What Drives Muscle Growth & What Doesn't | Dr. Mike Roberts

Perform with Dr. Andy Galpin · Episode 29 · July 8, 2026 · Transcript

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Dr. Andy Galpin
Is it then fair to say there are a subset of people who just simply cannot grow muscle from strength training?

Dr. Mike Roberts
I think the percentage of folks, when you look across different studies, the non-responders are pretty low. So that is to say that most people will see at least some growth. But I'm always devil's advocate. Yeah, okay, so they grow, but some people see a lot more growth than those people, right? So, there are clusters. There's-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... you can call it tertiles. You have low, moderate, high. There is that. But that is to say that maybe less than 5% of the population, if not even smaller, that will not grow.

Dr. Andy Galpin
The science and practice of enhancing human performance for sport, play, and life. Welcome to Perform. I'm Dr. Andy Galpin. I'm a professor and scientist and the executive director of the Human Performance Center at Parker University. Today, I'm going to be speaking with Dr. Mike Roberts. Mike has a PhD in muscle biology and has focused his research in his laboratory at the University of Auburn, mostly on how skeletal muscle responds to strength training and resistance exercise. Mike is by far my go-to reference when I want to talk about, understand, or learn more about how and why skeletal muscle grows in response to exercise. In this episode, you're going to learn a lot about that. He will cover many practical applications, such as what do we know about the style of exercise, how many repetitions, and how much volume is needed to maximize muscle growth. He'll also give you an extraordinary insight into the biology, molecular mechanisms, and cellular components that go into understanding why and how muscle grows in response to resistance exercise. So with all that in mind, I hope you enjoy today's episode with Dr. Mike Roberts. Dr. Mike Roberts, it is amazing to have you here, man. I really appreciate you flying halfway across the world to come hang out for a day. It's been a long time.

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Dr. Mike Roberts
It has.

Dr. Andy Galpin
If you've ever seen any of my videos or conversations on muscle physiology, there's a strong chance it's Mike's work that I'm talking about. So I just had to have you in. We're going to spend as much time as we can today on muscle. And I'm really excited because your lab has done such tremendous work in this area, covering everything from responders versus non-responders to exercise, right? So why are some people growing muscle and other people having a really hard time?

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
You guys have done a lot of work in aging. So how does this process change with age, with sex, with different nutraceuticals and nutrition and supplementation? But mostly what you guys have focused in on what I'll just call the molecular side-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... the equation, right?

Dr. Mike Roberts
That's where-

Dr. Andy Galpin
What's happening in the cell. So with that in mind, actually, I don't think I could think of another person in our field whose science I've seen misrepresented and misquoted more than yours.

Dr. Mike Roberts
Oh, wow.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Thanks.

Dr. Andy Galpin
So people love to use your stuff as fodder for whether it's a training recommendation or something else. And so I would really love for you to maybe set the table clearly on what some

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of your work does, what it suggests, what it doesn't suggest-

Dr. Mike Roberts
Sure

Dr. Andy Galpin
... and otherwise. So that's the playbook-

Dr. Mike Roberts
Okay

Dr. Andy Galpin
... in large part, and I think it would be best for us to actually just start with a broad understanding of how does muscle grow. When we say that, and we say this word hypertrophy, one of our muscles, presumably our biceps, because that's what everyone cares about, right? When it got bigger, how? Why? And then that, of course, will lead us into, if you wouldn't mind giving us an overview of what we'll call the molecular mechanisms of how that muscle grew, why it grew, and then that'll give us the table to get into all the nuances of how do we optimize that, how do we alter it, and change. So I'll set you up that way, and I'll let you lead from there.

Dr. Mike Roberts
Okay, sounds good. So how does muscle grow? The simple answer is mechanical overload. You will see that in the literature time and time again, which is to say that weight training for humans, or very, very intricate models in rodents, will allow the muscle to grow. So, when we say mechanical overload, if any of your viewers read that, we're referring to resistance training in the human. Consistent resistance training, and we'll get into programming, not my forte, like we talked about everybody, Brad Schoenfeld, who is very well-versed in that, but I have some ideas in terms of how to maximize hypertrophy, sets per week, that sort of thing. If you consistently resistance train, we've seen this time and time again with 10-week studies, 12-week studies, 16-week studies. We'll call it two to three days per week, full body. What you're seeing in terms of hypertrophy is mainly radial hypertrophy, which is saying that the cross-sectional area of the tissue is increasing in size. How do you measure that, right? So you can do muscle imaging. We do ultrasound in the laboratory. We have a panoramic, so we can actually look at the rectus femoris, the vastus lateralis, and we can see something to the tune of, we'll call it 15% increases in the cross-sectional area of that muscle tissue. And then from there, we can take muscle biopsies. That's mainly from the vastus lateralis, our lab does the vastus. And we'll see probably, I would call it 20 to 25% type II fiber cross-sectional area increases. So at the cellular level, those type II fibers, fast-twitch fibers, are increasing 20, 25%. And it's preferential for type II, because type I sometimes, depending upon training status, we won't see any hypertrophy, or in the untrained individuals, we'll see something like a 10% increase in cross-sectional area.

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Interesting. So you say, okay, the tissue's increasing in cross-sectional area. The cells are increasing in cross-sectional area. What's going on inside of those myofibers or muscle cells? Until recently, we frankly didn't know.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
And you had mentioned some of our research gets sort of misquoted a lot of times or misapplied. There are different modes of hypertrophy that we think exist. The conventional realm of hypertrophy would be that as your fibers, your muscle cells, as they increase in size, you are having a proportional increase in myofibrillar protein content, which are your contractile proteins. They allow the muscle to function. Right? So, and then the question became, all right, well, is it the preexisting myofibrils within those myofibers that increase in size or do you have an increase in the number of myofibrils? And, luckily, we were able to work with a very smart guy, professor at Wisconsin, Troy Hornberger. He had a fluorescent microscope technique where he did a really neat sort of resistance training model in his mice, and then we sent him some muscle from a training study that we did. Across species, what we see with mechanical overload in the mice and in the humans is that when you see this increase in fiber cross-sectional area, it is due to the increase in the number of myofibrils. So those myofibrils, in terms of their size, sort of maintain this sweet spot that's relatively conserved, and so applying resistance training, you're just going to see a larger radial increase in cross-sectional area of that cell, and that's due to the addition of myofibrils, if that makes sense. Other things that happen with resistance training, of course, is sort of this proportional increase in everything else in the cell. So we have the mitochondria. People conventionally look at it as like this is the powerhouse of the cell. This is Ex Phys 101. It produces the lion's share of ATP, which is certainly true. There are other roles of the mitochondria in terms of molecular signaling, ROS handling, things like that. But as you resistance train, that's been kind of one of our questions as well. What happens to mitochondrial content? Because some of the studies would indicate that you have a dilution effect, which is to say as the cells increase in size, certainly we have this proportional increase in myofibrils, but that comes at the expense of not expanding the mitochondria. We took different approaches throughout the years. One of the markers that has been conventionally looked at is citrate synthase activity, and a lot of studies showed that with GenPop, you take them through 10 weeks of resistance training, pre to post-training, you see a decrease in CS activity, which would then reflect the dilution of mitochondria, which is to say the myofibril, sort of the growth of the cell and expansion of the myofibrils outpaced the expansion of the mitochondria reticulum or whatever. But looking at it from immunohistochemistry, we have a 2021 paper by Brad Ruple. We were convinced that there is this proportional expansion of the mitochondria with hypertrophy, which sort of makes sense because you need that to produce energy for the

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growing cell. Right? So we think that everything with conventional hypertrophy, as it relates to fiber expansion, everything in that cell is going to expand proportionally.

Dr. Andy Galpin
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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
That's your outside thigh muscle.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Right? Here on out, friends, we're going to call that the VL.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
That's what we would always call it in the field, right?

Dr. Mike Roberts
Sure.

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Dr. Andy Galpin
So that's what we're talking about. It doesn't matter what muscle we picked. We don't actually have any indication that any of these things would be different across most muscles.

Dr. Mike Roberts
I would agree with that. Yeah. There's nuance, but yeah, generally speaking, that's fair.

Dr. Andy Galpin
Certainly, if you look at the gastroc or soleus-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... but close enough. Okay. So within that vastus lateralis, you've got how many individual muscle fibers?

Dr. Mike Roberts
I think a good guesstimation is anyone off the street, on average, would have between, we'll call it 400 to 600,000 cells in the VL alone.

Dr. Andy Galpin
So one individual muscle there is actually, we will call it a muscle-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... but really, we're looking at a half a million individual cells-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... that comprise that muscle. And so conceptually, it's easy for us to think about this muscle as one thing.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
But when you get into this side of the equation, you actually don't even consider the VL really a muscle. You're actually just paying attention to the individual tissue, the individual cells.

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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
The myocells-

Dr. Mike Roberts
That's right

Dr. Andy Galpin
... themselves. So you got 500,000, we'll call it, individual muscle cells. Now within those individual muscle cells, if you wouldn't mind, give us just the really quick overview of myofibrils, myofilaments, all that, so people can follow that jargon just a tiny bit. So then we'll come back to some of these questions.

Dr. Mike Roberts
So when we say myofiber, that is synonymous with a muscle cell.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Think about an uncooked spaghetti noodle that you would pull out of a box, right? That is what your muscle cells look like. So the diameter is relatively small when you look at the length of the fiber. Right? So they are very, very long cells.

Dr. Andy Galpin
And these are huge cells in all of biology, for the record.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Enormous.

Dr. Mike Roberts
Yeah. Sure. Yeah. Extraordinary.

Dr. Andy Galpin
Uncommonly large.

Dr. Mike Roberts
Yeah. Uncommonly large, right. Because of that, very unique to the muscle cell, though there are other cell types that have multiple nuclei, but they are multinucleated, which is to say that when

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you look at cell bio 101 books and you open chapter one, you're going to see this sort of organic-looking blob of a cell, and it's going to have this centrally located nucleus, which contains really a copy of the human genome. Right? So all 23 chromosomes, over 20,000 genes that are protein coding, et cetera, inside of that nucleus, inside of that cell. Muscle cells, and you've done a lot of work in this, right? If you image them under a microscope individually, you will see very, very long cells, and you will see that the nuclei are on the periphery of the cell, which is unique, and one of the sort of predominant theories in our field is we have this myonuclear governance of cell size. And so in order for that cell to grow, right, we need to add more myonuclei to regulate certain areas of that muscle cell in order to make mRNAs, which then are translated into proteins, and then you can have the deposition of those proteins, be it into the contractile apparatus. You can have metabolic enzymes residing in that area of the myonucleus, et cetera. But if you close your eyes and just think spaghetti noodle and you take a fine Sharpie marker and just draw dots on that, those would be each of the myonuclei, right? As you lift weights, right, just imagine the diameter of that spaghetti noodle increasing in size, and you draw more dots-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... on that spaghetti noodle, right? So people then ask, "Well, where do those nuclei come from?" Is a natural question. And by and large, they come from muscle stem cells or satellite cells. One good stimulus to activate satellite cells so that they fuse to that growing fiber is resistance training. Just tried and true. Certainly, a conserved mechanism, whether it be a rodent or human.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We're going to activate satellite cells to eventually fuse to those growing myofibers with resistance training. Now, inside the cell, you had said, what are the sort of nuance components? You're going to have 80% to 85% of that cell volumetrically occupied by myofibrils. I'm trying to go back to the spaghetti noodle. So imagine-

Dr. Andy Galpin
You have several more spaghetti noodles inside-

Dr. Mike Roberts
Yeah

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Dr. Andy Galpin
... your spaghetti noodle.

