Stem Cell Breakthroughs In Congenital Heart Repair Transcript

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Introduction to Congenital Heart Disease

All right, everybody, thank you for coming back to another amazing interview for Reversing Heart Disease Naturally Summit 2.0. This is Joel Kahn, medical doctor, your host.

And today I have the honor and privilege beaming in from Rochester, Minnesota, Dr. Timothy Nelson. I want to call him Dr. Dr.. Because whenever I meet people that have an M. D.

and a Ph. D., it's important to do that. This is a very highly educated man. It looks like he's about 35 years old. So I don't know how he got all this done early in life.

And we've never chatted the reversing heart disease, naturally, something about something when we talk about CHD we're always talking about coronary heart disease, the stuff that makes bypass stents and heart attacks.

But Dr. Nelson is an expert on the other CHD congenital heart disease. And I'll say very quickly and personally, I was born with a ventricular septal defect and I had a heart catheterization when I was nine months old.

And by the good graces, the little hole in my heart layered up because my poor mother wouldn't sleep until it cleared up. So she prayed it close. And I could have been the next one going for some sort of surgery or newer, innovative procedure.

So I have a personal reason to care a lot about congenital heart disease. This is a talk not very much about diet, not very much about necessarily exercise, but about flaws in development.

So thank you for being here. Dr. Nelson. It's great to be with you. Just give us like a couple of minutes on your path. I don't know if you've trained as a cardiologist.

I apologize for not knowing that. But, you know, how did congenital heart disease catch your imagination and intention? Well, I was training to be a cardiac surgeon as what I was training to be when I was in medical school.

Dr. Nelson's Path to Regenerative Medicine

And at that time, regenerative medicine, stem cell biology became the hot topic of the day when I was in medical school and I decided to make this a career choice as we went along the way in my training at Mayo Clinic and now we are running Heart Works and a physician scientist at Mayo Clinic with a vision of how to apply the next technology to not only rebuild the heart, but also preserve and protect hearts for the longevity that we expect our hearts to live through.

So, as you know, the regenerative capacity of the heart is limited. And as a science and technology is evolving not only from the things that we do to ourselves, our food, our diet, our exercise, but also the medicines and the treatments that we take.

How does that affect our ability to of our heart to regenerate? That's become my passion and that's become my career trajectory, to try to be a physician scientist, to make this reality a reality for us today and not for the future generation.

Incredible. Let me ask you the last question first. I'm going to interview you in 2034, ten years from now. And you're telling me what HeartWorks has achieved for children and some adults that survived congenital heart disease till adulthood?

What would you like to say our company has accomplished in advancing the care of people with Kengen real birth

heart disease. So in ten years from now it will be routine for various types of cell based regenerative medicine to be used at the time of heart surgery and catheter based surgeries.

It will be an adjunctive therapy, which means that we added on to the therapies that were already doing the operations that people will need. We will start with the sickest of the sick patients, the patients that are in the greatest need and for the complex congenital heart patients.

We will be using regenerative technologies to rebuild the heart. The goal will be to be able to make your heart no matter what. You're born with strong enough that you won't need to have your heart transplanted or removed from your body.

Because we'll be able to make it strong enough that it will be able to live up to the life demands. That's where this technology starts in the next ten years.

That's what our focus will be. But you can quickly imagine where this technology will be available to anybody that has pump failure, heart failure, that despite the best treatments, despite the healthier lifestyle some patients will have risk factors that will need additional therapies.

And the regenerative medicine technology that's available to us today will become more widely available in the next decade ahead. Wow. So we've got a very bright future.

So, you know, we're talking about, again, complex, congenital heart disease. There are children born with one ventricle pumping instead of two, for example.

And I know survival may be very limited. You know, we're hearing about heart transplantation. We know there have been a few people that have attempted in adults a pig heart into a human, having had very long survival.

But it's still early in the game.

Vision for Rebuilding Hearts with Stem Cells

Do you think we're going to be able to actually 3D print parts of the heart or maybe an entire heart and you know, what do you envision? How are you going to regenerate, you know, abnormal heart anatomy in these complex cases?

So here's our vision at HeartWorks. HeartWorks, We built hearts. We believe that we can use your cells, your body, to regenerate your heart muscle in the lab and transplant your heart muscle back into your heart to make it bigger, better and stronger.

The hope is that your heart will be able to be rebuilt, to be strong enough, to not ever have to be heart transplant it. Or we don't even need to do a 3D printed heart because our vision is that we can rebuild your heart from the inside out.

And the way we do that is we start with a piece of your skin. We engineer it into stem cells. We make it into your beating, contracting heart muscle, and then we surgically transplanted or implanted into your heart to make your heart bigger and stronger.

Now, there's multiple form factors that this is going to take in the future, but it's suffice to say it's like gardening or farming. We are planting seeds that can grow new heart muscle.

We literally are doing that right now. Our clinical trials are open and in the next ten years we'll be able to show who's going to benefit the most from this type of technology and how to make that more widely available.

So if we do, our job will eliminate the need for heart transplantation, will eliminate the need for pigs hearts, will eliminate the need for 3D printed hearts, because we're rebuilding your heart to meet the demands of your body

and your lifestyle.

That's a an amazing vision for Heart Works Inc So I'm no expert on what you do, but I read a little in general. So we taking a fibroblast and exposing it to Yamanaka factors and turning it into a pluripotent stem cell.

Those are some big words you use there. In a big words I know I listen to Davidson clear now and then I apologize. That's 100% right. So the best way I can describe it in layman's terms is we take a plug of your skin out like a biopsy.

If we were going to do a skin biopsy or remove a mole from your skin, we like to start with skin cells. We take the glue, the mortar that holds your skin together.

They're called fibroblast. And that glue and mortar that holds your skin together can grow really rapidly. When you put it on plastic plates in the lab, this grows out and we get hundreds and thousands of millions of cells that can grow in the lab.

And these cells then are the starting blocks that we reprogram back into what looks and feels like a stem cell or use the word pluripotent. These are called induced pluripotent cells.

We are doing that through a repro naming process. We don't create an embryo. We don't destroy an embryo. They're your cells. They're genetically identical to you.

But they now start thinking and behaving like they were when they were an embryo. And that means we can now train them to become any tissue of your body, but the one we like to train it to become is heart muscle.

And the way we know it's heart muscle cells is its beating and contracting under the microscope and contracting at the same rate that your heart can tracks in your body.

This then becomes the material that we've manufactured and can be able to use for surgical transplantation back into your body, which means your body won't reject it and your body won't recognize it as foreign tissue because it's genetically identical.

How Skin Cells Become Heart Muscle

It started from your body. Wow, that is so fascinating. So tell us about like a clinical trial. What's who's a candidate right now in a trial that you're doing or several trials?

So we've had five ongoing clinical trials to get to this point. The current clinical trial that we're conducting is patients that were born with single ventricle heart, congenital heart disease.

So these are patients that have a missing heart on the side. They're the most severe forms of congenital heart disease. There's probably 10 to 20000 of these patients living today in the United States.

These are the patients that are eligible for the world's first clinical trial that I just referenced, where will make their cells and will be able to transplant their heart muscle cells back into their heart.

They have a five horsepower engine. And our goal with this approach is to make their horsepower a ten, 20, 50 horsepower motor, to rebuild it, to make it strong enough.

So we're starting with the patients that have not very good options or no options. So they're the the patients that have very sick hearts. And these are the hard patients to find right now to be part of clinical trials as we as we prove that this technology can be safe and effective in that population, then we'll start envisioning how we bring it to more patients more rapidly.

Oh, wow. That's incredible. And this is something where you grow in the lab, but you actually have to take these

these generally young children to the operating room to apply these sheets of now beating heart muscle to their heart.

Yeah. So the clinical trial that we're starting with will be adults only. So we'll be moving it to kids when the time is right, when we have more data to justify that.

But in partnership with Mayo Clinic in Rochester, Minnesota, and under the Oversight of IRBs and the FDA oversight, this is adult patients with congenital heart disease that we're starting with today.

Wow. Yeah, I guess a little easier to start on a big target than start on a pinhead. So make some sense. And obviously the longevity of these adults is quite limited.

So I can understand that you have a separate I don't know if it's a company and organization and I'm going to say it wrong because it's a mouthful region There are Gnostics.

Yeah, that's a little different than what we were talking about. Heart working is hard work. Think of physical location. I mean, is there a biologic lab that is called a Heart Works?

Inc Yeah. So Heart Works is our nonprofit clinical stage company that is raised in philanthropic support, aligning academic institutions to work collaboratively to be able to show that this technology can be done safely and efficiently.

Current Clinical Trial for Single-Ventricle Patients

And so within that non-pro structure of heart works, we also have a wholly owned subsidiary known as Region Third Gnostics, where that's where we are, where we're holding the IP and we're building the manufacturing capabilities to be able to scale this to other diseases such as dilated cardiomyopathy or ischemia, heart disease or patients that are adults with more common conditions.

We do envision a day where we'll be able to expand our clinical trials beyond the congenital heart world of heart works and bring it to a larger patient's patients segment using the infrastructure that we're creating at region.

