[music]

Lightfoot — So we're pleased to welcome to the stage our next speaker, Dr. Sue Bodine from the University of California, Davis. Please welcome Dr. Bodine to the stage [applause].

Bodine — Thank you. So howdy.

S3 00:36 — Howdy.

S2 00:38 — So it's a great honor to be here on stage today with all these remarkable individuals. So today, I want to talk to you about skeletal muscle, a tissue that I have found fascinating for years but is very much underappreciated. So skeletal makes up greater than 40% of the body mass and is involved in many important functions in the body including uptake and storage of glucose and control of metabolism. But its most important function is the control of movement through the production of force. While many in this room, if asked, would identify the heart or the brain as the most important organ in the body, I would like to convince you that skeletal muscle is critical for living a healthy life because it allows us to live an active lifestyle and an independent lifestyle.

S2 01:38 — Skeletal muscles come in many shapes and sizes, so what controls the force or strength that a muscle produces? This is a topic that has interested me since graduate school. So, many of you have probably seen the outside of a muscle but I want to show you the inside of a muscle, maybe. Here we go. Here we go. So what this slide shows you-- oops. Here we go. So this is a cross section taken from a lower limb muscle of the rat. So I study the rat because it is a great model for human muscle but also because it allows me to actually investigate the mechanisms that control skeletal muscle size and function. So if you look at this slide right here, it shows a number of things. First, you can see the individual muscle fibers within the muscle which are outlined by yellow. If you look at these fibers, you see that they're not all the same size, that there's a diversity of size of these fibers. The other thing you see in this cross section is that there's a diversity of fiber types within a muscle. So, many of you have probably heard about fast-type or slow-type muscle. Fiber type is a property of a particular protein in the muscle called myosin, which is a contractile protein. And so we can use antibodies as shown here to identify the types of myosin that are expressed in individual muscle fibers. So in this section, the blue fibers are the slow fibers. The red, green and black fibers are all expressing different isoforms of the fast myosin heavy chain. I forgot where I was going to go with this.

S2 03:36 — Right, okay. So it turns out that the size of these individual fibers is a highly plastic property of skeletal muscle. So what controls the size of these muscle fibers? With respect to size, the saying or the phrase "use it or lose it" readily applies. If we do not use these muscle fibers, we will not maintain the size of these muscle fibers. This graph here shows the relationship between muscle mass and strength as a function of age. It's divided into three primary periods: early life, adult life, and older life. So what controls muscle mass during each of these periods? It turns out that it's not the same at each of our ages. So during early life, the increase in muscle mass and strength that we see is controlled primarily by hormones, such as growth hormone and testosterone, but also by increased activity and increased external loading. It is during this period of life that most of us will reach our maximum peak.

S2 04:51 — During adult life, now we go into a mode of trying to maintain that peak. In order to maintain that peak, we need to do resistance exercise. So it turns out that to maintain or build muscle mass, muscles need to contract against variable external loading. It is not enough just to activate these muscle fibers. So during this period, we need to do

resistance exercise in order to maintain muscle size. We've heard a lot about endurance exercise by the other speakers and this is, although very important for the metabolic properties of muscle mass, it is not enough to maintain the size of the muscle fibers. So the best way to do that is through a resistance exercise program that usually involves some type of weight training.

S2 05:49 During older life, our goal is to minimize the loss of muscle fiber size. Unfortunately all of us, no matter what our training state, will lose muscle mass as a function of age. And what makes matters worse is that as we age, our muscles also become less responsive to resistance exercise and so it's harder to build muscle. The other thing that this graph shows you is that there is a correlation between muscle mass and longevity. Recent studies have shown that people in the upper third of this population live a longer life, whereas people in the weakest third of this population live a shortened life. The reasons for this are not clear, but one of the reasons may be that with larger muscle mass, you are more active and also able to overcome a critical illness such as cancer or cardiovascular disease.

S2 06:57 Unfortunately, the loss of muscle mass, as I just said, is an inevitable consequence of aging. But the loss of muscle mass, or muscle atrophy, also occurs under a number of different conditions and diseases, some of them listed here. So a decrease in external loading or activity will induce muscle loss. This occurs under conditions of extended bed rest, but also can occur with immobilization of a limb such as may occur following an injury like an ACL tear and also under conditions of a neural injury which may occur during neurodegenerative diseases. But other factors can also affect the size of a muscle. Some of them being malnutrition, metabolic diseases, such as diabetes and obesity can have an impact on muscle health, cancer, and also cardiovascular diseases, and a decrease in muscle flow or blood flow.

S2 07:59 So unfortunately, there are no drug treatments or drug therapies to prevent muscle loss and there may be many reasons for this. One of them being that each of these conditions is a separate disease and difficult to study. But also that, in general, the loss of muscle mass has not been seen as a critical life threatening variable and thus, has not been studied in great detail. So what can you do to prevent muscle loss? So if we go back to this graph what can we do to stay in this upper third of the population? Today, the best remedy is resistance exercise. Where was I going to go with it? Excuse me. So best remedy here is resistance exercise. And when I refer to resistance exercise, what we need to do is to do intense resistance exercise, not just any type of resistance exercise.