Dr. Mike Roberts
Now what we're talking about-

Dr. Andy Galpin
Basically.

Dr. Mike Roberts
Is like, imagine the muscle cell at this point being a round cylinder that holds uncooked spaghetti noodles.

Dr. Andy Galpin
It's the package. So imagine if you got 50 noodles in a package.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And then you got a bundle of 50 of those packages.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And that whole bundle is the muscle.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
I'm working with your analogy here.

Dr. Mike Roberts
There you go.

Dr. Andy Galpin
So I'm doing my best I can.

Dr. Mike Roberts
So yeah, we have this long can that's a cylinder.

Dr. Andy Galpin
Yeah.

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Dr. Mike Roberts
Within the cylinder now we have spaghetti noodles that are uncooked.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Now what we're saying here is we're looking at one muscle cell again, and we're sort of zooming in, where this cylinder is the muscle cell. Those spaghetti noodles inside, those are the myofibrils.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
All right?

Dr. Andy Galpin
Right.

Dr. Mike Roberts
And if you pull out one of those spaghetti noodles, what you're going to see in series, right, Z-line to Z-line is sarcomeres.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Which contain your main myofilament proteins, actin and myosin.

Dr. Andy Galpin
Getting back now to the very place you started, which is the mechanical tension-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... idea, right?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So what you're saying is, and please interject if I don't do this perfectly, but you've got that vastus lateralis. It's got a half a million cells.

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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Each cell has a bunch of, if you want to think about them as sub-cells within them, like a bunch of individual kind of little circles within it. But on the outside of that cell are these nuclei.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
The nuclei are what hold your DNA. They control the cell's activity. Grow, shrink, die, repair, anything in between.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
And when you mechanically stretch that tissue, those nuclei effectively understand the fact that they can no longer control enough of that region. It's kind of like having a bunch of managers, and you're growing, and you're opening too many stores.

Dr. Mike Roberts
Yes. Good analogy.

Dr. Andy Galpin
And you have to say, "Hey, we have a new store opening. We need a new manager there."

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
That manager is the nuclei. The way you do that is you recruit satellite cells, turn those into nuclei, and now you've got more of these manager centers. These stem cells, these satellite cells, are what eventually turn into that. Is that a fair-

Dr. Mike Roberts
Perfect

Dr. Andy Galpin
... breakdown?

Dr. Mike Roberts
Yes.

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Dr. Andy Galpin
Okay. I know we've gotten a little bit deep early, but this is Mike and I's passion, so-

Dr. Mike Roberts
Sure

Dr. Andy Galpin
... I don't apologize. This is what we love to do.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
But this stuff is important because it will help us understand how we mitigate unloading.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Aging, muscle wasting. This stuff is all predicated on us understanding how the muscle is even growing in the first place.

Dr. Mike Roberts
Sure. Yeah. So I've heard in the field, you'll have to tell me the third, but basically, and I know Brad and I think maybe Jeremy Loenneke had spoken to this-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... a few years back. Mechanical tension and then this sort of metabolic perturbance.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
That could be-

Dr. Andy Galpin
Damage would be the third one.

Dr. Mike Roberts
And then damage. That's fair.

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Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Yeah, damage. Do you need damage to grow, right?

Dr. Andy Galpin
Right. In other words, maybe I'll translate right now. Do you have to break muscle down to build it?

Dr. Mike Roberts
Right.

Dr. Andy Galpin
Great. So you're going to answer that question for us, but go ahead.

Dr. Mike Roberts
Oh, God, I hope I can.

Dr. Andy Galpin
Oh, I think you're going to be fine.

Dr. Mike Roberts
Yeah. I am of the persuasion, and keep in mind, a group of us across the world, Karen Esser and I, she's at the University of Florida. She was more or less the godmother of the field of skeletal muscle hypertrophy. She trained Troy Hornberger, Gustavo Nader, John McCarthy, et cetera.

Dr. Andy Galpin
Kentucky lab for many years.

Dr. Mike Roberts
Kentucky lab, yes. CMB, exactly. So we got together in 2022, and we were looking to collaborate, and I said, "We need to write this update on mechanisms that we think contribute to skeletal muscle hypertrophy with mechanical overload." So 2023, publish a paper with people across five different continents, all of whom specialize in certain mechanisms that we talk about in that paper, and it's pretty evident that mechanical overload or mechanical tension is the prevailing mechanism. We didn't even speak to the metabolic aspects in terms of lactate accumulation. Is it involved? I've had conversations with Brad. There are a couple of studies, some rodent studies, in vitro work, so Petri dish muscle cell stuff, where they put lactate. They either inject it into rodents or put lactate in a Petri dish with muscle cells showing, oh yeah, we see this uptick in muscle protein synthesis, which is needed for hypertrophy. But there was a human study done in, it was in Europe, I apologize for forgetting the location, where they infused people, participants with lactate per exercise versus like a buffered saline as a placebo, showing

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that when they did the lactate infusions, they didn't see this enhanced post-exercise muscle protein synthetic response.

Dr. Andy Galpin
This is mimicry of blood flow restriction.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Right. Very similar idea. If you guys have heard of that style of training, that style-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... of exercise, very effective.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
We know that it works.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
The quest was why is it working?

Dr. Mike Roberts
Right.

Dr. Andy Galpin
And the basic idea was if you block blood flow, you eliminate the ability to get waste out of the tissue.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So that waste should accumulate.

Dr. Mike Roberts
Yes.

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Dr. Andy Galpin
One of the primary, we'll just call it waste right now, you're referring to is lactate.

Dr. Mike Roberts
Lactate, right.

Dr. Andy Galpin
So then the next step would be, well, what if we then induce the buildup and just inject it straight in?

Dr. Mike Roberts
Right.

Dr. Andy Galpin
Shouldn't that then result in muscle growth?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And it turns out-

Dr. Mike Roberts
I don't think so

Dr. Andy Galpin
... it didn't work very well.

Dr. Mike Roberts
Yeah. Again, you're going to see there was this Japanese group that did it in, I think it was in rats or mice, I apologize, and they did lactate injections, IP injections, and showed a little bit of an increase in hypertrophy. But the human study that was peri-exercise did tracer work looking at the MPS response after the exercise bout didn't show anything. If that makes sense.

Dr. Andy Galpin
So they're directly sampling muscle, looking to see, is protein increasing at all, muscle protein synthesis? And at the molecular level, it just wasn't.

Dr. Mike Roberts
It didn't enhance the post-exercise response after sets of leg extensor training-

Dr. Andy Galpin
Yeah

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Dr. Mike Roberts
... which reiterates the point that mechanical-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... tension was the driver, and we didn't see the enhancement with the addition of lactate to that. Yeah.

Dr. Andy Galpin
So if you induce the metabolic damage without the actual strength training component-

Dr. Mike Roberts
I don't buy it

Dr. Andy Galpin
... we don't see the growth.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Okay. You said at the very beginning, the contractile portion of this mechanical tension is-

Dr. Mike Roberts
Is king

Dr. Andy Galpin
... I think 80%-

Dr. Mike Roberts
Queen

Dr. Andy Galpin
... 90%?

Dr. Mike Roberts
Yes. Yeah

Dr. Andy Galpin
... of the driver.

Dr. Mike Roberts
Royalty.

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Dr. Andy Galpin
While we're here, let's touch on the damage side.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So what do we know about the adage, of course, you've got to break it down to build it, you have to do all that side of the equation. True, not true, somewhere in between? What do we know about that side?

Dr. Mike Roberts
I don't think it's true. Now, I'm going to say this based on what's in my brain cells right now, recalling information, but I do have one close friend at UCF, Matt Stock, that has done-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... concentric only versus mixed contraction model type stuff, showing concentric, at least according to ultrasound, is just as effective. I'm almost positive there are meta-analyses on this. If Brad hasn't done one, I know someone else has done one.

Dr. Andy Galpin
There are, yeah.

Dr. Mike Roberts
Does not seem like the eccentric portion is needed for hypertrophy to occur.

Dr. Andy Galpin
We certainly see almost no relationship between muscle soreness and relating growth.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Right. So more-

Dr. Mike Roberts
100%

Dr. Andy Galpin
... soreness is not equal-

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Dr. Mike Roberts
More growth

Dr. Andy Galpin
... at all.

Dr. Mike Roberts
Right. Which, growing up, we were going to the gym as teenagers, you and I probably like, "Oh, you have to be sore."

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
That's a prerequisite to look like Ronnie Coleman, right?

Dr. Andy Galpin
Yeah. Not necessarily the case. Now, when you do something that requires mechanical tension, that can often result in some soreness and some damage.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
But that looks more like a byproduct of doing the king, queen than it is an independent mechanism itself.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So if we were to go in, I guess another way to think about this, if we were to go in and isolate a tissue, a muscle cell, and you were to just damage it-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... you would not see any of the signaling cascade, any of the other stuff you've mentioned, probably kick on to an extent to where it would result in the muscle growing.

Dr. Mike Roberts
That's fair, yeah. And they've done that. There's certainly signaling that overlaps when you compare it to exercise, but it's a different signature. Practically speaking, I've had this

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conversation with people that train, coming to Auburn and asking, "How should I train students?" This, that, and the other. I wouldn't, unless it's something for stabilizing the joint, I don't think that doing pure eccentrics is going to maximize-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... hypertrophy, if that makes sense.

Dr. Andy Galpin
Yes.

Dr. Mike Roberts
Do it for something else, optimization purposes, but don't do it thinking that this is the way forward to get muscle growth.

Dr. Andy Galpin
Another area that you've spent a lot of time on is this idea of responders versus non-responders.

Dr. Mike Roberts
Oh, yeah.

Dr. Andy Galpin
If you can give us a basic overview, we'll start there, and then I've got a lot of specific questions within this, but the overview of What do we know about why some people, again, the responder phrase is some people will grow muscle. You mentioned at the very beginning.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Kind of an average rough number if you were to do 10 to 12 weeks of strength training.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
20% to 25% increase in muscle size. Is that fair? What would that number be? We'll just start there, and then I'll get in my responder question, actually.

Dr. Mike Roberts
Yeah. I think at the tissue level, it's fair to say 15%.

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Dr. Andy Galpin
15%?

Dr. Mike Roberts
Yeah. And then at the cellular level, and this is another topic we can get into, right? But you have a little bit larger increases in cell size.

