited to read the book.
I jotted it down and maybe to focus sort of on our mission
and our ethos, and we focus on disruptive innovation,
which is clearly what you're doing and changing lives.
So one of the things that we talked a little bit about
is how do we reduce time to market
for some of these new therapies?
And just wanted to ask if there were any sort of final thoughts
on that part of it because better sequencing,
better AI, better predictions for viable drugs,

from our perspective, it's something we're sort of ingrained
in our ethos and we think about a lot.
We've published on it a lot.
We think there could be like a 25% time-to-market reduction
with some of these convergences
and maybe even a 25% failure rates for less drugs
that go into the clinic that ultimately may not work.
So we'd just love to hear from you.
If you guys, I know at Moffitt, you're working on
tons of sort of mathematical innovation
and working in new sort of modalities into your protocols.
But if you have any sort of final thoughts
on how that can be improved, would love to hear of them.
Yeah, so this is really important.
It's everything actually because every day we can shave off
in an FDA approval is lives that can be saved throughout the world.
And so there is urgency to this.
And how can we do this?
Of course, we talked about AI, putting all the data together,
trying to predict better who to get.
What? Absolutely all of those things.
The other thing we can do is a novel trial designs.
For example, with CRISPR, we can take out 20,000 genes.
Well, we can't do those one at a time
and see how well those T cells work.
We're going to need to really have novel clinical trial designs
where we put in immune cells that have 100 genes knocked out.
Each immune cell with a different gene knocked out, right?
And then we can let the patient's body tell us
which ones are most effective by collecting the immune cells
at the cancer site and just seeing who's doing the hard work.
We can then fish out and figure out out of these hundreds.
Instead of doing 100 trials, one trial and figure out
which genes we need to knock out with CRISPR.
And so I think those kinds of novel trial designs
can greatly accelerate us, figure out which gene to take out,
and then really decrease the time from lab study to FDA approval.
And what's cool about that also is that CRISPR
can then also sometimes be the therapy.
So you can do the knockout study and then check
what the therapeutic, which one you would choose as a therapy.
So I think it can accelerate even from that perspective,
which is super interesting.

Absolutely.
Let's us define what the treatment really should be.
Right. Huge time saver.
So we'd love to know from a fun, personal side,
one cool thing that I learned about you is you're in a band
and you have a biotech conference.
So I know you perform at the biotech conference.
I don't know about your touring schedule other than that,
but it might be more extensive.
I think it's called the remissions. Is that right?
Yep.
So we'd love to hear just, you have a stressful job, obviously.
There are some great successes and some difficult times.
So we'd just love to hear about how you decompress.
That's one fun one I heard of, but we'd love to hear more
if you're able to share.
Thanks, Ellie. Yeah.
I've always been a musician and music's been a very important part of my life.
I've always kid, as an Asian son of immigrants, I had a choice.
I could either play violin or piano.
So I chose piano.
And as I grew older, in every job I've had,
I've had a band that we formed.
So at the NIH, we had protocol violation
because our drummer was the head of IRB.
When I went to MD Anderson, we had the checkmates.
And now at Moffat Cancer Center, we have the remissions.
And a remission is what every patient wants,
their cancer to go away.
And so I just put out a missive.
I said, you know, when I started a band,
as I started getting emails, hey, I sing, I play bass.
So everyone's a team member at Moffat Cancer Center.
Our drummer is in security.
Our lead singer is a mammographer.
Our bass player is a code nurse.
We just have a fun time.
We're practicing tonight, in fact.
And it's just really one of the most fun things that I do here.
It's just a totally relieved stress.
I also have a national band called The Checkpoints.
And we'll be playing at Buddy Guys in Chicago
at our big ASCO conference this June.

