Transcription results:

S1 00:18 [music] So our next speaker up is actually Aggie Class of '87. We were so thrilled this year to welcome back to campus Dr. Melinda Sheffield-Moore, who's the new department head of health and kinesiology. Please join me in welcoming her to the stage. [applause]

S2 00:35 Thank you. Howdy, Aggs.

S? 00:39 Howdy.

S2 00:40 Wow. What a wonderful community event to be held on Texas A&M campus. And the fact that we have partners from all over the state really speaks volumes to the work that Dr. Lighfoot has done. And of course, with the generosity of the Huffines Institute and the Hilliard family, we are able to bring together a wonderful group of scientists to talk about such fun topics. And today, I'm going to talk to you more about a fun topic that came out of my lab, and it's called aging skeletal muscle and the little blue pill. So when Dr. Lightfoot asked me to do this talk, I thought a TED Talk. Wow. That's a tough one. Because we as scientists, when we develop our talks, we give ourselves little triggers throughout our talks so we know exactly what we want to disseminate to you as our audience. And I was really struggling with how to do this, and I thought I could just do a stand-up comedy routine because that would be a really neat thing to do. And when I was looking through the American Association for the Academy of Sciences meeting that I'm going to go to in March, I saw an interesting session, and it was called Science Comedy Night. And it was a special session that they were going to be offering, and I thought, well, that's really cool. So I thought I would at least, if nothing else, try to have a little bit of a true more TED Talk environment. But unfortunately, I'm talking about science, and science is a little bit of a tough sell sometimes and difficult to make funny. Comedians are really good at what they do because of their delivery, but they're also really good because they have fantastic material. So I tried to pick some science that I do in my lab that's maybe a little lighter and a little more fun. So let's see how this goes.

S2 02:33 So one thing that isn't so funny is the fact that we're really facing what I would consider to be a global healthcare crisis. And this crisis is a disability crisis. And it stems from the fact that we have a rapidly growing population that is aging. And the estimates are that by 2050 that individuals over 65 will account for, I think, 25% of the population. And they will double. And individuals 80 and older will go from approximately, I believe the numbers are 10 million individuals to 30 million individuals. So if you look at this little cartoon, you see our baby boomers. Everybody else is flowing into the emergency room in a normal size ambulance. But the baby boomers are going to come rushing to the doors of our healthcare system, and we're not prepared for that. And so today I'm going to talk to you a little bit about how we can reduce things like mobility disability and medical disability by being physically active and how physical activity throughout our lifespan is our friend, but that when we reach sort of this metabolic tipping point in times of illness or chronic disease, that perhaps we may not have that luxury of exercise. And so what can we do in order to prevent this disability crisis. So I'm going to talk to you a little bit about some of this behind-the-scenes work that's going on in science. So skeletal muscle dysfunction associated with aging is associated with a number of different factors. But the one factor that I want to drive home today is that it's primarily associated with inactivity. And if you look at this depiction here, you can see that inflammation, oxidative stress, inactivity, anabolic resistance of skeletal muscle that occurs with aging, all of these

things can lead to something that we refer to as the sarcopenia of aging. And all that really means is the loss of muscle mass and physical function associated with age.

S2 04:47 And as you can see, the bar that goes to inactivity sort of feeds to the sarcopenia, this loss of muscle mass and loss of physical function. And one of the aspects of this that occurs with aging and chronic diseases, where we become disabled has to do with skeletal muscle fatigue or just generalized fatigue. And I have a colleague that was in my lab that was very interested in the role of fatigue in disability. And so as I said before when we reach that sort of metabolic tipping point if you will, and we don't have the opportunity to exercise as a means to prevent disability, to prevent sarcopenia, we as scientists are implored to come up with alternative strategies to help society prevent from having this disability crisis. So why is it important? Why do we need to maintain our skeletal muscle health as we age? Well, I've listed about five or six points here that are critical to my argument. But implicit in this is that we obviously want to maintain an independent living style. We want to keep our muscle strength. We don't want to be fatigued and feel bad. We don't want to trip over our own feet and break a hip. And we want to have a good quality of life. And we also don't want to add burden to the medical community by being inactive. And many of these other things that come about with inactivity, like obesity and other metabolic disorders, all lead us down that path of chronic disability or even things like acute illness. And these things are the things that put us over that functional or metabolic tipping point that can put us in the hospital.

S2 06:44 This shows just basically a depiction of the fact that there's a couple of ways that we can manage our muscle mass. So we can grow muscle mass, we know, nutritionally, with androgens such as testosterone, exercise, and blood flow. And skeletal muscle is this tremendous reservoir of amino acids and proteins that is very selfless when it comes to giving up these amino acids and proteins in times of need. And so, what happens is, is that when we're inactive or we fail to eat, so we're fasting, or we become inflamed because we're older and we become arthritic, or if we get a chronic disease such as cancer, where we have tumor factors, those are the factors that will cause our muscle to break down. And as I said, it's a very selfless tissue. But it's a tremendous reservoir of amino acids for us. And today I'm going to talk to you a little about a particular way that we believe that enhancing blood flow by a process of using a pharmacologic agent will help us mediate nitric oxide and grow skeletal muscle. So when you get tipped over in this little metabolic tipping point I keep referring to, there's not that many alternative strategies. So apart from exercise, we really have no other approved pharmacologic therapies to help us. My group participated in this 70-day bedrest study where we put healthy guys to bed for 70 days, and we had some strategies to try to prevent them from losing muscle. And one of the things that NASA has done is develop this vertical treadmill. But when you and I go into the hospital for 70 days or 7 days, we don't have the luxury of having this phenomenal treadmill that allows us to remain supine and keep our muscles working as we're ill.

S2 08:44 So, unfortunately, we're stuck with coming up with some alternative strategies, and as I mentioned to you before, Viagra or blood flow is one of those ways that we felt like might be a good way to grow skeletal muscle because there was some evidence with Viagra that it reduced fatigue. There was also some evidence from our laboratory and others that blood flow was stimulatory to skeletal muscle. So Viagra works because it works through a nitric oxide-mediated signaling process in skeletal muscle, and by doing that, it vasodilates our vessels in our capillaries in our skeletal muscle. And it opens things up, allowing for additional nutrients and things to be delivered to the muscle which helps it then grow. So today, I'm going to talk to you about a little bit of serendipity that has occurred in my lab. And when we first started this Viagra study,

we were really just interested in its ability to sort of mute fatigue that's associated with aging. And this was a very short acute study. It's a placebo-controlled, randomized study in younger men and older men, and we started with the lowest approved dose of Viagra or Sildenafil. And what we did was, we gave it once a day to these older and younger men, and we measured things like muscle performance with isokinetic, isometric strength, standard fatigue protocols on an isometric leg extension machine. But we also decided, fortuitously, I might add, to measure muscle protein synthesis because muscle protein synthesis-- I'm a muscle metabolism person, and that's one of the common things that we do as part of our clinical trials. But it's also one of the more difficult things that we do, and one of the more costly things that we do. And this was just supposed to be a proof-of-concept study to see if Viagra could reduce fatigue because we know that fatigue is one of the primary debilitating symptoms of chronic diseases such as cancer but also is a debilitating process in the normal process of aging.

S2 11:03 So we did the muscle performance measurements as well as, in the end, we looked at some muscle proteomic data. And I'm going to talk to you a little bit about that. So this is where the serendipity begins to creep in. Yay, we showed that Viagra-- when we look at skeletal muscle fatigue testing, Viagra, compared to placebo, is capable of allowing individuals to produce more repetitions in a leg extension exercise. Okay. Proof of concept. Yay. We're there. Way to go. But that's kind of boring, and we had already infused the isotopes. So we'd already incurred the cost. We'd already decided that we would-- let's just go ahead and measure and see what happens with muscle growth. No expectation whatsoever and the serendipity of the study is that we went ahead and measured this, ground up the muscle, put it on the mass spec. And lo and behold, my colleague Dr. Bill Durham got these results showing that the fractural synthetic rate or the muscle protein synthetic rate of skeletal muscle was greatly increased in response to seven days of Viagra at the lowest dose. We didn't believe the results. So we went back, and we measured them again, and then we had a lab meeting, and we talked about it and said, "This can't be true," and we measured them again. These are levels of protein synthesis that equate to even more than what we would see if I gave testosterone to a male acutely and looked at muscle growth. And so we got super excited, but we still didn't believe the results. So I sent them to a colleague of mine who runs a proteomic core lab at the University of Texas medical branch, and he ran some proteomic-- he ran some proteomics for me looking at abundance and nitrosylation. Because remember, I said that Viagra works as a nitric-oxide mediated signaling process in skeletal muscle. And so we were not only interested in total abundance, but we were interested in the nitrosylation, and we wanted to know which of these key growth pathways in skeletal muscle were affected because of Viagra.

S2 13:23 And what we see is that Viagra is actually capable of remodeling skeletal muscle in a very functionally adaptive way. And what that means is that when we look at the pathways that are most affected-- those pathways are things like muscle development, the makeup or the morphology of the muscle, things like that. So these proteomic results confirmed what we saw with our mass spec results and also confirmed what we saw with our fatigue results. So what we now have is serendipity in the little blue pill. We have Viagra's ability to reduce skeletal muscle fatigue. We have its ability to stimulate muscle growth in humans and to remodel the skeletal muscle proteome. This makes it a viable pharmacological intervention for individuals who maybe are hospitalized and are unable to utilize exercise or a vertical treadmill to stimulate muscle growth and to prevent disability and muscle loss. So this unexpected road means that essentially my moral of my story is that the next time that-- you should stay healthy and fit and exercise throughout your lifespan. But the next time

that someone you know takes Viagra, my guess is you're not going to be thinking about sex. Thank you very much. [applause]

S1 14:53 Thank you Dr. Sheffield-Moore.

S2 14:55 Certainly.

S1 14:55 The phone is starting to light up here. The first one we got in-- please tell me your name and where you're from, so I can give you credit. This is coming in several times. Are you now worried about Viagra being used as a performance-enhancing drug?

S2 15:10 The athletes are way ahead of us in this field. I think Viagra probably is already being used as a performance-enhancing drug. The athletes are usually well ahead of the scientists in this department. So yes, I'm worried about that, but that doesn't prevent me from wanting to sort of help society as a whole and to prevent disability. So the athletes can do what they need to do, and the rest of us will still work towards helping overall society, others.

S1 15:40 There was a question that came in earlier, and I wanted to get to it. Excuse me while I page to it.

S2 15:51 I forgot to mention that-- while you're paging to it, we're going to-- I was supposed to say the word penis, sex, erectile dysfunction, and several other things, and then you were supposed to count how many times I said them. And then Tim, Dr. Lightfoot, was going to give you a prize if you could give me exactly how many times I said those things. But if you noticed, I managed to give my talk without saying anything but sex at the very end, so.

S1 16:16 Too late for that party [laughter]. Okay. This is from Arash Bandegan. And given what you just said - he's from Western University - especially if you're talking about helping frail older individuals, what do you recommend as a noninvasive surrogate approach to measuring muscle protein degradation in frail patients in place of muscle biopsies? So that's the population you're working with.

S2 16:38 Well, so if I understand what he's asking, we've done this in space flight years ago, even with John Glenn. We had a study where we used an isotope drink that then we can collect blood and/or urine to be able to measure and model muscle protein breakdown. So we've done some of those studies in space flight already because in space flight, we really don't have the opportunity to take muscle biopsies. So that's a great question.

S1 17:08 I've gotten this question three times from unattributed sources. So we're going to ask this question. How would Viagra affect women in this case?

S2 17:16 So some of the results that I can't talk about because we have some intellectual property issues going on-- or not issues but some good things, are some of these future studies that we've already started. And we have put women on Viagra. And the number one question I get is, "Does it grow their muscle?" And I can't answer that yet, but number two is, "Do they have a similar effect that it-- does it have a similar effect on women that it has on men?" And the answer is probably from a skeletal muscle standpoint, the answer is yes, but from a ability to desire more sex, the answer is no. So we don't have-- it doesn't work in that same manner for women from a sexual behavior standpoint--

S1 17:59 But it develops muscle? May develop muscle?

S2 18:03 It may develop muscle.

S1 18:04 Excellent. And we'll leave it with that.

S2 18:05 Right. We'll leave it at that.

S1 18:06 Please join me in thanking Dr. Sheffield-Moore.

S2 18:08 Thank you. [applause] [music]