Dr. Andy Galpin
Okay. So if you were to take an individual muscle cell, that cell might be 20% or 25% larger.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But if you're looking at your leg-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... your vastus lateralis, after three months-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... 10% to 15% increase.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Right. Depending on lots of variables, and I'm just trying to give you a rough idea of how to picture this in your mind.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Right. Of course, much larger. So the fundamental question of responders, non-responders is, if you say the group average was 15%, and then you start looking at every single person-

Dr. Mike Roberts
Yeah

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Dr. Andy Galpin
... somebody was probably at 25%.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And somebody was at five.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So again, the question is why?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
What do we know about why some of these people are these hyper-responders, why people are these non-responders?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And then ultimately, I want you to tell us then what do we do training-wise?

Dr. Mike Roberts
Excellent. So I need to tip the cap to Markus Baumann, who really brought attention to this topic at the molecular level. Priscilla Clarkson and Monica Huebel, they published really the first paper in the mid-1990s on this, just showing after resistance training, when they're looking at hundreds of people, and you plot the individual responses, what happens is exactly how you described it, right? You're going to have this sort of mean response where 70% of these individuals fall, 60 to 70 are right in the middle there, sweet spot.

Dr. Andy Galpin
It's a bell curve, right?

Dr. Mike Roberts
It is a bell curve, yeah. And then you have, we'll call it 10 some odd percent, maybe 15 that respond quite well, and then on the other side, you have people don't respond-

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Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... at all. It's almost like they didn't train when you're looking at the hypertrophy response. So Markus Baumann also presented in Finland. He was the first, in the mid-2000s, him and Jay Kim, his postdoc, showing, and I still think this holds true, that the highest responders hypertrophy-wise to resistance training, this would be 16 weeks in their study, had this very exaggerated satellite cell activation response. And not only that, but they started training with more satellite cells, which is to say that if you were somebody that has never trained walking into a gym, and for whatever reason, genetically, that you have more satellite cells in your muscle tissue, that could be a huge advantage in terms of gaining muscle mass when you activate those satellite cells, right? So you're sort of primed with more satellite cells. You train for 16 weeks. You activate a subpopulation of those to fuse to myofibers, adding mononuclei, which we talked about being important, and then those cells can grow. I think in his paper, the extreme responders saw a 60% increase in fiber CSA.

Dr. Andy Galpin
That's crazy.

Dr. Mike Roberts
That is nuts. Yes. So satellite cells are critically important, A. B, we think that ribosome content and the response to training is important. So ribosomes are macromolecules. Some people call them organelles. They reside inside of the cell. They themselves have 80 proteins glommed together. You have this large, small subunit. When the large and small subunits sort of coalesce around messenger RNA, it translates that messenger RNA into protein. So that's muscle protein synthesis when you talk about that inside of a muscle cell. We published a paper, Brooks Mobley, in the lab, part of his PhD work, showing that in our hands, the high responders to 12 weeks of resistance training saw the greatest response to training in terms of increasing muscle ribosome content. So now our theoretical framework is if you have the muscle ribosome response to training, and if you walk into the gym with more satellite cells, you should be primed, if you train consistently, to be a relatively higher responder. Okay? Other mechanisms, we've looked at a lot.

Dr. Andy Galpin
I was going to say, give me the null-

Dr. Mike Roberts
And this is where the null hypothesis comes into play. So there has been some back and forth as to whether or not the androgen receptor inside of muscle cells-

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Dr. Andy Galpin
Walk us through what that is.

Dr. Mike Roberts
Yeah. So the androgen receptor is a protein inside the muscle cell, and it is activated once testosterone from the blood diffuses into the muscle cell, binds to the receptor. The receptor then is activated. It can translocate into that nucleus or myonuclei across a cell, and it can turn on a gene program that is anabolic. Hence why you take 600 mgs per week of test and ante, you see hypertrophy when you resistance train.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Shaly Bassim did those studies back in the day. So-

Dr. Andy Galpin
Can I pause you right there?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
I want you to continue on with the story, but actually, people are going to jump off the roof right now if I don't stop you. Let's actually go in order, if you don't mind.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
With testosterone, and then we'll get into receptors, and we'll kind of follow that pathway through. If you want, we could actually even go into fiber type as a thing, but we'll kind of go up the chain. Another way of saying this is, is one of the things that determines a responder versus a non-responder or super responder testosterone? Walk me there, and then we'll get to the receptors.

Dr. Mike Roberts
Okay. I'll give you the short answer-

Dr. Andy Galpin
Great

Dr. Mike Roberts
... so people, it'll stick. So when we look at the younger male, and we look at the younger male

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that doesn't supplement with testosterone, that physiological range is not a predictor. Which is to say somebody walking in the Um, door and has, you know, 500-

Dr. Andy Galpin
Total testosterone, 500, 600, which would be-

Dr. Mike Roberts
Milligrams per deciliter.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
And then you compare that to somebody that has 900. If we train them the same way, that variable difference between those two did not drive the differential response in hypertrophy.

Dr. Andy Galpin
We want to know who will get bigger or smaller based on-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... total testosterone.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Nor free testosterone.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And can I go ahead and just assume the same answer would be the case if we looked at estrogen in women?

Dr. Mike Roberts
That is correct.

Dr. Andy Galpin
So the total amount of circulating hormone at normal physiological levels-

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Dr. Mike Roberts
This is in the young adults.

Dr. Andy Galpin
In the young. Yeah.

Dr. Mike Roberts
Yes. And when I say young, I'm saying we're talking about 18, and we'll call it up to peak muscle mass, which is 35, 40.

Dr. Andy Galpin
Great. So if that caught you by alarm, that's been pretty well established, in my opinion.

Dr. Mike Roberts
Yes. Now, here's the deal. There's a caveat there. Let-

Dr. Andy Galpin
There's several. Yes.

Dr. Mike Roberts
Yes. So, there have been aging studies in the Northeast. I think Baltimore Aging Study is a good example of this, whereas when you look at the lifespan in the male and you track from the age of 18 to 90, there is a relationship with testosterone in the blood and muscle mass in people just walking around. That's tough to disentangle because you're like, okay, well, it matters obviously, but when you look at resistance training, it doesn't matter. And the answer is, it's just not a predictor of the hypertrophic response. Which brings me to the most important point here, and it comes back to mechanical tension.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
The driver is mechanical tension, and then there is about 20% of the recipe that has to deal with perhaps metabolic byproducts, perhaps hormones, et cetera. Right.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Today's episode is sponsored by LMNT. LMNT is an electrolyte drink that has an ideal electrolyte ratio of sodium, potassium, and magnesium, but no sugar. Hydration is critical to performance,

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both physical and mental, and countless studies have shown that even a slight degree of dehydration, even as small as 1%, can lead to decreases in physical output and mental performance. We also know that electrolytes are critical to proper hydration, which I've been harping on for years. But you can't do that, proper hydration, by only drinking water, especially if you sweat a lot. You need to get the right amount of electrolytes in the right ratios, and that's why I'm a huge fan of LMNT. In fact, many of you might remember that I featured LMNT in my YouTube series on hydration nearly six years ago. I featured LMNT in these videos because their blend of 1,000 milligrams of sodium, 200 milligrams of potassium, and 60 milligrams of magnesium really is unique and different than any other electrolyte on the market, and it has great scientific support. I use LMNT on nearly a daily basis, especially when I'm doing really hard training in the heat and I'm sweating a lot. If you'd like to try LMNT, you can go to drinklmnt.com/perform to claim a free LMNT sample pack with the purchase of any LMNT drink mix. Again, that's drinklmnt.com/perform to claim a free sample pack. I can predict your answer here, but it would be inappropriate or ill-advised to alter somebody's training approach simply based on how much total testosterone they have in their blood if they're-

Dr. Mike Roberts
I agree 100%. Yeah.

Dr. Andy Galpin
And that's the practical outcome here.

Dr. Mike Roberts
So that, again, assumes normal physiology. They're within range.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Now, if they're using exogenous testosterone-

Dr. Mike Roberts
Oh, they're going to hypertrophy more.

Dr. Andy Galpin
It works incredibly well.

Dr. Mike Roberts
And then that becomes its own question. Okay, well, why? And this gets to the androgen receptor, what the androgen receptor does.

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Dr. Andy Galpin
Great. So time right there. That's where I'm going to walk us to.

Dr. Mike Roberts
Yeah. Sure.

Dr. Andy Galpin
The opposite could also be true. If you are subnormal-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... so if you are a 20-year-old male walking around with a total testosterone of 100, we would anticipate much less hypertrophic response.

Dr. Mike Roberts
Yeah, because at that point, you're hypogonadal, and there's studies done-

Dr. Andy Galpin
You're subclinical.

Dr. Mike Roberts
Yes. And Phil Atherton, over in England, they've inhibited testosterone production endogenously through pharmacokinetics, and they show that that does-

Dr. Andy Galpin
In non-humans, I assume.

Dr. Mike Roberts
No.

Dr. Andy Galpin
In humans?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Woo.

Dr. Mike Roberts
And this is published, right? So when you bring levels way down into that, okay, we are certainly hypogonadal, almost not producing anything, then we do have somewhat of a blunted hypertrophy response, but there's still hypertrophy. Bingo.

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Dr. Andy Galpin
Do you remember how low they brought them?

Dr. Mike Roberts
I want to say it was under 100.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We could look that up. But yeah, this is through pharmacology, right?

Dr. Andy Galpin
Of course.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Yeah. Wow. Amazing IRB. Good for you. So those are the things that, the part of the story that gets missed. If you are, again, way above or below, especially if you're above because of pharmacology-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... we'll just call it that, or below, getting back to a normal range will likely impact, but it's not like you go to zero either, right? So if you're subclinical-

Dr. Mike Roberts
Right

Dr. Andy Galpin
... you're not going to zero muscle growth.

Dr. Mike Roberts
Yeah. You will still have muscle growth. Yeah.

Dr. Andy Galpin
It's still there because 80% of the driver is the tension.

Dr. Mike Roberts
Mechanical tension and the mechanisms associated.

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Dr. Andy Galpin
Testosterone, in this case, would be folded into one of those subparts, whose subpart at best explains up to 20%.

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
So the other 80, you're still driving some growth.

Dr. Mike Roberts
Fair.

Dr. Andy Galpin
Okay. Is there anything we need to add to this from the female side of the equation, or is the answer the exact same in women? Because the example we've been giving are young men.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Same thing happening in young women as well?

Dr. Mike Roberts
Yeah. Hot take. I think muscle growth is conserved across men and women at the younger age and across species, which is, there's beauty in simplicity, in my opinion. Programming doesn't have to be mega complex. That's a topic that's becoming very hot. Brandon Roberts, Greg Nuckols, they probably have the best meta on this. The young female population can hypertrophy on a relative scale, just as good, if not a little bit better than men.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? Same training stimulus.

Dr. Andy Galpin
I'm a little insulted you didn't mention my paper on that, but you-

Dr. Mike Roberts
It's okay. I'm saying-

Dr. Andy Galpin
That's okay. It's fine

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Dr. Mike Roberts
... no. And you guys published before.

Dr. Andy Galpin
That's fine. Give him all the credit. It's fine.

Dr. Mike Roberts
Andy Galpin also has a great meta on this topic, crowd. Go read it.

Dr. Andy Galpin
Nonetheless, yeah, the muscle growth effectively the same, right?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Certainly strength on those Estrogen, it's a similar story here.

Dr. Mike Roberts
Yes, and the receptor too does not predict in muscle.

Dr. Andy Galpin
So as long as you're in, we'll just globally call these anabolic hormone ranges.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
If you go below or above pharmacologically, the story changes.

Dr. Mike Roberts
The story changes.

Dr. Andy Galpin
But they themselves, I'll come back to what I said earlier, I think the practical implication we want to take from this is we simply shouldn't alter training variables and how you're lifting weights if you're intending to grow muscle simply by a blood test that looked at one of these. And really, honestly, you could pick any endocrine marker here.

Dr. Mike Roberts
That's right.

Dr. Andy Galpin
And I really don't care.

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Dr. Mike Roberts
Yeah, no. And Stu Phillips, he did this, they looked at, I think, HGH in the blood. They looked at free tests, they looked at total tests, they looked at cortisol. We have looked at myostatin in the blood. None of these markers predict the hypertrophic response-

Dr. Andy Galpin
Okay

Dr. Mike Roberts
... or the acute muscle protein synthetic response according to what Stu had published too. So-

Dr. Andy Galpin
Right. So if you look at the molecular mechanisms that happen immediately after exercise-

Dr. Mike Roberts
Yes. It's all inside the muscle cell that's the magic. That is the sizzle of the steak-

Dr. Andy Galpin
That's right

Dr. Mike Roberts
... if that makes sense. Yeah.

Dr. Andy Galpin
Okay. So it's not the signaling from outside the cell.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
No matter how you cut it there. Something is secretly happening inside the tissue that determines how much it grows.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And we could actually probably play this game for a very long time, and you have across your career. You've looked at a lot of-- We mentioned three or four, but you've looked at a lot of them, and we're so confident here, you are particularly, because nothing has stuck. Like nothing has landed-

Dr. Mike Roberts
Yeah

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Dr. Andy Galpin
... outside the cell.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So now let's move to the cell.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
On the cell membrane-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... and we'll be careful not to call it a cell wall so you biologists don't-

Dr. Mike Roberts
Yeah. Don't do that

Dr. Andy Galpin
... biologists will kill us on that. We're humans, so we have a membrane.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
You have receptors, and in the example of testosterone, testosterone needs to bind to that receptor for that receptor to then move to the nucleus-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... to tell it to turn on its genes-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... to get the ribosomes moving to synthesize and make new proteins, which ultimately makes

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those myofibrils larger.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So then the next stop in the equation, and we'll just keep going this route, is there something unique on those cell membranes that is then predicting it? And I'll let you answer it, but I'll finish real fast here. Example could be maybe the amount of testosterone doesn't matter. What does matter is how many testosterone receptors you have. Theoretically-

Dr. Mike Roberts
Yeah, it didn't matter

Dr. Andy Galpin
And he just-

Dr. Mike Roberts
I told you I want to be a buzzkill

Dr. Andy Galpin
... I took all that time.

Dr. Mike Roberts
I know.

Dr. Andy Galpin
I took all that time.

Dr. Mike Roberts
That was really elegant, though.

Dr. Andy Galpin
Thank you.

Dr. Mike Roberts
That was beautiful. So yes, to your question directly, what about the hormone receptors? Initially, Stu Phillips said there does seem to be a correlation with muscle biopsy, testosterone receptor content, and the hypertrophic response to training. And that led us, with Cody Han when he was in the lab-

Dr. Andy Galpin
Yep

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Dr. Mike Roberts
... we did a study in trained individuals. It was a secondary analysis of his main dissertation. We didn't see in trained individuals when they did a six-week very high volume training study that muscle androgen receptor content or testosterone receptor in the muscle in trained men, college-aged, we didn't see it predict hypertrophy. Since then, we've worked with Clayton Lombardi's lab, who's down in Brazil, University of São Carlos, and he had a really nice elegant study where we had 40 individuals, 20 men, 20 women, college-aged. They did an acute bout of exercise. We took a pre-intervention biopsy walking in the door. They did their first bout, and then 24 hours later, we took a biopsy. That's T2 biopsy.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
T3 biopsy was after the 10 weeks of training, leg extensor. And there was hypertrophy. When looking at the biopsy markers, be it the estrogen receptor in the muscle or the androgen receptor, there was zero, not even close association with hypertrophy.

Dr. Andy Galpin
So that also answers our sex question.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So this is not a male-specific answer at this point. And not only is it not a receptor-specific, but it's not gender-specific-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... at all either.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
Strike number two. With even the anabolic hormones or receptors, you can answer both sides now.

Dr. Mike Roberts
Sure.

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Dr. Andy Galpin
Does this story change in midlife or later in life or-

Dr. Mike Roberts
Yes. Oh, that's a great question. So I and Juha Tynälä, he's a great colleague at Hyvaskyla. He's the one that we did the conference with. He and I organized on the response heterogeneity to resistance training for background information, but he's also looked at this a lot. He has shown that across the age span in skeletal muscle, you do seem to lose androgen receptor content, and there does, across the age span, young versus old, this is where we get outside that just young window, the relationship becomes a little bit more evident there in terms of less receptor could be detrimental to growing muscle. Which we'll get to that topic, too, because so far this conversation has hinged upon when we're young and vibrant and trying to optimize peak lifetime muscle mass, it doesn't seem to matter. Things change at our age-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... and beyond, our future, right? Proteins in the muscle may be a little bit more important, and we have some data that I'll get into on that front, too.

Dr. Andy Galpin
The fundamental question I'm getting at here is, again, if we're trying to get better programming-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... the concept, whether this is supplementation, recovery, or the actual exercise intervention itself, if we understand who's going to be a better responder-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... if we understand who's going to be a worse responder, if we can preemptively give different recommendations.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And so the quest here is to figure out, well, what's causing that to begin with?

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Then theoretically, this could lead to potentially a screening process.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Where we could run some tests on somebody. Obviously, very few people have access to a muscle biopsy.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
But at least we had to figure out what we're trying to do in the first place-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... before we can come up with a screening tool. And let's say magically one was possible, we could say, "Okay, you've been flagged as a non-responder because of XYZ, whether this is you or whether this is now you because you're aged."

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Then we could say, "Okay, start this way." And we'll get into what those this way versus that ways are.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Protocols. But that's ultimately what we're getting at. So with the aging question, if we're still just figuring out, and kind of what it sounds like is there's something there. There's potentially something there with the testosterone story across the lifespan.

Dr. Mike Roberts
Yeah, 100%.

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Dr. Andy Galpin
Something there with the androgen receptors potentially across the lifespan.

Dr. Mike Roberts
Instead of 20% in that young vibrant, we're saying up to 20% of the variance could be related to the receptor-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... thing. When you become older, that explains more-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... in terms of the response.

Dr. Andy Galpin
Still not a single point variable.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
While we're here, actually, I've seen these done, but how do you feel about direct to consumer commercial genetic testing-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... and similar things that will say, "You're an XYZ, therefore you should train this particular way." What are your current thoughts on those?

Dr. Mike Roberts
We are totally not there yet, dude. That scares me, because we actually have, us in collaboration with Stu Phillips, and Chris Van was the lead on this. He's at Duke post-docing. We did the first GWAS study, so looking across the entire genome to see if any gene or genes predicted muscle fiber hypertrophy or DEXA lean mass changes to 10 or 12 weeks of resistance training. And we found one gene sort of weakly did. It's called GLEE3. Now, that needs to be validated because for a GWAS-

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Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... study, it was only 110 or 20 people. But what we showed was people that had a certain GLEE3 genotype, right? So ATCG, I think if it was like a CC, meaning that-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... mom and dad's copy of GLEE3 at that locus spot in the GLEE3 gene had a cytosine. You were a good responder, and it dealt with the satellite cell response, so that's kind of cool.

Dr. Andy Galpin
Okay. Similar story.

Dr. Mike Roberts
Because now we have genetics, satellite cells, and response heterogeneity. Before we put that and package it into a genetic test, though, I do want to see it validated.

Dr. Andy Galpin
Okay. So I'll translate that in my own brain.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Humans have, we'll call it 20,000 unique genes.

Dr. Mike Roberts
Yep, that code for proteins.

Dr. Andy Galpin
Right. And of those 20,000, you ran an analysis of people where you, the GWAS-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... the genome-wide thing. So you looked at all of them basically.

Dr. Mike Roberts
Yeah, we looked at all of the 20,000.

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Dr. Andy Galpin
And of the 20,000-

Dr. Mike Roberts
And as well as non-coding regions of the genome, too.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
So that's a difference.

Dr. Andy Galpin
Which is even larger number.

Dr. Mike Roberts
Yeah, 100%. Yeah.

Dr. Andy Galpin
And of those, one of them potentially explained 1%?

Dr. Mike Roberts
Yeah, I would say it was under 10%.

Dr. Andy Galpin
Under 10%.

Dr. Mike Roberts
If I were to do the math on that, yeah.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Okay. So hopefully, that answers at the current state, if you're buying direct to consumer testing that tells you how to train to optimize muscle growth from a genetic perspective-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... you've wasted 96% of your money? Maybe?

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Dr. Mike Roberts
Yeah, it's fair.

Dr. Andy Galpin
Yeah. Okay.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Okay, great. We'll just move on from there then.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Continuing back to some of our null hypotheses here.

Dr. Mike Roberts
Oh, another null hypothesis, by the way. Sorry about that. Yep.

Dr. Andy Galpin
Oh, yeah. We missed that one, too.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Presumably, we'll get better at that.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
You mentioned it needs to be validated. There'll be other things pop up, but there are some things gene testing can tell us and we can offer for. But simply whether or not you're going to respond well to strength training from a muscle growth perspective-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... is such a nuanced question.

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Dr. Mike Roberts
It is.

Dr. Andy Galpin
That single polymorphism or site mutation, I'm not sure what it was, rare mutation.

Dr. Mike Roberts
Yes. A SNP. Yep.

Dr. Andy Galpin
It's not going to tell you anything.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
All right. So don't use that. We'll call that intellectually interesting.

Dr. Mike Roberts
It is.

Dr. Andy Galpin
But not clinically relevant.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
Going back to our responder story, the androgen receptor concentration or density didn't seem to pan out. And that's actually really interesting because that's one of the things I was referring to at the very beginning when I said people are misquoting your stuff so frequently.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
This seems to be what, I don't know why, but in pop culture, it's the receptors that get all the answer, right?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
It's like, "Well, your total testosterone doesn't matter, and the reason it doesn't do ABC is because it's actually all about how many receptors you have." And so there's been a race for

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private companies to try to develop all kinds of assays where we can actually measure that in blood.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And the assumption is we're going to answer this, and I get a little bit frustrated because I'm like, "Yeah, but have you seen the papers?"

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
You're trying to solve a problem that we already know actually doesn't matter.

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
It's like you're just way too far behind. So that part gets very frustrating. Relevant, interesting, I can say, but it's not the thing that's describing whether or not you're responding-

Dr. Mike Roberts
Yeah. That's fair

Dr. Andy Galpin
... to exercise or not.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Let's continue down the chain then.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So is it something in the signaling or gene side of the equation-

Dr. Mike Roberts
Yes

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Dr. Andy Galpin
... that is answering? What do we know about that?

Dr. Mike Roberts
Long story short, I think the original question, it finally popped back in my brain, was is there anything at the cell membrane?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Receptor, be it receptors. We talked about receptors. We don't think any of the receptors play a big role. I had a student, Josh Godwin, did a very elegant two-year project, deep dive, where we took, it was a small cohort of humans that we had trained already. We had sort of biobanked the muscle biopsies. And ah pre-post training, we isolated the cell membrane from the tissue and-

Dr. Andy Galpin
Interesting

Dr. Mike Roberts
... and we did proteomics on it.

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
So resistance training in these folks, the aggregate numbers were what they were in terms of VL hypertrophy, fiber CSA growth, looked pretty average, but there was response heterogeneity. We then did proteomics pre-post intervention on the cell membrane proteins. The total cell membrane protein pool significantly increased, which I thought was cool. I looked at the literature and said, "Oh, wow, this is kind of the first time that we're seeing things that happen at the cell membrane."

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
May be important to know, by the way, from cell membrane down to signaling to muscle protein synthesis is important, right? The transduction of the mechanical tension down to the ribosome in terms of increasing protein synthesis. So, Josh did proteomics on that, and we found a couple of proteins, one of which was called vimentin, VIM, that we saw a small sample size regression seem to be associated with myofiber hypertrophy.

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Dr. Andy Galpin
Mm.

Dr. Mike Roberts
We did some elegant studies showing that vimentin, it's an intermediate filament, meaning that it should exist-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... in cells. But what we found was it seems to be deposited in the extracellular matrix, and it seems to come from satellite cells. I don't know if the satellite cells secrete it. We didn't answer that question, but we saw, using John McCarthy's Pax7DTa model of satellite cell ablation or getting rid of satellite cells in a mouse. We got rid of satellite cells and applied mechanical overload. We didn't see vimentin in the extracellular matrix hardly at all, and they didn't hypertrophy as well. Now, there's other factors that play into that mouse model. The lack of satellite cells prevents myonuclear accretion, so that certainly is also driving that lack of hypertrophy. But it is coinciding with the loss of VIM being associated with hypertrophy. So we think more research needs to be done from VIM.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
There's also some other studies, and I want to say they're in Petri dish embryonic fibroblasts, but VIM has been linked to stimulating mTORC1, which we know is needed for bolstering MPS or protein synthesis in any cell. And so there's that linkage between this protein and mTOR. So we're really excited. That seems to be part of the mechanical tension story that we think needs to be further investigated-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... if that makes sense. Other than that, Marty Boppart does elegant work, with the integrins-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... that are spanning the cell membrane. The notion being, you have this integrin protein that sort of communicates with the extracellular matrix, and then once tugged upon, will start this

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phosphorylation cascade that can transduce the tension signal-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... into anabolic signaling in muscle-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... cells. And so that's always been in the backdrop, I'd say for the past decade, in terms of potentially being a driver of how we get tension into anabolic signaling, right?

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
Other candidates, and we talk about this stuff in the review that we wrote in-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... 2023, Karen and I's review. Other candidates would be calcium, so stretch-activated calcium channels. When you contract muscle, you have this influx of intracellular calcium. Now, some of that is used to activate calpain-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which are calpain proteases, and you see this proteolytic response. But in addition to that, there's a tie-in with the influx of calcium and mTOR activation. So there's a little bit of that going on as well. But all of this sort of, mechanisms aside, this is cool stuff. These are academic questions. These are just sort of reinforcing the notion that it is the mechanical tension, right?

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
That is feeding into this anabolic signaling, which is then bolstering MPS, muscle protein synthesis, which is then leading to the deposition of more myofibrils, which is then leading to the-

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Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... expansion of the myofiber. And once we reach a critical threshold, call it like a 10% increase in myofiber size, we have the stem cells fusing, starting to tether additional nuclei so that more proteins can be produced-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... and so on and so forth, right?

Dr. Andy Galpin
Okay. Are there any other major candidates? Myostatin I threw out there.

Dr. Mike Roberts
Yeah. Okay. So golly, myostatin. John Petrilla was a PhD student with Marcus, and that early landmark, again landmark hypertrophy molecular paper by Jay Kim and Marcus showing modest, low extreme responders to 16 weeks of training in terms of muscle fiber CSA increases. One thing that they showed was that myostatin signaling pre, post-intervention, I believe, I'll have to go back and look at this in detail. There were differences between extreme and low responders-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which is to say that the myostatin response seemed to be partly diminished in those extreme responders. We have since taken an interest in myostatin. I mean, golly, right, if you overexpress follistatin, which inhibits myostatin in a mouse, or if you knock out myostatin-

Dr. Andy Galpin
Mm

Dr. Mike Roberts
... genetically, or if you have this selectively bred dog or Belgian blue cow that has a mutation in myostatin and therefore doesn't have a functional myostatin protein, they are jacked.

Dr. Andy Galpin
Yeah.

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Dr. Mike Roberts
They are completely yoked, right?

Dr. Andy Galpin
If you don't know what we're talking about, go just Google the-

Dr. Mike Roberts
Google

Dr. Andy Galpin
... word myostatin and hit images. You're going to see, you mentioned the cows, the bull weevils. There's humans-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... that have this.

Dr. Mike Roberts
The German, I think, child that-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... we've all lost touch of. There was like a cool pub and then-

Dr. Andy Galpin
I actually did a little update on him in one of my shows last year.

Dr. Mike Roberts
Is he yoked?

Dr. Andy Galpin
I'll save it for the surprise.

Dr. Mike Roberts
Okay. All right, good.

Dr. Andy Galpin
So this can happen, as you mentioned, naturally.

Dr. Mike Roberts
Yeah.

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Dr. Andy Galpin
This is just a lucky part of the job, but- You can also induce this, right? We can cause this, we can gene block this.

Dr. Mike Roberts
In mice, to be clear. Yeah.

Dr. Andy Galpin
Well, in humans.

Dr. Mike Roberts
Yeah, in humans too. You have CRISPR-Cas9.

Dr. Andy Galpin
Nonetheless, because myostatin is what we call a negative inhibitor.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Right? It's backwards, so it blocks muscle growth. So if you block the blocker, it can take off. So what you're indicating here is if you presumably have a lot of that-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... then you would be a lower responder to growth, right?

Dr. Mike Roberts
And I think, even though you're going to hear me say this, I always catch things, we always need a little bit more data-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... just to be more certain.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? Because I want to speak truths, and I don't want to spread falsehood. Based on the John Patrella data, as well as just data showing that when you resistance exercise, you are

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down-regulating-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... myostatin at the mRNA level. You are up-regulating follistatin, which is the inhibitor of myostatin at both the mRNA and protein level. We have a 2023 paper, Mason McIntosh, showing that. The pathway is certainly a conserved response to a bout of training. You are-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... certainly, yeah, working on that pathway.

Dr. Andy Galpin
Yeah. This is a way of saying this is a natural biological phenomenon, not specific to humans. You're going to see this as a general physiology. Why that matters is that gives us more confidence to say it is a thing.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
This is not a random thing we saw in a human.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
It is a real biological phenomenon.

Dr. Mike Roberts
Across multiple labs, you'll see this.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So I think we've done a pretty good job of that. I could go more, but we'll progress now because I have a lot more areas to go.

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Dr. Mike Roberts
Sweet.

Dr. Andy Galpin
It's a fundamental problem. Let's round out this responder versus non-responders. You've clearly done a lot of work in this area. We're starting to learn more. We've crossed some things off the list. We've added some things, some things in your data, some things you're really excited about that are coming of interest. But let's go to the implications of this stuff. Is it then fair to say there are a subset of people who just simply cannot grow muscle from strength training? In, again, normal humans-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... without clinical medical conditions. If that's the case, elaborate. If that's not the case, elaborate that side as well. So how do we overcome that? What do we do about it if we are a non-responder? I just think there's a lot of questions in the implication side, so I'd love to go there.

Dr. Mike Roberts
I think the percentage of folks when you look across different studies is getting honed in a little bit more now that our lab has done a lot of this work, Abby Mackey's lab-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... Marcus Bauman obviously has done a lot of this work. Yuha Tainan's done it. Clayton Labarde's done it. Like you said, we're a small community.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We're all friends.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Stu Phillips, right? So I think Stu wrote a recent review, and I think the indication is this, the non-responders are pretty low, and same with Abby's data. So that is to say that most people will

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see at least some growth. But I'm always devil's advocate. Yeah, okay, so they grow, but some people see a lot more growth than those people, right? So, there are clusters.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
You can call it tertiles. You have low, moderate, high. There is that. But that is to say that, rarely would you see the person, maybe less than 5% of the population, if not even smaller, that will not grow. And oh, by the way, Clayton Labarde did this with Marcus, and they published this maybe a year ago, showing that the lower responders to lower volume training actually could respond to more training volume. So there's your practical implication. If you're not growing, then you may not be training either correctly, or you may not be having enough volume implementation to maximally stimulate hypertrophy, if that makes sense.

Dr. Andy Galpin
When you and I were in school, I feel like the number we would always hear all the time is 30% to 40% of people are going to be low responders. And I remember thinking, "That sounds crazy."

Dr. Mike Roberts
That's crazy.

Dr. Andy Galpin
And I hear this in the outside world really often, right?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
A third of people won't respond, or some wild numbers. To be really clear, probably looks more like less than 5%?

Dr. Mike Roberts
The people that just show minimal growth.

Dr. Andy Galpin
Minimal.

Dr. Mike Roberts
Yeah, minimal growth.

Dr. Andy Galpin
So it's really, really uncommon.

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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And-

Dr. Mike Roberts
And oh, by the way, they get stronger.

Dr. Andy Galpin
For sure.

Dr. Mike Roberts
Because we've done that study, right?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We've done the, okay, this is what happens at the VL level in terms of ultrasound, and now let's look at their 1RM changes. Well, the low responders got stronger.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Neurological adaptation, whatever you want to call it, right?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
There was a positive response to resistance training there.

Dr. Andy Galpin
Today's episode is brought to you by TruMed. Lately, I've been thinking about what actually drives performance. It really comes down to two things, the quality of your training and how well you recover from it. And both sides of that equation matter. And the tools you use to train and the tools you use to recover, high-quality fitness equipment, sleep support, recovery tools, can get expensive. And that's why I love what TruMed is doing. Their whole mission is to make health more accessible by helping you use pre-tax HSA or FSA dollars on eligible health products. So instead of thinking about this as extra spending, you're using money that's already set aside for your health. For a lot of people, that means saving an average of 30% on those purchases, depending on your finances and eligibility. I always thought HSA and FSA funds were

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But we'd still predict them to get very strong.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So those folks that are in that camp are saying, "No way. I follow my program, I hired a coach, I train so hard, and I'm just not growing as much as possible."

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
First stop on that train to solution is probably then saying maybe this is a volume issue.

Dr. Mike Roberts
If you can tolerate it.

Dr. Andy Galpin
Right. If we can tolerate it. And then the next stop, we'll get there, but with that, we've said this a number of times, would you define what high volume is here? Can you give me some bumpers as to how would someone know if they're up high, up low? What are these things? I think you guys actually put this out in one of your papers, some-

Dr. Mike Roberts
We did. This is Cody Haun, and he's-

Dr. Andy Galpin
Yeah

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Dr. Mike Roberts
... really, he's doing great. He's in Alabama running his own company, but he really opened my eyes to this world. He had trained with Mike Stone at ETSU. Masters, came in. He was into programming. He taught me, his professor, this is what a deload week is. And I'm like, "This sounds so stupid. Why are we letting them sort of rest for a week?" Sure enough, it seems to work in terms at least psyche and-

Dr. Andy Galpin
Sure

Dr. Mike Roberts
... we're not getting aches and pains throughout a 12-week intervention. Okay, so Cody comes along, and one of his sort of sub-questions to his dissertation is, look, if we take these well-trained individuals, these are all college-age men, and we do six weeks of training with them, where week one is something that they would do typically in the weight room three days per week-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... three sets per exercise, maybe four sets per exercise. Every week was an increase in volume. So by mid-study, it was like 20 sets per week per exercise. By week six, it was like 32 sets per week per exercise. Oh, by the way, back squats, all the way down, all the way up, think about 32 sets per week of that, 32 sets per week as well of bench press, 32 sets per week of deadlift, 32 sets per week of cable pull-downs.

Dr. Andy Galpin
Very easy program.

Dr. Mike Roberts
Awful. So-

Dr. Andy Galpin
Sorry, before going on.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Intensity was, I'm assuming, reasonably high. Like, they're trying very hard, so it's not like they're lifting light weights.

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Dr. Mike Roberts
Yeah. So we try to keep it within a 10 RM, which is to say the-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... the typical hypertrophy programming, 10 reps.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Right? Plus or minus two reps per set.

Dr. Andy Galpin
Yep. Okay.

Dr. Mike Roberts
Okay.

Dr. Andy Galpin
So they're lifting at, we'll call it, 80% effort at least.

Dr. Mike Roberts
We had said 60 to 65.

Dr. Andy Galpin
Okay. Yeah.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
No, sorry, when I say 80% effort, I don't mean percentage of 1RM max.

Dr. Mike Roberts
Okay.

Dr. Andy Galpin
I meant reps in reserve or-

Dr. Mike Roberts
Oh

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Dr. Andy Galpin
... RPE kind of thing.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Like, they're trying really hard.

Dr. Mike Roberts
Sure. Yeah. So the reps in reserve, I would predict after every set, once you get in the last week, was like one or two. So-

Dr. Andy Galpin
Yeah. So RPE is-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... nine out of 10.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Yeah. RPE is how hard was this?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Just emotionally, right?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So you're really trying hard-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... for 32 sets per exercise per week.

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Dr. Mike Roberts
And we did some mood disturbance stuff, some validated questionnaire. It did, it affected their mood-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which is a different-- I'm not a-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... psychological person, but I was like, "Oh yeah, they're starting to really-- This is accumulation-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... that's leading to..."

Dr. Andy Galpin
And how many weeks was it total, you said?

Dr. Mike Roberts
It was six.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
It was six, so we accelerated quickly. Yeah, we accelerated quickly.

Dr. Andy Galpin
The ramp.

Dr. Mike Roberts
Yeah, it was certainly the ramp. So, and we had done like 30 people in this study. But long story short, Andy, what we did was we took biopsies at pre-intervention, week three, and week six. And then we had a deload week where half of the 30 folks did like 25% volume, and then half of them did nothing.

Dr. Andy Galpin
So 25% volume or 25% drop?

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Dr. Mike Roberts
75% drop in volume.

Dr. Andy Galpin
Okay, so they went almost on the floor.

Dr. Mike Roberts
Almost on the floor.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Just sort of-

Dr. Andy Galpin
Something

Dr. Mike Roberts
... going through the motions.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Yeah. We'll get to that week seven after the deload week later on if you want. But to summarize, not only did we do biopsies, but we did DEXA, and then we did total body water, intracellular water, extracellular water testing using bioelectrical impedance with Jordan Moon, who is-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... one of the thought leaders in this field on that. And based on number crunching, to our best guess, 20 sets per week per exercise seems to maximize hypertrophy, I got to be careful, without this extraneous increase in extracellular water, which gets into a different story-

Dr. Andy Galpin
Sure

Dr. Mike Roberts
... which is apparently hot topic right now.

Dr. Andy Galpin
Yeah.

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Dr. Mike Roberts
And misrepresentation.

Dr. Andy Galpin
Nero fiddles with others.

Dr. Mike Roberts
Yeah. So that is to say, I am of the persuasion that Brad Schoenfeld would say it only takes six sets per week at minimum perhaps to stimulate hypertrophy appreciably, and then I would add to the other end of that and say, yeah, it goes from six, like he's saying, and work all the way up to 20. If you're a non, or I shouldn't say non, if you're a lower responder, not seeing results and you're at eight sets per week, why don't we try 12? Let's start there.

Dr. Andy Galpin
Six is enough to get something there-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... but that's not necessarily the same thing as saying optimal either.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
I think optimal would be, and again, this is probably there's probably response heterogeneity here, but I think it's safe to say 20. And Cody's study wasn't perfectly designed to answer that because-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... it was all those same participants that continued to scale. We didn't have parallel groups. One group did 20 per week, one group-

Dr. Andy Galpin
Yeah

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Dr. Mike Roberts
... did 32 per week, if that makes sense. I think Eduardo de Sousa, though, at Tampa, has some data, and I think they're landing around 20, if I'm not mistaken as well-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... in terms of optimizing.

Dr. Andy Galpin
When we say 20, we're talking about number of working sets per week?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Per muscle group?

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
And do we have an indication about how that is best split up? Those 20 throughout the week. Can I do all 20 sets one day? Should I do four sets a day for five days? Any thoughts on how we should break that up?

Dr. Mike Roberts
I think practically speaking, two to three days per week just makes sense, would be my thought. Again, Brad would be a much better-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... candidate to answer that question.

Dr. Andy Galpin
If you just think about this from a human perspective-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... if you got to do 10 working sets per muscle, because you're trying to split this up into two

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sessions per week-

Dr. Mike Roberts
Right

Dr. Andy Galpin
... this starts to get-- That's a day.

Dr. Mike Roberts
Yeah, that's a day. So if you're optimizing hypertrophy, this goes back to the split routine where you do two upper, two lower.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
The math works out favorably in that regard-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... where you're not spending three hours in the gym.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Alternatively, 10 working sets per muscle per day is doable.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
If you do three sets of 10 of three exercises, that's not completely off the stratosphere. And I bring that up because every time I mention these types of things, the comment section explodes, right?

Dr. Mike Roberts
Yeah.

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Dr. Andy Galpin
And they're like, "Well, it's actually not-- It is hard."

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But it's not that crazy of a thing to do. It's probably not that different than what most people are doing. And I'll also remind you, because this will be the next most popular comment, not every rep of every set is taken to maximum failure.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
You can't do that.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
You're not going to last to the 20.

Dr. Mike Roberts
And that gets into another interesting question, which is training three to four RIR according to the Zortos scale.

Dr. Andy Galpin
Here's my next question.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
You have published on this.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
High load versus high volume. What do we know? We can take this from the responder, non-responder route or some of the other pathways you guys have taken this. But how should we be appropriately thinking about if, again, the goal is muscle growth?

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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
We'll get about strength adaptations and other things, bone, maybe a different time. But how should we, based upon the data you've seen, think about load versus volume?

Dr. Mike Roberts
When we talk about load, what we compared was the 30% 1RM training-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... where if you go do squats, you're doing 40 reps.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
If you're lifting-

Dr. Andy Galpin
Because you're taking them to failure.

Dr. Mike Roberts
You're taking them to almost failure, close to volitional fatigue, as we would say it.

Dr. Andy Galpin
So if you're at 30% of your one-rep max, you're going to have to do a lot of repetitions-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... before you get to failure.

Dr. Mike Roberts
And they suck.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Do you?

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Dr. Andy Galpin
They suck after rep like 12.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Or you can do your 12s, 10 to 12s of 80%. That right there gives you an answer-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... practically speaking. If you want a hypertrophy, according to our data, according to Stu's data, you can do 30% 1RM training close to failure, or you can do 80% close to failure, whatever you like. If you're sadistic, you're a 30% person, right? With the 80%, though, the key point here is you tend to get a little bit more strong.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? So that's the added benefit of doing higher loads.

Dr. Andy Galpin
Yeah. So presumably, when you're lifting 30% of your max, it's not going to stimulate much strength because you're not challenging overload.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
And do we have actual cellular data to suggest that that 30% is sufficient to induce mechanical tension?

Dr. Mike Roberts
Casey Sexton published his dissertation in our lab showing we did one acute bout, and these were in well-trained individuals, pre-biopsy in the morning. They then did either 30% or 80% squat and leg extensor training, and then we took biopsies six hours post and-- Excuse me, three and six hours post. We looked at the global mRNA expression signature in that biopsy, exactly the same. We looked at the mTORC1 signaling from those biopsies, exactly the same.

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We looked at the myostatin markers in terms of downregulation of the pathway, exactly the same. So that tells you indirectly that the mechanisms associated with mechanical overload respond in a similar fashion when you do 30% fail training or 80% fail training. In addition to that, Stu Phillips has shown that the muscle protein synthetic response is relatively similar. And what is interesting, Andy, is that when you do the volume load calculations-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... whether it's 80 fail, 30 fail, it's actually the same volume load.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
When you do the reps multiplied by the weight, there was not a statistical difference there.

Dr. Andy Galpin
So do we have then information, understanding of what the tension is directly? Because it's not the androgen receptors, it's not that side. There's something happening at the membrane itself-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... that is physical. This is not electrical.

Dr. Mike Roberts
We think it's a mechanical perturbation effect.

Dr. Andy Galpin
Tell me more about that, and how is that perturbation the same if I'm lifting light versus heavy and taking to fatigue? Because what you're saying here is there's a fatigue component, so something to this, if we want to call it that. What is that actual perturbation, the best we know?

Dr. Mike Roberts
Yeah. So the perturbation, again, it gets into the integrins and some of Marty Boppart's stuff and others. We think that that protein that spans the cell membrane is tugged upon with the matrix of muscle cells. The extracellular matrix is transducing the signal to the interior portion of those integrins, which are these complexes, and then you can have sort of this signaling event leading eventually to mTOR and muscle protein synthesis. Your question's a good one, which is to say, okay, we're doing time under tension, for instance. It takes a lot longer to do 30 fail training if

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we're doing 40, 50 reps per set. Why then are we not getting an enhanced response? I think that whether it's 80 fail training or 30 fail training, on the signaling side of things, you have met some sort of minimal threshold-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... at the cellular level, and then it's almost like the all or none, right?

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
We've turned it on, and it's going to do its thing now.

Dr. Andy Galpin
So if that is the case, we'll just call this a physical stretching of the tissue Causes some change in the membrane, which then kicks off an entire signaling gene and ribosomal cascade that-

Dr. Mike Roberts
Sure. Yeah

Dr. Andy Galpin
... eventually results in that.

Dr. Mike Roberts
MPS. Yeah.

Dr. Andy Galpin
Why couldn't I simply stretch?

Dr. Mike Roberts
You can, but the stretch protocols are going to be brutal.

Dr. Andy Galpin
Tell me more.

Dr. Mike Roberts
You've seen the quail studies.

Dr. Andy Galpin
Sure.

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Dr. Mike Roberts
So my postdoc mentor, Frank Booth, Jim Carson.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
Now, it's stretch under load. There's something, again, that is magical about stretch under load that leads to extremely massive hypertrophy. Joey Antonio, one of our common friends, he did this with Bill Gonia.

Dr. Andy Galpin
Mm.

Dr. Mike Roberts
I've never seen this, but the quail wing model where they put weight on the wing and it stretches the ALD muscle in the back, and they will see such-

Dr. Andy Galpin
Sorry. I wanted you to draw that point out. What are you specifically saying here is happening?

Dr. Mike Roberts
We are taking a muscle and stretching it, basically with a weight.

Dr. Andy Galpin
We're tying a weight on a wing.

Dr. Mike Roberts
Yeah. Let me see if I can do this in human terms. Okay.

Dr. Andy Galpin
To do it in the animal terms is totally fine.

Dr. Mike Roberts
Let's get on an incline bench and let's put 120 pounds in each hand and look up at the ceiling in pain for seven days.

Dr. Andy Galpin
So you can do this work.

Dr. Mike Roberts
And you will hypertrophy, I guarantee you, if-

Dr. Andy Galpin
100%

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Dr. Mike Roberts
... you don't drop the weight, and if-

Dr. Andy Galpin
You don't move

Dr. Mike Roberts
... your muscles don't rupture.

Dr. Andy Galpin
That's right.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Or tendons or anything along that pathway.

Dr. Mike Roberts
There you go.

Dr. Andy Galpin
If one could do this, let's just say we're doing a hurdler stretch, we're stretching our hamstrings. If one could hold that with that overload, again, for many days if not weeks on time, I think people are going to be very surprised to hear that that will not only result in some muscle growth, but a very large amount.

Dr. Mike Roberts
100%. And this is getting into some key topics that are at the forefront of physiology that my good friend Troy Hornberger is working on at Wisconsin, which gets into not only do we see some radial hypertrophy, but now we're seeing the addition of sarcomeres in series and longitudinal hypertrophy, which is, again, going to be a very hot topic. And not only that, but okay, how are the sarcomeres increasing in series? Meaning how are we lengthening the myofibril in the cell? How are we making the spaghetti noodle-

Dr. Andy Galpin
Longer

Dr. Mike Roberts
... longer? And Troy is doing exceptional work in that area. So he has a preprint published more or less indicating that the anabolic signaling response to making the spaghetti noodle bigger in diameter is canonical mTOR signaling, but longer is not mTOR signaling. It's some other signaling cascade. So, more to come there. Troy also has some crazy, awesome images

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showing how we have the addition of sarcomeres with longitudinal hypertrophy, as well as how we have the addition of myofibrils with radial hypertrophy. So if you geek out about our conversation, Andy and I's conversation, follow Troy Hornberger's work. He is doing it. He is driving the field in this area, if that makes sense. So Brad, Brad Schoenfeld. So they did interset stretching and showing it was a somewhat pretty decent effect when you did interset stretching versus not on hypertrophy outcomes using the ultrasound.

Dr. Andy Galpin
This is humans. So this is you lift some weights-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... and when you're resting, you sit down and stretch the muscle.

Dr. Mike Roberts
Yes. And then Danny Plotkin, one of my students, and Dakota T, they've told me, and I need to do a better job of following up on this, but for instance, imagine a mobilization boot, but that puts you into dorsiflexion.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And that apparently can cause some hypertrophy as well. So yeah, stretching is a component. And again, I think it operates through the tension, the tugging-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... extracellular matrix, all the way to anabolic signaling that can explain some of this stuff.

Dr. Andy Galpin
All right. You got me fired up. There's three ways I want to go with this.

Dr. Mike Roberts
Okay.

Dr. Andy Galpin
I'm going to probably forget them.

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Dr. Mike Roberts
All right.

Dr. Andy Galpin
But the first one that I cannot pass up this opportunity to get into. I don't know if you know this about me, but I am a day one diehard hyperplasia guy.

Dr. Mike Roberts
Oh, yes. Here we go, dude.

Dr. Andy Galpin
Okay. I'll frame it a little bit. You've been talking a lot, and you're using these phrases like radial increase.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
This is the spaghetti noodle getting thicker.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Right? It's getting-

Dr. Mike Roberts
To be clear. Yeah

Dr. Andy Galpin
And you've used CSA a lot.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Cross-sectional area. Same thing.

Dr. Mike Roberts
Same thing. Spaghetti noodle is getting thicker.

Dr. Andy Galpin
Thicker.

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Dr. Mike Roberts
That's our muscle cell. Yes.

Dr. Andy Galpin
If it's a circle, the circle is larger.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Right. And that is functionally how, again, your shoulder muscle is bigger is because those got thicker.

Dr. Mike Roberts
Radial hypertrophy is the bodybuilding hypertrophy that we classically think of.

Dr. Andy Galpin
Amazing.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Where we have some controversy, I'll say, and when you brought up Joey, you made me think of this, is the idea of hyperplasia.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And that is the fact that you would not necessarily make the spaghetti wider, though that could happen as well, but that you would add spaghetti noodles. This is you would add additional new muscle fibers. For the last 50 years, we've been told that that does not exist in humans in response to exercise. We have certainly seen it in humans in other models. Aging or, I guess, the opposite of aging.

Dr. Mike Roberts
Yeah, the loss of myofibers. Yeah.

Dr. Andy Galpin
We know it happens when you're a young baby, an infant, and stuff like that. The question is, in an adult human in response to exercise, we've also seen excellent evidence, well, good evidence, I should say, of it happening with exogenous testosterone-

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Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... or some evidence. Excellent was too strong there.

Dr. Mike Roberts
Well, no, that's going to be the paper that I end up referencing. So keep-

Dr. Andy Galpin
Okay

Dr. Mike Roberts
... going. Ask the question, and then-

Dr. Andy Galpin
All right

Dr. Mike Roberts
... we're going to go there. Yeah.

Dr. Andy Galpin
So now the thing I've been burning on is I'm waiting for us to be able to officially identify, and Kevin and I and a couple of my other muscle physiology friends, Kevin and Jimmy, we've always talked about this.

Dr. Mike Roberts
Oh, yeah.

Dr. Andy Galpin
You know Kevin.

Dr. Mike Roberts
I know Kevin, yep.

Dr. Andy Galpin
I'm just like, he's always sending me stuff and like, "Look, more evidence." I'm like, "Come on, man. Give me the paper that like does it." So break my heart or-

Dr. Mike Roberts
I'm not going to break your heart

Dr. Andy Galpin
... fill me with joy. Where do we really stand, if you had to guess, does hyperplasia happen in humans in a normal exercise response?

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Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Oh, my God.

Dr. Mike Roberts
Now-

Dr. Andy Galpin
Keep going

Dr. Mike Roberts
... I am going to-- And by the way, Kevin Murach would know more about this because he worked with the synergist ablation model.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
There is a backstory, but instead of like, there could be public banter, there could be Instagram stuff on this, or X or whatever, but there is actually a pretty considerable debate with our small group of friends.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
So Troy Hornberger and Stu Phillips, they're no-gos.

Dr. Andy Galpin
No, I know.

Dr. Mike Roberts
No hyperplasia. But then Kevin-

Dr. Andy Galpin
See, when Troy says no, I get scared.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
No offense, Stu. But when Stu says no, I'm like, "Oh, whatever. I don't care." Like you're-

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Dr. Mike Roberts
Well, Stu would admit this

Dr. Andy Galpin
... closest to this guy.

Dr. Mike Roberts
I'm saying no because Troy said no.

Dr. Andy Galpin
Yeah, 100%. When Troy says no, I'm like, "Argh!"

Dr. Mike Roberts
So Kevin.

Dr. Andy Galpin
So I'm always like, "Kevin, tell Troy he's wrong."

Dr. Mike Roberts
I think the famous interchange here that really got a lot of us thinking about this was Kevin had put out a paper, a review article sort of summarizing what happens with synergist ablation.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And oh, by the way, we see the number of muscle cells in this massively hypertrophied rodent plantaris when you remove a portion of the gastroc, the plantaris takes over in terms of ambulation, and there is almost a doubling of the mass of the plantaris. Not only do we see an increase in the thickness of the spaghetti noodles, the cells, but we see more spaghetti noodles, thereby fiber splitting is responsible for some of this massive hypertrophy. Well, Troy put a pretty big soggy wet blanket on that because he and Kent Jorgensen, awesome-

Dr. Andy Galpin
Ah

Dr. Mike Roberts
... student of Troy's, put out this rebuttal, and they had this mathematical model saying, look, you're looking at a muscle that has a pannation angle. You have to think more in terms of three-dimension, right? When you have massive hypertrophy, that is going to force changes in pannation angle. And when you do that, and you look at the number of muscle fibers-

Dr. Andy Galpin
Yeah

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Dr. Mike Roberts
... in cross-section, you're going to change the number just by mathematics, changes in angle, pannation angle. He mapped it all out. He did some SohCahToa. And sure enough, it seemed to check out, at least according to a lot of independent reports, some saying, okay, when you do synergist ablation, this is the percent change in pannation angle. Then when you look at Kevin's work, this is the number of fibers that he observed with synergist ablation. And so if you sort of do all of this mathematical stuff together, it would explain almost all of the increase-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... in myofiber number. However, here's the deal, man. Time and time again, if you take a biopsy from somebody that's well-trained, 10 years lifting weights, then you take somebody off the street that doesn't lift weights. Okay. The person that lifts weights has, we'll call it 30% larger muscle, VL muscle.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And the fiber size differences between those two individuals does not explain why that muscle's larger. Therefore, there seems to be more muscle fibers in the trained person time and time again. In addition to that, the paper from, I think it's from Norway, again, I apologize, lost the citation in my head, but you see some interesting things with large muscle fibers. You see fissures, you see centrally located nuclei. We had talked about, hey, look, man, this spaghetti noodle, Sharpie marker, all those little dots, those are myonuclei on the periphery. This group, I think it was in the mid-2000s, had histological evidence showing that as myofiber size increased in these powerlifters who were on steroids, limitation, those large fibers started having the invagination of the cell membrane looking like the myofiber was splitting into two daughter cells. And to me, it looked convincing enough. Then you look at Joey's work with the-

Dr. Andy Galpin
Oh

Dr. Mike Roberts
... LD model in Quell, and he shows he's plucked out myofibers that are branching.

Dr. Andy Galpin
Yeah.

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Dr. Mike Roberts
That seem to be splitting. We cannot dismiss this and say it doesn't occur. This is all evidence, right?

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
And so we have to be fair on both sides of the coin. I've said, look, I think a lot of stuff doesn't matter appreciably, but it may play a-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... small portion of the variance. And on the other side of the coin, if we have evidence across independent laboratories-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... different epochs, right? Going in the '70s and Kevin's work with John McCarthy and Charlotte Peterson and the Norway study in the early 2000s. We need to look at this and we need to consider it when we do future work, right? More innovative methods, histologically, et cetera. But I don't want to dismiss it yet.

Dr. Andy Galpin
I think that there's something there. I don't think it's a lot. It's not explaining half of muscle growth or anything close, but I think it exists. So I feel very validated that you're supporting me in this.

Dr. Mike Roberts
I do, and I support you firmly, and here's the deal. When you look at that Norwegian paper, I think it was controls, and it was also these bodybuilders. The number of-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... we'll say the number of splitting fibers per 100 fibers in these individuals, right?

Dr. Andy Galpin
Yeah.

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Dr. Mike Roberts
It was perhaps 1% in the controls.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And like 2 or 3%. And so people would say, "Oh, that's a rounding error." Or sorry, "That's a technique error," or "That could be variance," da, da, da. No, but if you say, "Hey, look, this is a snapshot and this is a dynamic process." We're just getting a snapshot, biopsy picture.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
But if we consider this dynamic 2% over years, right? If the number of fibers that are splitting at any given time are 2%, well, over years-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... compounding interest is a powerful thing.

Dr. Andy Galpin
Thank you for letting me run that.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
I appreciate it. Makes me feel better spiritually. I want to come back to the stretching thing.

Dr. Mike Roberts
Okay.

Dr. Andy Galpin
Because this is very counterintuitive and interesting, and it has some implications that I know you guys are currently working on in your lab.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So we want to get into this. We've established the fact that if you literally physically stretch

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tissue, muscle, skeletal muscle specifically, that you will see muscle growth. Until Brad's paper, didn't really think this had any human practical implications-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... because you can't, again, stretch-

Dr. Mike Roberts
Who's going to sit there looking at the ceiling with 120 pound, having dumbbells there.

Dr. Andy Galpin
Even if you stretch for an hour a day-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... this is not going to do it, right?

Dr. Mike Roberts
Right.

Dr. Andy Galpin
You need weeks, and traditional models with this, by the way, when we do this in cell culture, it would be things like you tie tissue, a muscle fiber to something, hang a weight on it, and come back in a month, and these are the types of things that we're talking about. With that said, what does this tell us about things like range of motion with our exercise selection? Is it fair to make the stretch then to say, hey, maybe larger ranges of motion in our exercise technique or selecting exercises that allow us to go through larger range of motion, should that then result in more growth than partial range of motion?

Dr. Mike Roberts
Yeah. Okay. So Brad has done a good bit. I'm familiar with some of the stuff indicating that partial squats, for instance, seem to be just as effective as deeper squats according to the meta. And I also know that he's done lengthened partial work, which is to say that imagine yourself going to the gym, and oh, by the way, this is a study we're doing, so Daniel Plotkin, all of the glory to Daniel, he wanted to pursue this pretty much from day one when he came from Brad's lab after his master's into my lab for his PhD. He has taught me a ton on lengthened partials.

Dr. Andy Galpin
Mm-hmm.

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Dr. Mike Roberts
Apparently, there's a lot of good evidence at the ultrasound level that lengthened partials, which is to say you go to the gym, you get in the leg press, the hip sled, all that weight loaded on, you sort of unrack it, and then you start working in this range of motion, knees to chin, and that's the lengthened partial for the quadriceps.

Dr. Andy Galpin
This is the opposite of how most people think about it. In the traditional way, people would do a shorter range of motion. It'd be the other end. So maybe with the leg press, you let it come down halfway.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And then go back.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
What you're saying is the opposite. You let it come all the way down.

Dr. Mike Roberts
All the way down.

Dr. Andy Galpin
So your knees are on your chin.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
And you only extend halfway.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Instead of a full lock out of your knees, not even stopping lock out, you're not even going, we'll call it roughly halfway.

Dr. Mike Roberts
Right.

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Dr. Andy Galpin
So you go up a little bit and then come back down.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
Which means you're spending most of the time in a really deep stretch.

Dr. Mike Roberts
Deep stretch, and this sort of integrates the notion of, okay, if we can't sit in the gym, look at the ceiling, hold 120-pound dumbbells for seven days straight, what if we adapt the training over 10 weeks, right? Where all of our movements are lengthened partials. And again, this is Danny Plotkin.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
I said initially, "Eh," and then I thought about it, and he showed me some literature that he had dug up on the topic, and I thought, "Oh, this is cool. This is actually kind of interesting because the time under tension, yes, with one bout isn't that much, but then you take this out to eight weeks, 16 weeks, a year, train like that all the time, can you see enhanced hypertrophy?" So his dissertation right now, we're currently analyzing, and what we did was we had within-subject design, which is a great way to run studies for you young folks out there that are doing dissertation projects or whatever. One leg of the participants did lengthened partial leg press, and then leg extensor. The other leg did full range of motion. Before and after the intervention, we did MRI scans, and we did it actually from knee all the way up to the hip, and so we're going to get across the entire quadricep regional hypertrophy differences, which I think is critical. We also did mid-thigh muscle biopsies. Obviously, it would've been cool to do five biopsies at a-

Dr. Andy Galpin
Sure

Dr. Mike Roberts
... different sites. Couldn't do that. But we're analyzing the main players, satellite cells, ribosomes, fiber CSA, myonuclear number, okay, and then we're going to look at MRI. Too early to tell as of yet, except I will say this, at least numerically, not statistically, but ribosome content increased in the lengthened partial leg, which I think is promising. Can't quote you on the p-value, effect size, stuff like that. Got to go look at the satellite cell stuff, and we're still doing the MyoVision fiber analysis, myonuclear numbers, stuff like that. But yeah. I guess stay tuned. I think it's an interesting way to train if you do want to maximize hypertrophy because aside from

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what we're doing, so Danny is going to be publishing the most sort of mechanistic study on the topic, but other laboratories, including some Japanese papers that he had made me aware of, and then I think Brad Schoenfeld just published something in '25, showed whether it's triceps or biceps, that lengthened partials seem to confer some added benefit to hypertrophy.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Which then you say, okay, well, if I want a hypertrophy man, when I was coming up, I was like, I want to look like Ronnie Coleman.

Dr. Andy Galpin
Mm.

Dr. Mike Roberts
Right? And if I wasn't growing, well, then up the volume and maybe integrate some lengthened partial training into your program and see what happens.

Dr. Andy Galpin
You mentioned the fact that you can wear a boot and you put it in flexion, so dorsiflexion. Plantar flexion is a confusing term, but just make your toe point to your face, right? Imagine if any of you have ever had plantar fasciitis, and they put you in a little boot, and then it constantly stretches you.

Dr. Mike Roberts
Stretches you, yeah.

Dr. Andy Galpin
So we've used that in that model, and I won't go into if that's a good idea or not for that injury, but those things have been around for a long time.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But what you're talking about, though, is using that boot actually and then seeing hypertrophy.

Dr. Mike Roberts
Of the plantar flexors, so think about gastrocnemius and things like that.

Dr. Andy Galpin
Yeah. Your calf muscles, right?

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So then here's my question If it works, can I wear that boot for, I assume, several weeks before that effect takes place? It's not going to happen in a couple of days.

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
Is this something we should be thinking about for unloading individuals? So when someone gets a major surgery or an injury-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... and a tissue, you can't lift weights. Of course, space flight is the one that we will always use-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... for this model, and you and I could probably share stories about some of the funny suits that have been tried to put on astronauts in space to alleviate this. But we'll stick to the planet.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Is this a reasonable thing for someone to think about if they're in one of those situations, either short-term or kind of long-term, from an injury or other unloading situation? Is that a reasonable thought process?

Dr. Mike Roberts
I think it is. We're getting outside my comfort zone

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
Because this is like PT, but we did a disuse study, by the way-

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Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which we can sort of-

Dr. Andy Galpin
No, yeah. Tell me.

Dr. Mike Roberts
I can strategically left turn on this.

Dr. Andy Galpin
Of course.

Dr. Mike Roberts
What I do know is that the angle of fixing a brace or a cast is at play, and it's because of that reason. If they're trying to preserve joint function after surgery, they don't want to put you in this contrived angle. And if they do, that may influence outcomes afterwards. So I think function is the main concern rather than hypertrophy, although hypertrophy plays into function.

Dr. Andy Galpin
This is going into the broader question on this topic-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... which is just simply disuse models.

Dr. Mike Roberts
Yes. So you're going to geek out on this.

Dr. Andy Galpin
Yeah, cool.

Dr. Mike Roberts
Max Michelle, he's post-docing with Marcus, just finished his dissertation, and his dissertation was this, Andy. We had people with resistance training history, men and women, it was 11 of them, come to the lab. We had controls that had no training history come into the lab. We put a knee brace on them for two weeks, and then after that two-week knee brace, took it off, and recovery resistance trained them for eight weeks. Now, strategically, biopsies, walking in the door, right after the knee brace, and then right after the eight weeks of training. And what Max wanted to answer was this: Does training history play a significant role in the retraining

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response? Well, does it mitigate the atrophy?

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Right? And then does it give you a conferred advantage when you're growing the muscle after the atrophy? This was in young healthies. It was non-complicated disuse, meaning there wasn't trauma to the tissue.

Dr. Andy Galpin
No injury.

Dr. Mike Roberts
Yeah, no injury.

Dr. Andy Galpin
You're just putting a brace on them-

Dr. Mike Roberts
Just putting a brace on them

Dr. Andy Galpin
... on a healthy knee

Dr. Mike Roberts
Some limitations. Fascinating results that bucked all kinds of preconceived notions. The rate of atrophy, the rate of VL atrophy, was the same whether you had prior training or not. But the key point there is your tissue bank was larger. So even though folks lost the same relative amount of muscle mass being either-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... trained or untrained, the absolute levels are still higher in those that had training experience.

Dr. Andy Galpin
So we'll pause you right there.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
This implication would suggest if one were to go into a surgery or something like that, whether

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you started trained or started untrained, how much muscle you lose as a result of this, in your case, two weeks of being in a brace.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
It didn't matter your previous training status.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
But if you start off with a lot more muscle and you lose, we'll call it 10%, then you're going to end up with still a lot of muscle.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
If you don't have much muscle coming in and you lose 10%, you don't have much total muscle left.

Dr. Mike Roberts
That is correct.

Dr. Andy Galpin
Okay, great.

Dr. