

Disruptive: Sports Genomics

Host Terrence McNally interviews George Church and Jonathan Scheiman.
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McNally:

Hello, I'm Terrence McNally and you're listening to DISRUPTIVE the podcast from Harvard's Wyss Institute for Biologically Inspired Engineering.

Can sneaker endorsements, cereals, protein powders or electrolyte cocktails get any of us closer to the peak level performance of our favorite athletes? Despite billions in sales, the answer is probably no. But how about an elite athlete's biology?

With 100 trillion cells in the human body, bacteria outnumber our own human cells 2 to 1, and bacteria in our gut affect all our key organ functions. They play a role in our health, development and wellness, including endurance, recovery and mental aptitude.

What if we could tap the gut bacteria of elite athletes to produce customized probiotics - and what if those probiotics could give recipients access to some of the biological advantages that make those athletes elite?

A former NBA hopeful in the lab of George Church at the Wyss Institute asked that question a couple of years ago and the lab is now moving toward a startup to bring such products to market.

In related news, consider this: With 2015 sales of \$115B, sports-based nutraceuticals made up the largest share of the global nutraceutical market, but probiotic-focused sports products made up less than 1% of those sales.

I'll talk with Wyss Research Fellow JONATHAN SCHEIMAN and - a previous guest on Disruptive - Wyss core-faculty member GEORGE CHURCH.

Our bodies — and all living systems — accomplish tasks far more sophisticated and dynamic than any entity yet designed by humans. The mission of the Wyss Institute is to: Transform healthcare, industry, and the environment by emulating the way nature builds.

Jonathan Scheiman, a research fellow at the Harvard Medical School, has worked on transformative sequencing technologies and programmable cellular engineering, with publications in journals such as *Science* and *Nature's Methods*. But that was not his dream growing up - [2:02]

Scheiman:

I wanted to play in the NBA. I went to St. John's University in New York. I played for the basketball team. We won a Big East championship my freshman year, an NIT championship my senior year, but I didn't make the NBA, so as I tell everyone, my backup plan was getting a PhD in molecular biology, which is I guess the traditional route for most basketball players.

I went to NYU for grad school. I focused on molecular oncology. Then, when it came time to look for post-docs, I really wanted to get into genomics, next generation sequencing, and synthetic biology. George Church obviously has a great lab for doing all those things, so I had a chance to do a post-doc in his lab and be a part of the Wyss Institute, and kind of been in the lab now for the past four-and-a-half years working on all sorts of cool technologies for reading and writing DNA. [2:54]

McNally:

But now you're bringing your two worlds together...

Scheiman:

For me, I think after a few years in the lab, I kind of wanted to circle back into my background and obviously that's athletics, so I've thought about ways in which we could bridge together the science and athletics community, and in particular use the tools we develop in the lab maybe for applications in athletics. [3:16]

McNally:

When was the first moment that you thought about cultivating the gut bacteria of elite athletes?

Scheiman:

It's pretty funny. I should also say, while in grad school, I actually coached high school basketball with my brother for around eight years - to give you a sense of how long I was in grad school. I was really big on working with kids and education. My parents are teachers. My brother's a teacher.

I don't know, maybe around three years ago, something just dawned on me. I was thinking, "Why am I in George's lab? What am I doing here?" Obviously other than learning a lot and helping develop technology.

It kinda dawned on me, maybe it is to bring these communities together. I first had an idea and I told this to George. I was like, "You know, I want to sequence LeBron James's genome. Imagine what that could do just for education and promoting the sort of technology we develop and the science to the masses." Obviously professional athletes have a tremendous amount of influence in society and education.

I told that to George and he said, "Yeah, that sounds like a great idea, but why don't you focus on multiple athletes, not just one?" Then it became a matter of brainstorming what would be a feasible project. [4:26]

McNally:

But he's not looking at the whole genome these days. He's focusing -

Scheiman:

It felt like the gut microbiome is probably one of the more translatable fields in research right now. Also, the microbiome is dynamic in nature. It's something we can change. Something we can modulate with diet. It's something we can extract and give to other people. Those were the rationales for focusing on athletes as well as moving towards the microbiome in general.

To take it a step back, I think if you look at biomedicine right now... A lot of times, and I come from a molecular oncology background, we're looking at, let's say, diseased physiology. To look for deficiencies and then finding ways to correct those to promote health, and that's great. That's absolutely things we should be doing.