Oh, well, I will be at ASCO.
So I'm excited to see it.
I'll come.
It's June 4th.
We're playing at Buddy Guys.
And the last three years in a row, Buddy has come up
on stage with us for a song.
So it's been a ton of fun.
I will definitely put that on the calendar.
And it's kind of cool to see your trajectory of names, right?
You went from sort of like regulatory to therapy to remission.
So it sounds like you're at the best possible place.
So that's pretty cool.
And maybe I'd be curious to know, obviously,
you're at Moffitt now, which is in Tampa, Florida.
I would love to hear, I think, one of the things
that you've been doing and working really hard at
that has been gaining a lot of traction
is getting really great people to the region
and sort of building up biotech within that ecosystem.
So I'd love to hear about how you're working on that,
maybe even how we work on that together.
But I think building a really great biotech ecosystem
within the region is really important and something
I think you're really excelling at.
Thank you.
Florida is a very entrepreneurial state.
I think the whole country realizes that.
People are moving into Florida, including you guys,
which we're so excited about.
So it is really ready to take off to be the next hub of biotech.
Biotech, there's so many.
We're at a very unique time in history
where the science is so good.
We will be able to continue to cut these cancer deaths down.
And a lot of that's going to go through biotech.
We're going to take ideas and start to put them into patients.
And so we do have a 750-acre campus
about 35 minutes north of our main campus.
It's going to be called Spiros.
It's in Pasco County.
We're really excited about that.
We're going to have a proton center there, a clinic,

a big 300, 1,000 square foot research building.
And we are welcoming biotech companies in,
as well as Big Pharma in to work in partnership
to build this community within the state of Florida.
And we think it's going to be very successful
and impactful to the region.
And hopefully, we'll come up with a lot of new treatments
to help patients in the future working together.
That's fantastic.
And obviously, you know about the ARC Innovation Center
that's being built in St. Petersburg.
So I'm sure we'll have a lot of opportunities
for collaboration.
So really exciting.
We'll have to follow up on that.
But you know that you're busy.
So I just maybe one final question.
You have any advice to give to young scientists,
young clinicians, and or even to patients
and their families who are going through either
considering or undergoing immunotherapy currently
would love to hear sort of support
to sort of younger scientists slash clinicians
and then maybe even some thoughts
for patients and their families
undergoing these difficult treatments.
OK.
Thank you.
First to a potential scientists and clinicians out there.
If you're in middle school or high school,
science is fun.
It's inspirational.
And it's often way better than they teach it in school.
So I feel like I just play every day.
We're coming in.
We're doing clinical work.
We're doing scientific work.
It's a ton of fun and you can save a lot of lives.
And so it's one of the most fulfilling careers ever.
So go into STEM, become a scientist or a health care
worker.
There are many different aspects that you can do
in the field from the person who takes the x-rays,

the person who reads the x-rays,
the person who handles the test tubes in the lab.
It's really very exciting area.
So go after things that you really love doing.
But science and health care is fun.
To patients, make sure to advocate for yourself.
Cancer is extremely complex.
The treatments are changing every month.
We're getting more FDA approvals than ever.
So make sure you're going to a place where the doctors have
seen thousands of cases like yours,
such as a large cancer center like Moffa Cancer Center.
We have hyper specialization and I only see advanced melanoma.
We have other doctors that only see breast cancer,
but other doctors that only see lung cancer.
So you can really say up to date on the cutting edge
and also get access to clinical trials,
which often are the most exciting agents because
they're available to patients 10 years before their FDA
approves.
So often the best approach for a patient
is an agent that's only available on a clinical trial.
So I really urge patients to advocate for yourself.
Don't just go where a doctor referred you to,
but just do some research.
Make sure you're going to a place that has specialized cancer
care, such as Moffa Cancer Center.
Excellent.
And with that, I just want to thank you so much for your time,
your expertise and your insights that you've provided today.
I know they'll be really helpful for a lot of people listening.
So we appreciate you.
We think of you as an ally in the community
and we're just excited to create further collaborations together.
So thank you.
Well, thanks so much for your time today, Allie,
and can't wait to work more with you and your innovation center.
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