So it's a really interesting, unique hybrid model between a nonprofit academic environment and a four profit scale up manufacturing to be able to move efficiently and cost effectively to build bring this type of technology to as many patients as possible. And when do you think the first adult with congenital complex heart disease, single ventricle, might actually be in an operating room getting this implant from a region?

Their Gnostics Well, we're talking the end of 2023, right now as we sit here and we are open for enrollment in this clinical trial. And so we envision through 2024 and 2025, we'll be enrolling patients and executing this clinical trial.

So the clinical trial is open, the permissions are all intact. We are at the clinical stage a development of this. And we're recruiting patients that meet the inclusion criteria today to be able to make this a reality.

And how long is the the lab process before a patient gets scheduled for operating room? Is it take months, weeks to go from this skin biopsy to another tissue to take them to the operating room?

It's a very perceptive question that you're asking right now. It's not short. It takes us nine months to manufacture this process. And let me tell you why.

It being the first in the world that we're doing this, there's biology involved of taking the cells through this process that we just simply can't shorten.

But we also do a lot of extra steps to make sure that the product is safe, that it doesn't have infections or contaminations. And we do all the testing in that nine months before we would release it to a surgical treatment.

We do many other products. We've treated hundreds of patients out of our lab with other cell types. And so we have good processes in place to be able to make sure that this can be done safely and reproducibly.

And so with this world's first clinical trial, it is a long time. It's one product for one patient, and we can probably shorten that quite significantly as we scale it and as we start doing it for more patients in the future.

But right now it is a nine month process. Every day these cells are taken care of in the lab to make this happen. Wow. How big is the is the team? And again, the team would be under the region.

There are Gnostics. We were say. We work side by side, but region is wholly owned by artworks right now. So we like to think of everybody is as working for our congenital heart mission today.

So we have nearly 60 people and across the whole team, it's a seven day a week manufacturing process in-house. We don't outsource that to anyone. And so we're really building the infrastructure to be able to do this type of work with our team from the ground up.

Manufacturing Timeline and Mayo Clinic Trial Setup

And that makes our artworks very unique and very different. But that's really important to be able to accelerate the learning of what it takes to do this type of technology, to be able to bring it to a larger market more quickly.

Where do you think the first surgery will happen? Will happen at the Mayo Clinic? Yeah, we have only one site open for this protocol right now. And that said, Mayo Clinic in Rochester, Minnesota.

Our clinical colleagues in the Department of Surgery and Cardiology are working side by side with us to make this happen. Wow. Wow. Well, this has been in incredibly exciting.

I think everybody listening again, this is a reversing heart disease summit. And we typically talk about reversing high blood pressure, reversing cholesterol, reversing diabetes, reversing atherosclerosis.

But we don't talk a lot about reversing commonplace congenital heart disease. And you've painted such an exciting future for us that, number one, if anybody were to know a family relative that has complex congenital heart disease, how do they contact know somebody in the research department?

The easiest place is to go to our web page. We build hearts dot org. We build hearts dot org and there's contact information on that page that will direct you for us to get you more information.

Okay, well, that's exciting. And actually it took me over to Heart Works Inc dot org, but it is right there. We built hearts. I had looked at your other websites.

I apologize. You have a nice association with Porter family vineyards. I have to give you a shoutout for picking a nice, uh, a nice red varietal to raise money.

But one in 100 children. That's what I always you know, we always say 1% of babies born are born with congenital heart disease. So it's not rare. And there will be many, many that will be potentially able to benefit from this down the road.

It all takes time and careful research. And of course, you accept donations, right? Yeah. Heart Works as a nonprofit that makes all of this work for these early phase clinical trials.

That's hundred percent right. Is you never know if Elon Musk or Jeff Bezos signs up for some summit. They might ring your email right away and make it in.

Tim Nelson, uh, professor of Regenerative Medicine, Mayo Clinic. Good deal. And you said a couple of things during the first part of the interview, and I wanted to just go a little deeper with it.

You know, more common and complex congenital heart disease and no less compelling is that large market of adults with weak hearts, weak cards from a previous large heart attack or suffer heart attack, weak hearts from a viral infection.

And we cards from kind of the unknown cardiomyopathy, as we call it. And that may be, you know, further down the road. But it's such a big market, of course, leading to congestive heart failure, leading to the need for defibrillators now, leading to sometimes a very short life span with a reduced quality of life.

Expanding to Adult Heart Failure and Future Applications

What is the leap of technology from approaching complex congenital heart disease now to the next phase of starting to use it as an alternative to heart transplant or pig transplant into humans with weak hearts and advanced congestive heart failure?

You know, the thing that makes us most concerned with that leap is the risk of arrhythmias, right? So we are rebuilding the heart with electrically active tissue.

And so when you have a patient with with a heart attack and a major loss of heart function, many of them are dealing with multiple forms of arrhythmias and these cells could potentially exacerbate that.

So we're working through how to reduce that risk of arrhythmias, and we're working through what are the right models to be able to test that and gain confidence that this electrically active tissue that we're engineering does not cause additional problems with patients that have had heart attacks.

That's going to be perhaps the most difficult patient to get after. But as you said, there's other patients with viral myocarditis or dilated cardiomyopathy or other genetic forms of of heart disease that have weak heart muscles that are that are affected less by scar tissue.

And these might be the patients that this technology becomes relevant for as the second tier, if you will. The first tier will be congenital heart. The second tier will be nonischemic cardiomyopathy.

And then ultimately, we do have to be able to rebuild the scar tissue that has formed from patients that have had a scheme at heart disease. But, you know, the thing that I get most excited about is we can start predicting and intervening earlier and earlier than we ever thought possible.

And by having access to technology like this, how do we bring technology to patients in a preventative strategy rather than trying to rescue them from the ultimate failure at a crisis moment?

And so this is where personalized manufactured tissue, I think, becomes really exciting, is at risk patients. Patients at the earliest forms of of forming a weakened heart muscle that we start rebuilding it with multiple doses at a at a prescribed regimen.

When you show that this can be done safely and efficiently, that changes the paradigm of how we think about it. So getting away from the crisis mode, thinking of a heart transplant and getting towards more of a longevity, rebuilding, strengthening the heart, that's where this technology, I think, really, truly becomes a game changer.

Wow. That is such an exciting future. And, you know, the challenges that you have to bridge will be very interesting to see and hopefully work out and sooner than later.

And I just hope you made another statement during the first part of our interview that you have a team of 60 and you've treated or you've involved other conditions, other patients, maybe I didn't understand that.

But other than this push for complex congenital heart disease, what does region theory gnostics, what's the rest of the scope of what they're working on?

Yeah, so we started out 2013 was the first patient we treated. That was a decade ago using tissue collected from the cord blood at the time of birth. So babies with congenital heart disease diagnosed in utero before they were born, we were able to collect their own autologous cord blood and process those cells.

And we've used that in many, many protocols.

HeartWorks, Region Therapeutics, and How to Get Involved

We've done phase two B clinical trials. We did a 50 patient controlled trial using that product, and we're following those patients right now. To complete the follow up on that.

I think of that as fertilizers. The cord blood itself does not cause new heart tissue to form, but it is able to fertilize the hearts. And in this case, we were treating three month old infants, three month old infants with congenital heart defects at the time of open heart surgery.

We injected the cells in at the time of a Glenanne operation to try to use the fertilizers of the cord blood cells to fertilize and rebuild and strengthen the heart of a three month old infant.

We've done that over on a over a hundred patients so far, and that's really been the Pathfinder for us to develop the manufacturing, develop the clinical teams, developed a clinical quality oversight to be able to take on the bigger project, which is this bioengineered project that we've talked about.

Wow, this is really, really exciting. And so actually some of the most exciting stuff we've ever discussed in this segment. So. Well, thank you for your time.

Thank you for your expertize. Thank you for sharing again. And just one more time for those wanting to pursue further either maybe they have a family member or friend, maybe their own heart is been damaged and they want to follow this closely.

As you make further progress, tells us again where to look for more information. Yeah, come see us. webuildhearts.org All one word. webuildhearts.org You'll find out our full story.

You'll find out ways you can engage with us. And we've got some really exciting opportunities with virtual lab tours. People can join us and we'll bring you in.

The lab will show you the manufacturing of the cells. You simply sign up on the website and we'll get you in the lab and show you firsthand exactly what we do.

We'd love to have all of you join us for a virtual lab tour, and there's many other activities and educational seminars that you'll find out on that website to learn more.

So we appreciate spreading the word because it takes all of us together to to pull these things off. And you are you're helping contribute in a massive way to to share this story and to reach out to anyone anybody knows with congenital heart disease.

And thank you, Joel, for sharing your own personal story on this, because it's connecting all of these families that makes this possible. No problem. We all have to care.

And this will reach tens of thousands of people who may not have known much about congenital heart disease and probably knew nothing about the groundbreaking work you're doing.

So keep it up. Thank you very much. Thank you. Can get this project done soon. We are working on it. It never moves as fast as we we'd hoped. It never does.