I think another approach is: what if we look at extremely beneficial phenotypes or extremely healthy people and fit physiology? Certainly, if you're looking for that, I think professional and elite athletes are certainly one form of elite phenotypes and certainly for all intents and purposes, these are superheroes. They can run faster. They're stronger. They can jump higher. They're mentally tough.

I think the notion of trying to understand what makes these elite athletes unique from a molecular standpoint, and then the really exciting thing is extracting that information and then looking to provide it to others to benefit and promote general health and well-being, not only in athletes but maybe one day in the general population. [5:51]

McNally:

I turn to George Church for the big picture.

Church is Professor of Genetics at Harvard Medical School and Professor of Health Sciences and Technology at Harvard & MIT. He's Director of the U.S. Department of Energy Center on Bioenergy at Harvard & MIT and director of the NIH Center for Excellence in Genomic Science at Harvard.

He has co-founded a number of companies, and coauthored hundreds of scientific papers, more than sixty patents, and the book, "Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves." [6:18]

McNally:

Now, we're talking about the ingestion of cultivated gut bacteria from elite athletes. Let's set this up. First, what is the microbiome? [6:30]

Church:

Well, the microbiome for humans are all of the organisms that live on your

skin and inside your gut, and all over your body that can contribute positively and negatively to your health.

McNally:

I think we've even talked in a previous podcast at some point, George, about the fact that for much of our time, we perceived them as negative, as threatening, and so on, and there's been quite a sea change in our perspective over the last few years. Why did that happen? What changed? Was it technology? Was it asking the right questions? What changed? [7:09]

Church:

I think one of the big things was the improved technology that allows us to analyze all those organisms. We knew they were there, but it was too tedious, expensive to assay exactly what organisms were there, when, in various people, in various activities. Now that's all changed. The cost has dropped by over a million-fold, and the second thing that's happened is some experiments have been done where you reconstitute a microbial population so that it has physiological inputs...positive impact. That was missing before. So both the motivation and the wherewithal technology to do it have changed dramatically in the last few years. [7:58]

McNally:

I've read – "...with 100 trillion cells in the human body, bacteria outnumber our own human cells two-to-one."

Church:

Well, I think it's a little deceptive in that they still are a minor fraction of the weight. It might be a couple of kilograms out of a 50-100 kg body.

McNally: [8:15]

I did an interview with neuroscientist, Antonio Damasio, and I remember him saying something to the effect, and I'm not quoting exactly, of that, while we are each an individual human life form, we also contain, or are made up of trillions of other life forms. I'd never thought of it that way. Is that an accurate way to look at it, that they exist as entities just as we do?

Church:

Oh yeah, well certainly. They probably look at us as a convenient package to carry them around and distribute...

McNally:

We are locomotion to them...

Church:

And they have all kinds of strategies for making sure that we distribute their progeny where they want them to be distributed. They trigger all kinds of reflexes having to do with sneezing, coughing, rubbing our nose, all sorts of things having to do with defecation, and so forth.

We are their tools, and to some extent, they help us in return. Not always. Some animals absolutely depend on their microbiome, but most of them you can rid them of their microbiome, and they will survive. Not necessarily thrive, but it's not absolutely essential. Nevertheless, anything that gives you a slight edge in this world has been heavily rewarded, both during evolution and today. That's what we're talking about is things that can impact your health, well-being, mental, as well as physical and athletic well-being.

McNally: [9:48]

Now, it seems to me, when our perspective shifts to where we, on the one hand, see that there are all these other entities within us that have their own goals, and that bacteria are not all negative, this is actually, it seems to me, a big conceptual shift in our relationship to microbes, to bacteria, to the rest of nature. Am I wrong?

Church:

Oh yeah, it's a huge shift. I'm not sure that anybody is really overstating it yet. We don't really know how far it goes, but it's big in the sense that quite a bit of what we've tried to do with human genetics is limited if the studies don't include major analyses of the environment, and microbiome could be considered part of your body, a part of your environment, depending how you look at it, but it has been historically neglected in human genetic studies.

McNally: [10:43]

I also noticed that when I think about the microbiome, I almost always, in my head, think gut microbiome. Why is the emphasis, it seems to me so far, on the gut...?

Church:

Right, well, part of the reason for the emphasis on the gut is that's where 99% of the microorganisms are. There are some known physiological components in the skin. There are all sorts of microorganisms in your sinus cavities, and your lungs, blood even. Blood and urine are sometimes thought to be sterile, they're not always sterile. When they're not, it's quite important. Dental decay is important. Urogenital tracts are important, both positive and negative.

Yeah, the gut is a major reservoir, and if you talk about being in equilibrium with our blood, just by mass, that's where you can have huge impacts, including positive. You could take metabolic disorders and fix them with microorganisms. [11:48]

McNally:

Jonathan Scheiman outlines some of the biological areas for which they see potential microbiome applications -

Scheiman:

When I talk to athletes, in addition to the general population, I focus on three

major tenets that the gut microbiome influences. One of them is energy metabolism. For instance, a majority of carbohydrates and fibers that we consume as humans, our body actually doesn't break down. We have co-evolved with bacteria that contain specific enzymes to actually break down these carbohydrates and convert them into energy molecules for our body. That's one aspect. Influencing how we eat, energy metabolism, how we process these foods, convert them to energy.

Another one, a huge application is gut/brain access. 90% of serotonin is actually fermented by bugs in our gut. Applications with regards to brain functionality, there are all sorts of studies coming out now with how the gut microbiome influences anxiety, depression. There's a recent paper on Parkinson's Disease development, autism, and things of that nature.

Finally, I like to say immunology. 70% of our immune system is basically activated and primed by bugs in our gut. First of all, these bugs, collectively as a community, could prevent opportunistic organisms and pathogenic infections and competing them out of our system. Also, they could interact with immune cells. They contain certain molecules on their surface to regulate inflammation, certainly not only in the gut but also at distal locations in our body. Those are just some of the things, and obviously there are applications in obesity, diabetes, malnutrition... There are so many things that the gut microbiome influences in our body. [13:31]

McNally:

Within immunology, Scheiman mentioned inflammation, of significance to athletes and non-athletes alike.

Scheiman:

Having spoken with several athletic trainers at the professional level, one thing they say that they look at as far as not only training regimens but also dietary implementation is trying to prevent and reduce inflammation in their athletes.

Absolutely if we could understand how the microbiome influences inflammation in our body and then identify bugs - and this is one of the applications we're looking into - bugs that have anti-inflammatory properties is something that we could potentially give to athletes as a form of probiotic. You're looking at things that could benefit their careers but then ultimately help other people as well. [14:13]

McNally:

Yeah, it's those other people, it seems to me - seniors who just wake up with aches and pains. Seniors who stop exercising because the recovery takes too long, and then of course that's a vicious cycle that gets worse and worse.

Scheiman:

I can tell you myself. I'm thirty-five so I'm not a senior, but I wake up with a

lot of aches and pains as well. I think a lot of people could benefit from this.

McNally: [14:36]

The most successful example so far of transferring healthy microbiome is in the treatment of *C. difficile* infection.

Scheiman:

I should say what everyone points to in the field is the notion that already, we can basically with 95% efficacy cure *C. difficile* infection through fecal transplants. Essentially what that is is basically transferring a healthy microbiome community of organisms into someone that's infected with this pathogen and basically curing them.

C. diff is something that affects around 500,000 people a year. It basically occurs when people take antibiotics when they're in the hospital for surgery. It wipes out their gut microbiome, and then this opportunistic pathogen colonizes the gut and causes all sorts of inflammatory aspects and ulcerative colitis. Obviously something that greatly afflicts a lot of people and right now you could cure it by gut microbiome transfer.- I think that's the gold standard in the field.

McNally: [15:35]

You mentioned the fecal implant. I've read about it for a few years and it is just what it sounds like it is. My question always about this is what happens? In other words, you take a fecal sample from someone with a healthy microbiome, you implant it... What's the middle process between what you remove and what you implant?

Scheiman:

I'll give a shout out to a non-profit company called Open Biome right now. They're probably the leaders in this field right now. In general, I think the process is, you recruit healthy donors, and *obviously to quantify how they're healthy, you put them through a questionnaire to determine different things about their health, their diet, and other background issues. Then once you confirm these donors are healthy, you essentially collect fecal samples from them. You could then basically resuspend these fecal samples into some sort of buffer and get rid of all the particulate and insoluble matter in these samples, and then basically freeze them and do a bunch of important tests to make sure they're safe. Once you determine that, that resuspended fecal sample can essentially be shipped to hospitals*

McNally:

So not a lot of processing, really. In other words, it isn't that you change much about them, right?

Scheiman:

Yeah. Here's a fun fact by the way. I think 60% of fecal samples by weight are bacteria. There's a lot of microorganisms. It's the basic principle that in this particular case, just repopulating the gut with a healthy and complex

and diverse community...

It's also been shown that increased diversity of bacterial species in the gut is associated with health, and certainly the notion of taking antibiotics, wiping out a lot of bacteria, and allowing these opportunistic pathogens to take over is the opposite of that.

The field needs to move more towards a precision medicine sort of approach, where rather than just take an entire community in a fecal sample and giving it to patients, which works in the case of *C. diff*, we need to start to identify individual organisms or communities of organisms that cooperate synergistically, that can then be purified, extracted, and then delivered in nutritional forms and stuff like that.

For instance if you recruit an ultramarathon runner, someone who runs 100 miles at a time, I'm going to venture to say that their microbiome in terms of processing carbohydrates to convert to energy, they're going to have some bugs in their system that aid them in that process for applications and endurance. In fact, some of our studies have identified bugs that are elevated in these athletes that actually help in energy metabolism.

Certainly, if you look at gut/brain access and the notion of mental toughness applications... Professional athletes and elite athletes, if you look at the pressure that they face on a daily basis with competition, I would reason that perhaps they have some bugs in their gut that could help them stay calm during these times of high anxiety. Certainly, they could benefit from bugs that may be able to calm them and help them with mental toughness.

Certainly from immunology... We spoke about inflammation and the notion that you can identify bugs that change maybe between performance and recovery phases, that either modulate endurance, recovery, fatigue, or inflammation. That's sort of transitioning to what athletes may have in their microbiome that could be unique that would be useful for, let's say, beneficial applications. [19:00]

Once you do in fact recruit an athlete to give you their fecal samples, we also collect a lot of, let's say, metadata. We collect information as it pertains to their health, athletic and dietary history. All of these athletes answer a questionnaire with over 100 questions that can give us a lot of background on them. Also, every day that they hand us a fecal sample, they actually fill out a daily annotation sheet that lets us know what they ate for breakfast, lunch, and dinner that day, what snacks they had ...

McNally:

How much they exercised -

Scheiman:

How much they exercised, their workout, how they feel. This gives us a lot of background information that could help us distill which microbe is

associated with their athleticism or sports-related functionality versus what they eat, which obviously plays a large role in your gut microbiome community as well.

Then, once we have all that information, then the real fun begins. Then we take these fecal samples and - we mentioned that each sample has millions of bugs in them. On one hand, we could then extract the genetic information from these fecal samples, the bacteria present within them. Once we have that genetic information, we could do all sorts of cool things and use next generation sequencing to basically decode that genetic information and then run it through, for all intents and purposes, search algorithms and bio-informatics to basically then identify all the microorganisms present within the fecal sample derived from an elite athlete. That's the way of identifying what's in there, what are they doing, and what is the potential of these bugs and how these athletes differ from other athletes as well as non-athletes. [20:34]

McNally:

That seems to me, that's the first half.

Scheiman:

That is the first half. Once we have those candidates from next generation sequencing, what we then do is we can go back to these fecal samples and, believe it or not, actually grow them out in the lab under Petri dishes under special conditions, and then start to isolate and purify individual bacterial colonies, which we can then select, grow up, and basically now start to have these purified bacterial cultures that we can then start to do all sorts of cool functional validation studies in initially animal models to test for safety, but then ultimately, once we prove that they're safe, start to do studies within athletes to see if we could provide these probiotics to them to help them with performance and recovery applications. [21:17]

McNally:

Where when we talked about *C. diff*, it was just the cleaning it up, purifying it, and then putting it in another human being. This one, you're extracting, you're cultivating, so you're creating, if you will, ingredients for a new probiotic.

Scheiman:

Absolutely. I think you hit it on the head. All we're doing is basically using next generation genomics to identify novel probiotic candidates that could serve as ingredients for, let's say one day, sports nutrition products.

I will say something provocative, though. I'm not excluding the possibility that fecal transplants of elite athlete microbiomes into non-athletes may have beneficial effects. I'm not going to exclude that possibility.

McNally:

That the very simple replacement might actually have an effect, and you just

don't know yet.

Scheiman:

We know probiotics work. There have been studies on probiotics... There's been longitudinal studies with people that eat yogurt on a daily basis and showing that they're less prone to becoming obese. There have been follow-up studies showing that probiotics have anti-inflammatory effects in the gut. There have been studies which spoke about gut/brain access and mental toughness, that they influence calmness and anxiety levels in people. There's a lot of study out there, but again, there's not a lot of diversity, and I think there's a dearth of innovation and implementation of technology in the field, and that's really where we're looking to be disruptive. [22:41]

A couple of things that I want to touch upon in terms of the functionality and functional validation of what we're doing. I mentioned the marathon study, where we collected samples from athletes before and after they ran the marathon and we looked for changes in their gut microbiome. One interesting finding that we discovered is that in all of these athletes, and it even extends beyond marathon runners. It goes to the rowers training for the Olympics as well as the ultra-marathon runners, is right after these athletes compete, we find a spike in their biome of this one particular bug. Several bugs, but one in particular that actually its natural ability is to break down and ferment lactic acid.

Which is kind of interesting if you think about it because obviously after physical exertion and intense exercise, there's an increase in lactic acid in the blood, which is associated with soreness and fatigue, but what we're finding is there's almost this natural response in the biome of these athletes to increase the abundance of this bug that breaks down lactic acid. A couple of things come to mind as far as applications. Imagine you could purify this one bug and then give it back to athletes before they run a race to actually prevent lactic acid accumulation, prevent fatigue, prevent soreness, but to aid endurance and recovery.

In fact, this is one of our lead candidates. We've already purified it. We've lyophilized it. We've shown that it's stable on the bench for a month, and we're introducing it now to animal models to show that it's safe and then ultimately do functional studies to see if maybe these animals could run longer or have reduced levels of inflammation or reduced levels of lactate in their blood. Then obviously move that into humans as well. Those are some of the things... how we're translating the discoveries through sequencing into now isolation, purification, and ultimately functional validation.

McNally:

That seems to really be in line with Wyss's model of biological inspiration. You're finding the body does this. It does it after the fact. What if you can take what it does after the fact, after the exertion, and have it in the body prior and during exertion... [24:42]

McNally:

After discovery, extraction, and analysis, George Church talks about the next steps in bringing a product to use –

Church:

It's like introducing a new food or drug. The Food and Drug Administration is some level involved. Some, in fact, many foods, and some microbiome treatments are not regulated by the FDA. They are exempt. The safest thing is to follow all the FDA guidelines, and do double-blind placebo-controlled randomized clinical trials where you establish direct safety, and cause-and-effect efficacy where it accomplishes a particular goal. [25:29]

McNally:

Once you've gotten that there might be a positive benefit and there's safety, are you ready at that point to try them in humans? That seems like a quicker process than in many sorts of lines of research.

Church:

Right, so many of the microorganisms we're talking about are already considered safe. They are generally recognized as safe. It's got an abbreviation, G-R-A-S, GRAS... and they are present in many probiotic formulations, things like yogurt. We might have a new strain that might be a little more effective. To a first approximation, that doesn't need to be reevaluated for safety, although it probably will be in the course of any new study. If it's sufficiently potent, then it particularly demands...The more you want to claim that it does, the more you have to establish its safety and efficacy. [26:28]

In principle, you can bring products out immediately if they're just equivalent to existing products, just the existing products would derive from ordinary members of a species of bacteria, and we're getting the bacteria from elite athletes. You could do that without proof, and likely, without any harm, and possibly without any benefit. The point is, it might get people talking about the science, thinking about it.

Then, in parallel, you could be doing experiments to see which of the new bacteria that you're introducing have how much impact, if any. I think the important thing is to engage the public in any way we can to be more scientifically literate. The *Wheaties* box has pictures of athletes on it and engages people a little bit more in their product from a personal standpoint. This could do the same thing initially, getting the public, and the athletes, the scientists, all in a shared, common discussion, and then, as the data starts rolling in, and evaluating what to do next. [27:39]

McNally:

One of the thing that's inherent in this project is actually attempting to be more specific, more customized, more targeted, correct?

Church:

Right, so... A fair number of nutritional supplements and probiotics are taken without rigorous proof they're benefiting. Others, there is at least anecdotal, or in some cases, even research data in the literature that gives one hope. It is very different from double-blind placebo-controlled randomized clinical trial, which is the gold standard.

Some of the cases, the dosing is unclear. There are some opportunities for personalization. This is the era of precision medicine and personalized medicine. Even foods certainly affect your body. Shape, size, activity, all those things are influenced by your food. To some extent, our food should be treated with the respect that we give to drugs. They have just as big an impact on your body composition and physiology.

McNally: [28:44]

Is there any research that tests or shows that such probiotics, including these extracted bacteria from elite athletes, that such probiotics do enhance performance in athletes or non-elite athletes? Any research yet that shows that?

Church:

No, this is brand-new. That, I can fairly competently say, it's not in the literature and peer reviewed journals. I think it will be soon.

McNally:

Do you think it's inevitable that the product will have positive results?

Church:

I think it's inevitable that the metabolism of a microorganism can influence the host. If you're willing to make unnatural micro-organisms, you can do almost anything you can do with any other drug delivery method. You can think of it as the microorganisms delivering things to your gut, your skin, and that goes into your blood. It's just another delivery device.

Whether that could be done with naturally occurring organisms, taken from elite athletes, which would be particularly compelling and easy to get buy-in from the community, scientific and public, that's, I think, a little more speculative. I think it's likely enough that we're pursuing it quite intensely. [30:00]

McNally:

I return to Jonathan Scheiman to learn about the path forward -

What stage are you in in your research and what questions do you need to answer, and how are you going to go about doing that?

Scheiman:

The next phase is showing safety studies in animals. Obviously you want to show these bugs are safe before you give them to people. My presumption is, since they're actually derived from our bodies and derived from our gut,

chances are they're going to be safe. Then to your point, starting to do trials with athletes and showing that, for instance, these athletes can run longer or could run faster, or even things in terms of mental toughness.

McNally: [30:35]

One of the things that I noticed in reading some stuff is that sports nutrition is big business and so is probiotics, but the overlap is small. Probiotics is a very small part of sports nutrition. This seems like an opportune situation.

Scheiman:

Yeah. I think currently, probiotics as an industry is around a \$60 billion industry a year. 90% of it is derived from two types of bacteria. We have trillions of bugs in our gut basically waiting to be discovered to disrupt that industry that have all sorts of cool functional applications and beneficial applications in our body. Sports nutrition is a \$115 billion industry. Gatorade makes \$3 billion a year. To your point, less than 1% of that industry is made up of probiotics. There's a tremendous opportunity.

McNally: [31:26]

The form that this is likely to take once you hit on some formulas that seem to be effective is a drink or something like that. What's your ideal timeline? When might a product actually emerge?

Scheiman:

That is something that could happen fairly rapidly. Actually, for our first set of probiotic candidates, we would imagine being able to commercialize them in this form within 18-24 months. Again, the great thing about the probiotic industry is that the manufacturing and delivery capabilities and large-scale fermentation, a lot of that stuff has been established.

McNally:

So you're saying 18 months to 24 months from the time we're having this conversation, there might be something available?

Scheiman:

I would say 18-24 months between the time we potentially commercialize the technology out of the Wyss Institute to getting a product to market. That's a process as well, but we feel really good that we could get to market certainly in an accelerated fashion comparable to other biotech companies, but the great thing about it is we could continuously innovate with our R&D and obviously not only just probiotics, we're talking about applications with the microbiome to look for, let's say, personalized nutrition applications, performance diagnostics, and then maybe one day applications beyond athletics. There's a lot of cool things we could do. Things we could do fairly quickly, but then obviously long term a lot of really transformative things we can do as well.

McNally: [32:57]

When these are finally available and an athlete takes it, what are some of the

effects we can actually expect? What are you aiming for on an athlete's performance or their biology?

Scheiman:

I think the applications that we're focused on currently are those of endurance, recovery, mental toughness, strength. Can we help athletes run longer? Can we help them extract energy from food better? Can we help them break down proteins and peptides better to aid with, let's say, muscle building and strength? Can we reduce lactic acid to prevent fatigue and soreness? Can we reduce inflammation to accelerate recovery levels?

McNally:

What has been the response of athletes? I would imagine that's two questions. One is to participate, to give you their samples. Two, to actually down the line be customers and seek improvement.

Scheiman:

It's actually quite amazing. The response has been overwhelmingly positive. For instance, we were in Rio for the Olympics. We were talking with some of the best athletes in the world about what we're doing... We spoke about recruiting athletes. We're in the process of following up with a lot of Olympic athletes and teams and institutions, and not to mention professional athletes as well.

They're so used to consuming nutritional supplements or doing training regimens with not a lot of functional validation behind them. When we tell them about the science, where we're coming from and what the applications are, I think they're just like, "Where do we sign up?" They're more than willing to provide us with an abundance of fecal samples. We've got freezers full of it.

McNally: [34:33]

I've got to say that, in keeping with their enthusiasm for this, I imagine somewhere down the road there'll be the question of is this performance enhancement?

Scheiman:

Yeah, we've received that question. The first thing I say is, "If it ever gets to the conversation of whether or not this is performance enhancing, it means we're doing something right."

McNally:

That's right. That's a victory.

Scheiman:

Exactly, because it means that we've actually identified, isolated, and developed functional probiotics that could help athletes. I could tell you right now, I've been into several NBA locker rooms and I've seen kombucha tea probiotics in them. Athletes are already taking probiotics. They're already

taking nutritional supplements. All we're doing is introducing technology to improve them. As you said, there are applications beyond athletics here. It's a question that we're not concerned with and we would obviously welcome if it ever comes up.

McNally: [35:25]

Jonathan, in other podcasts, I've spoken to teams at the Wyss who were in the later stages of spinning off startups. The startup is about to burst... You're in a much earlier stage. What is it like at the Wyss in your process? You assume there's a startup down the road, but what is it like in this stage in that process?

Scheiman:

One thing I could say is that, man, I can't imagine doing the work I'm doing and trying to translate the work I'm doing in any other place. In George Church's lab and the Wyss Institute.

The first time I met George Church for an interview and he invited me to the lab and ultimately the Wyss Institute, I said, "George, my background is in arts and athletics." He said, "Great, that's good. That's what we want." He's like, "We want people that think differently."

I've got to say, the Wyss Institute as a whole, it just really encourages people to think differently, and then think of ways that ... Part of what we're doing, and I know George's lab is big on this and the Wyss is big on this. We're scientists, but we don't want to be bottled up in a research lab and do things that won't have any applications in the real world. I think there's a real push and encouragement of scientists to think of ways where they can translate their science. Obviously this is the mission statement of the Wyss.

To that end, there's a tremendous amount of support. Not just scientifically, but also ways to think about business development, commercialization strategy. In every aspect of this, the Wyss has just been supportive along the way. Even to this podcast, take what we're doing and get it out there in the real world. It's just a tremendous environment for thinking differently, and then importantly trying to translate that work, ultimately for the benefit of the general population. [37:09]

George has been around the block a time or two as it comes to disruptive technology and also translating it and starting companies, so in terms of a mentor and an advisor, it's hard to find someone that would be better suited to help me in the process.

George is just, again, there's no idea that's too crazy for him. He's always challenging you to think bigger in ways that this could be impactful, and he's really big on that too. He's really big on developing technologies that ultimately are going to help people and will be educational. He's done stuff with the Personal Genome Project. He has something called PTP Ed, which also looks to educate people about genomics and genetics.

There's just been a tremendous amount of support in all regards. I could talk about one of my basketball coaches at St. John's when I first told him about this. The joke is, I asked him. I was like, "How can I work for the NBA?" He said, "John, you work at Harvard. Why don't you just invent something and have the NBA work with you?"

McNally:
Okay. Thanks a lot, Jonathan.

Scheiman:
Great. Thank you very much. [38:10]

McNally:
George Church sees probiotics that include gut bacteria of elite athletes as just one of a wide range of possibilities -

What's your big picture of where this field might go in the next 5 or 10 years?

Church:
The applications of human microbiome therapies, can range from fixing diseases, to athletic improvements, to mental components, to aging reversal. Almost every aspect of health and wellness and aging could be impacted if we get off to a good start, with the small number of therapeutic applications that are out there already looking very promising.

McNally: [38:56]
Finally, a question that always comes up for me is the Wyss is dedicated to translation and development of products and therapies that impact the world. How does that or has that influenced the path a momentum of this project?

Church:
The Wyss Institute really is a wonderful place to do basic research and swiftly move that into a translational environment where you can get it out and have an impact on society. Even at the very earliest formulation of the basic research, you've got your eye on the ball, you can see where it could go, and that can influence all the choices you make early on in the projects. It's a terrific incubator of ideas and collaborations among disparate backgrounds and disciplines.

McNally: [39:45]
How do you see your role as a mentor at the Wyss?

Church:
Well, right. Whether I'm advising postdoctoral fellows that are doing basic research, or as they transition into... all the way out to decisions about startups, marketing, getting things into the hands of the public. There are definitely some similarities where we're envisioning and debugging the

science. There's some differences where marketing is less of an issue for most post-docs. At most, you're worrying about whether you can market it to the peer review journals. To some extent, you want to complement them. If they're already going in one direction and that's healthy, you leave that alone, but if there's a new direction, that could open their mind...

I think one of the things I did with Jonathan was, he was focusing extremely on getting very clean and extensive mouse data. I said, "a) that's going to be expensive and take a long time, but b) it may not be that relevant, and we're dealing here with something that people are already eating. Maybe we could move more quickly into human clinical trials." I think that took him a little bit by surprise. He noodled on it, and I think that has influenced the path that we're taking.

McNally: [41:13]

Now, for Jonathan, this project is close to his heart as a basketball player. Is there a sport in your present or your past...? You've used yourself as a test subject before. If you tested this on yourself, what sport are you looking to improve in?

Church:

Well, right. I have participated as guinea pig number one in a project called PersonalGenomes.org, Personal Genomes project. It has included microbiome components, not specifically aimed at that project, not specifically aimed at sports. In my past, I was on the varsity track and wrestling teams in high school, and at the beginning of college.

I think what I'm most excited about is wellness, things that might result in reversing the aging process or extending youthfulness, and anything that could help with mental acuity. There is an axis between athleticism and mental acuity. The two interact in many ways that are only partially understood.

McNally:

For me, the part that strikes me as most exciting is the recovery part. Whether it's injury prevention or exertion recovery or fatigue recovery, all those sorts of things seem to me is an enormous market, much larger actually than the athletes who want that 2%, 3% gain in something. It just seems to me the general population that wants to be able to remain active for as long as possible.

Church:

Right, well, there's recovery in the ordinary sense where you run a few laps, and then your lactic acid gets back to normal levels. Then there's recovery from injury. To some extent, almost any athletic event involves minor injuries that you aren't even aware of, ranging all the way up to life-threatening injuries. And your body's ability to recover from those allows you to train harder, and again, allows you to extend the useful years of your life.

McNally: [43:20]

If one of these products comes to market, might this be something you would take, and what would you be looking to get from it?

Church:

I would be interested in taking it before it makes it to market. I'm interested, not just in the athletic components, but the aging and mental components as well. That may be an unintended consequence at the beginning or it may be something that's very intentional somewhere along the line. I'd be interested to be a guinea pig at any stage.

McNally:

Yeah. I must say, so would I. Might get me back out on the court. Thank you very much, George Church. It's a pleasure as usual. I really appreciate it.

Church:

Thank you, it was great being with you. [44:00]

McNally:

You've been listening to DISRUPTIVE: Sports Genomics. I'm Terrence McNally and my guests have been JONATHAN SCHEIMAN and GEORGE CHURCH.

You can learn more about their work with the microbiome, as well an exciting range of other projects at the Wyss website - wyss.harvard.edu - that's W-Y-S-S dot Harvard dot edu - where you'll find articles, videos, animations, and additional podcasts. In fact, George Church has been featured in a couple of other episodes of DISRUPTIVE.

To have podcasts delivered to you, you can sign up at the Wyss site or on iTunes, Googleplay or SoundCloud.com

My thanks to Seth Kroll and Mary Tol-ee-kas of the Wyss Institute and to JC Swiatek in production, and to you, our listeners. I look forward to being with you again soon. [44:45]