S2 09:14 So why do I say intense resistance exercise? So let me show you here. So here is a cross-section taken from an adult muscle of the lower limb and it shows two different fiber types, the green fibers and the black fibers, both of which are fast fibers. What you see two things here, that the black fibers generally occur in isolation or in groups of two or three and the green fibers are significantly greater in size. Now I'm going to show you a section from an older muscle and this illustrates a number of points. One is that there are fewer green fibers and also that the green fibers are smaller. The other thing that you see are that the black fibers, there's more of them, but also they're clustered together in groups. What is responsible for this fiber-type grouping with age?

S2 10:12 Well, what happens with age is that we start to lose motor neurons, and in particular, we lose motor neurons that innervate these large green fibers. As these motor neuron die, these green fibers become denervated and so existing motor neurons sprout and reinnervate these fibers. And as they reinnervate, they modify or change the myosin that's expressed in these fibers and so you see fiber-type grouping. So this is an indication that there's been some type of neural injury and remodeling.

Unfortunately, what happens with age is that motor neurons continue to die and with advanced age the existing motor neurons fail to sprout. And so muscle fibers become permanently denervated and eventually die. And so with aging, not only do we see a decrease in fiber size but we also see a decrease in the number of muscle fibers. So is there anything we can do to prevent this from happening?

S2 11:20 As I mentioned, there are no drugs to treat muscle loss and there are no drugs to treat age-related muscle loss. So the best thing that you can do is resistance exercise, but this resistance exercise needs to be intense resistance exercise. And why is that? Because these large, fast fibers are only recruited when the muscle produces heavy loads or high loads. And so in order to activate these motor neurons, you need to do resistance exercise. So it's been shown, recently and over the years, that endurance exercise is good for cognitive health and for neurons in the brain. But for the muscle, we need to activate specific sets of spinal motor neurons or specific sets of motor neurons in the spinal chord. And this can only be accomplished through high-resistance exercise. So my theory is that if we could activate-- if you can retain or if you can activate these fibers, that somehow we would help these motor neurons and prevent them from retracting. And hopefully, prevent the loss of these terminals and these motor neurons.

[silence]

S2 12:54 So, in conclusion, the main point that I would like to leave you with today is that you need to continue to use your muscle fibers in order to prevent muscle atrophy. There is much that we still don't know about age-related muscle loss and the loss of motor neurons. But what we do know is that resistance exercise is good for muscle and can help improve the strength of muscle. So to date, as I mentioned, there are no effective drugs to treat age-related loss of muscle mass and strength. So the best thing that you can do is stay active and be sure to include resistance exercise in your routine. What I hope to leave you with is the message that proper skeletal muscle function is important for a healthy life and for living a high quality of life. It also may be important for a long life. Muscle health starts at a young age, but it is not too late to ever start exercising. So I hope that no matter what your age, you will be active and include a resistance exercise training in your activity. Thank you.

[applause]

S1 14:22 Thank you, Doctor Bodine, how are you?

S2 14:23 Thank you, good.

S1 14:25 Good. This is from Brandon N. He's here and I must say that this question-- you may have to explain a little bit because-- but I think he was prepared. I think he's been reading your papers because 30 seconds after you walked up, I got this question.

S2 14:38 Oh no.

S1 14:38 How can mTOR affect the rate of muscular regeneration from satellite cells?

S2 14:44 How can mTOR-- okay. So what many of you in the audience may not know is that mTOR is a kinase that has been shown to be important for muscle growth. So it needs to be activated and it is activated in response to resistance exercise. So with respect to regeneration, whether or not mTOR is important for satellite cells, we know that satellite cells are important for regeneration. And we know that mTOR needs to be activated in order for muscle fibers to grow during that process. So I'm not sure what the link between mTOR and satellite cells are, but they both need to be activated.

S1 15:29 Excellent. Okay. We have a question here from David F. at Michigan State University,

who by the way was our stage manager here for the first two years of the Huffines Discussion. "With muscle function being set in early life, should we promote an intense exercise prescription for children in order to minimize muscle loss as an adult?"

S2 15:49 That's a very interesting question. So I think that it is important to have some type of resistance training at a young age. And when we look at that graph and we say "early life" many of you in the audience still are in that category. So I think you can start resistance exercise too early, too young. But I think incorporating resistance exercise early is important and there's some people that theorize that this early exercise may cause changes in the muscle - epigenetic changes - that have long-term consequences. And so early activity may be beneficial later on. For example, if you take a period of inactivity and then become active sometime later.

S1 16:39 Excellent. The phone is blowing up now [laughter]. You stated that there is a correlation between muscle mass and the longevity of the life of an individual. With that said, could the use of anabolic steroids or other PEDs affect an individual's lifespan for the better?

S2 16:56 Good question. While I think anabolic testosterone and growth hormone are very important for growth in pre-puberty, I don't personally believe that there's good data to show that anabolic steroids or testosterone is needed to maintain muscle mass in the adult. So if you're somebody that has very low testosterone levels, I think giving somebody testosterone with resistance exercise will improve muscle health, but I don't think just using anabolic steroids by themselves are going to improve longevity or improve muscle mass.

S1 17:35 Super. Thank you so much.

S2 17:36 Thank you.

[applause]

[music]