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Tim Lightfoot. We are so pleased to have one of the giants in our field in exercise physiology, Dr. Jim Hagberg who is a Professor in the Department of Kinesiology at the University of Maryland. Welcome to the podcast, Jim.

Jim Hagberg. Good speaking with you, Tim.

Tim Lightfoot. Yeah. Dr. Hagberg and I go back more years than I think that either one of us want to remember, but I want to tell everybody a little bit about Jim and some of his accomplishments. Jim is one of the few scientists that has been funded by NIH, the Veteran Administration, the American Heart Association and the U.S. Olympic Committee. He has been awarded the American Colleges Sports Medicine Citation Award, which is one of our highest honors in our field. He has received the University System Maryland's Regents Award for research. He has won many other awards over his time. He has over 170 research publications. His PhD and Master's degree in Exercise Physiology is from the University of Wisconsin in Medicine and he did an NIH post-doctoral fellowship at Washington University's School of Medicine. And so Jim has actually been on the forefront of our field for many years and we'll talk about some of that work today. But why don't we get started with a really easy question, Jim. You ready?

Jim Hagberg. Sure.

Tim Lightfoot. Was there any specific event in your life that made you really interested in studying exercise? What got you into this business?

Jim Hagberg. Well it's a story that I use to tell students to open doors and stick their necks out every once in a while. I was a…I went to a very small college in the University of Wiscon-, in Wisconsin, I was a terrible distance runner but I loved it, I got injured and I went to the coach's office and said, could I help coach? And he said, of course. I can use all the hands I can get. So I went into his office, was helping him set up workouts and I saw this stack of books behind the desk and I said, well that looks interesting, could I borrow that and read it? And he goes, of course. I read that book and a couple of weeks brought it back and took the next one and then took the next one and by the time I got to the third one, he told me, he said that's an area called exercise physiology that you're reading in and the University of Wisconsin, about 100 miles up the road, has one of the best training programs in the world in it. And bells and whistles and light bulbs and everything started going off in my head because at that point in time, I was a sophomore or junior in college I had no idea what I wanted to do. So a bit fortuitous. So that's why I say try things. You just never know what might click somewhere along the way like that.

Tim Lightfoot. Well it's great that you walked into the office and volunteered to help.

Jim Hagberg. Well it's kind of what I am, I guess. I don't know. A volunteer along the way.

Tim Lightfoot. But I think that an important concept for the people listening many of which are students in that so many times the doors that you open on your own just to walk in and say hello, are sometimes the doors that gets you the furthest down the road.

Jim Hagberg. Yup I agree with that totally and I think if a lecture's going on on campus or something like that and looks interesting, go take a shot. You may get 15 minutes into it and say yeah that's not what I thought it was and that area's isn't what I thought it was and in 15 minutes you may have learned something you don't want to do and that's fine also but you just never know when all of a sudden you find what I call, what makes your heart pump peanut butter. What really gets you motivated and want to do it. And people are interested in what they heard about and if you haven't heard about it you can't be interested in it so go out there and hear about some other things.

Tim Lightfoot. Well and in that, one of the great things about being at a university, because I know probably like us at Maryland there are probably all kinds of seminars going on and especially in exercise science all the time and it's a little distressing to sometimes see the people that don't take advantage of that exposure.

Jim Hagberg. True, very true. I mean we have very few undergraduates show up at these and then they…some of them complain at the end that they weren't exposed to other opportunities. Well the opportunities were there you just needed to open that door a little bit. But is what it is.

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Tim Lightfoot. That's right, yeah. So let's talk about your research. You're well known for research in a couple different fields. So…well let's start with what you're working in now.

Jim Hagberg. Yeah. We're actually…our work right now is centered on some circulating adult stem cells.

Tim Lightfoot. Okay. Are those the [??? 00:05:31] cells…

Jim Hagberg. Yeah.

Tim Lightfoot. … that we read about?

Jim Hagberg. We now call them circulating angiogenic cells. This is a rapidly evolving area and the terminology changes too frequently and you almost need a program to keep up with what's going on but these are adult circulating stem cells so they're in all of us and when you take them out and culture them appropriately, we use them to play our little brand of science fiction because we grow blood vessels down the hall from our office.

Tim Lightfoot. Cool.

Jim Hagberg. And these cells are being used in infusion methods to treat cardiovascular disease and our goal is to try to learn more about why they function so well in athletes compared to others and perhaps…excuse me…perhaps then we can use that knowledge to help improve the function of those cells that are infused back into patients.

Tim Lightfoot. Wow. So…well there are so many questions there that you just raised. So and athletes seem to have more of these or the ones…these stem cells that they have function better?

Jim Hagberg. Yeah that's…mostly the function better type. There's a lot of issues on identifying these cells and counting them and the like and, so most people now…at the beginning it used to be focusing on number, now it's pretty much focused on the function of these cells and these cells just, under the same conditions, grow more blood vessels which if you think about endurance trained athletes they have more capillaries and better blood vessels so it's not surprising that when we get to this level they end up ahead of the game there also.

Tim Lightfoot. Is that one of the reasons that…or do you think it's one of the reasons why exercise is why they call it cardio protective or helps you grow collateral blood vessels in the heart?

Jim Hagberg. I definitely think it's possibly part of it. Yeah, yeah. I mean they're certainly not anymore close to definitive on that yet but things are certainly headed in that direction for that line of thinking.

Tim Lightfoot. Yeah. So you talked about athletes. Are these people that have just undergone endurance training or these are regular elite athletes that these stem cells work so much better? What I'm getting at is, can you take someone who really hasn't been fit and start having them do exercise training and these stem cells become better functioning?

Jim Hagberg. Yeah there's some evidence on that right now. We're using kind of a model that we've used…assessed a bunch of risk factors over the course of my career so we're taking a lot of older athletes and then having them stop training for 10 days and we see reductions in the function of those cells even over that short time period. And we're doing the flip side also. We're taking some older sedentary people and having them exercise for 10 consecutive days and looking at whether the upside of that response is also rapid. I'd like to be able to give you that answer right now but I don't know that answer just yet.

Tim Lightfoot. But you're working on…

Jim Hagberg. Working on that one right now.

Tim Lightfoot. So I guess hypothesis a little bit about how this will help elderly folks because that's what you're looking at is the older athletes and older non-athletes.

Jim Hagberg. Yeah I mean the question really is a cardiovascular disease question. It's not really so much an exercise question. I mean, again, this method is being used in cardiac patients. They take the individual cells out then isolate them down, purify them down and put them right back into the coronary arteries where the damage has occurred in a heart attack and the thought is these are regenerative cells so it should help that area regenerate. Well, we also know that in the patients that have heart attacks these cells don't really function very well. So it's great that you purify them down and have a nice pure solution of them to go in, but if the cells don't work, it's not going to help that much.

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We actually have some patent applications out to take these cells out, rev up some enzymes, tone down some enzymes to more mimic the function that we see in these cells in athletes and then be able to put those cells back into the individual and hopefully with a lot better function and a lot better chance for enhancing the regenerative capacity there in their cardiovascular system.

Tim Lightfoot. Really neat. So is this…you said that you're working on patents and obviously you're doing some things in humans. Do you think this will be a clinical procedure in the next three, four, five years? Longer than that?

Jim Hagberg. I mean this method called autologous intracoronary stem cell transplantation is being used now but again with mixed results. Had great hopes when it started but the hopes have waned a bit so yeah, we were hoping two to three years to be able to try this in some actual patients. I mean now we're trying it on their cells, extracted from them, but not being put back in at this point in time yet.

Tim Lightfoot. Wow that's really phenomenal.

Jim Hagberg. We're kind of having fun with it.

Tim Lightfoot. Yeah. So this is…you read a lot about the diverse responses in cardiovascular disease in different ethnic groups. Would this same process work as well in African-Americans as it does European Americans?

Jim Hagberg. I don't have a clue yet. Sorry I can't give you a very good answer on that one.

Tim Lightfoot. No that's fine it's just I'm sitting here thinking about…out these things as we're talking it's one of the things you always see about it is the difference in the cardiovascular risk factors amongst those two ethnic groups.

Jim Hagberg. Yup. I mean I'm not even really aware of much data at all yet on differential functions of these cells across the racial or ethnic groups. It's a very plausible hypothesis at this point in time I would say.

Tim Lightfoot. Yeah. One to think about. So that's really exciting and you have been involved in many different exciting areas of research and one of which I want to talk to you a little bit about for the sake of the audiences about one of your early papers, in a group of subjects called McArdle Syndrome patients. Really has become a classic study in exercise phys. Can you tell us a little bit about that study?

Jim Hagberg. Yeah at the time way, way long time ago in ancient history…

Tim Lightfoot. You notice I didn't say the year.

Jim Hagberg. Thank you. There's this concept called the anaerobic threshold and anyone whose exercised knows kind of the feeling of the anaerobic threshold. As you exercise more and more intensely when you cross some point all of the sudden you really start breathing much more rapidly, much more quickly, things get out of control, kind of [???ventaltory 00:13:09] wise and cardiovascularly and metabolically and it was proposed that's where a person went anaerobic or where they started to produce energy without the use of oxygen. Nice concept. Something most definitely happens at that point around 70 percentish of a person's maximal oxygen uptake? When you cross that breakpoint you can't exercise anywhere as close to as long as you could below that breakpoint. And again, it was proposed to be that when black lactate levels went up that was the indicator of anaerobic metabolism and the consequences of that were that you couldn't exercise very long.

Tim Lightfoot. Now let interject here for the audience. That anaerobic threshold theory was proposed in like 1968 and it really took root in exercise phys. circles. I mean you still see it in some textbooks as a matter of fact so that was very much foundational at that point.

Jim Hagberg. Yeah it was and it…I still…well I'll get to it at the end but I mean I still…there's something going on there. I guess I would just say we still probably don't know totally what it is exactly. But I was at Washington University in St. Louis and was actually doing some work with a neuromuscular disease center there and they had this population of patients with various neuromuscular disease and some of them that came in to be tested too, before we got our little thinking caps on and realized what we had. Two of them had this disease called McArdle Syndrome and it's a disease where they're missing one specific enzyme in muscle.

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And the bottom line is they can't produce energy anareobically. They lose part of the metabolic pathway to break down glucose into lactate. And so someone said to me, a good friend of mine, actually John Ivey up the road there a little ways at the University of Texas said, wow, he said, that could be a really interesting way to study the anaerobic threshold. And so we got four of those patients together and for those students out there saying wow I'd like to do a study with just four subjects. Well, at the time there had been 50 of those people described in the world so

we had about 10 percent of the whole world's population in our study. So think of it that way rather than the N04.

Tim Lightfoot. You had a good sampling of the population.

Jim Hagberg. Of the population which started off pretty small. So we put…subjected them to a progressive [??? Pychologemeter 00:15:59] test just as people did to assess V02 max and anaerobic threshold on a bike and clearly if it's the production of anaerobic metabolism or the increase of anaerobic metabolism that causes this breakpoint in ventilation, then these McArdle's patients should not have one.

Tim Lightfoot. Right, right.

Jim Hagberg. But they do. And I presented that at a meeting of the American College of Sports Medicine in Miami and it was a rather contentious affair.

Tim Lightfoot. He says modestly.

Jim Hagberg. But it was interesting because I had about four or five people come up to me before and they said since we've seen your abstract we've actually tested two McArdle's patients and we see exactly the same thing you do so we'll be in the audience just in case it gets too heated. And I said, thanks guys.

Tim Lightfoot. Nothing like validation in the audience, huh?

Jim Hagberg. Yeah that helps.

Tim Lightfoot. Yeah.

Jim Hagberg. So yeah it was a bit heated. Science is not supposed to get heated but sometimes it does. And the bottom line though is I think there is still something definitely going on there. It relates to distance running, performance and all other kinds of endurance performance but I just don't think the cause is as simple as what it was proposed to be. I mean there's a lot of things that changed dramatically at that breakpoint. Catecholamines and a whole bunch of other hormones and substrates and if they were as easy to measure as lactate, we might have called this the catecholamine threshold or some other hormone threshold or some other substrate threshold if they were as easy to measure as lactate was.

Tim Lightfoot. Yeah. Well and I think for the audience, especially those that aren't in exercise science, what I want people to understand is the impact that that one study with…admittedly it was only four subjects, but the impact that that study had on exercise phys because that really caused everyone to relook at that theory and shortly after that we started seeing study after study after study in a variety of different ways looked at, showing that that theory probably didn't hold water.

Jim Hagberg. Yeah, yeah it was, it was kind of encouraging to me that it kind of opened that door to get people to look at things a little differently and a little more open mindedly and come up with a true underlying physiology of it. I mean that's what it's all about. I wasn't…my goal wasn't to blow somebody out of the water. It was to find out if the answer, the explanation is really true. Had nothing to do with personalities or individuals. It was the theory and the hypothesis that they had and the interpretation.

Tim Lightfoot. Yeah that's what science is supposed to be about, isn't it?

Jim Hagberg. Amen.

Tim Lightfoot. Yeah and unfortunately during that and that's the other thing I'll share with the audience is during that time, there were a lot of people that didn't look at it that way. As you say you were…I think, like I said, understated and when you said contentious there were many meetings that I was at that I thought speakers were going to come to blows over these things.

Jim Hagberg. Yeah there were some…not to appropriate interchanges of points of view. Let's put it that way.

Tim Lightfoot. Yeah, yeah. That was…and those things…those are very disappointing sides of science that every once in a while we see though, right?

Jim Hagberg. Yup. Of course. I mean it's people's life's work. They do get invested in it even though you're supposed to kind of distance yourself from it but if you're working out of 40 or 50 or 60 hours a week it's hard to step away and say oh, what I just thought was totally wrong and somebody blew me right out of the water. Well that's not a good feeling.

Tim Lightfoot. Right, right. Well like I said that's why I'm so glad you're on the podcast because it's not often that you get to talk to someone who's done a seminal study like that that really did change the paradigm. That word paradigm is used a lot but I think that was…the publication of that article was really a turning point for so many studies in that area. So great job.

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Jim Hagberg. One other interesting story about that. I had a few days before that meeting was to take place, I had a death in the family, an older grandmother, so it was not a terrible surprise, but I didn't actually know if I was going to be able to make it to the meeting to present it. And the second author said, you damn well better be there, he says, because that's one presentation I don't want to give. And I did make it and it was all good.

Tim Lightfoot. And they were supporting you. They were just standing behind you the whole way, right?

Jim Hagberg. That's right. Way behind me.

Tim Lightfoot. Well Jim it's been a great honor to have you on the podcast today and as we do with all of our speakers at the end of the podcast we give them a chance to give us their take home message. So what would be your take home message for today?

Jim Hagberg. I think you got to find the phrase I used before, what makes your heart pump peanut butter. To me coming to work is not a job. This is fun and I've been doing it for quite a number of years. We won't go into exactly how many but quite a number of years and it's still fun and I enjoy interacting with the younger students whether they're undergraduates or graduate students because it helps to keep me young and that's a good thing. I don't want to curl up in a ball somewhere and be an old person. So open doors, track down what makes your heart pump peanut butter and find something that gets you to the point where it's not a job, it's fun and it's what you enjoy doing.

Tim Lightfoot. Great take home message and I hope everyone is listening and takes heed of that. Thank you again Jim for being with us today.

Jim Hagberg. No problem. I enjoyed it, Tim.

Tim Lightfoot. Been great to have you. And for all of you that are listening, thank you so much for taking the time to download and listen. Our regular listeners know that at this point in the podcast we always have a podcast question of the week and here with our podcast question this week is our producer, Kelly.

Kelly. What cells do not function as well in patients with cardiac problems?

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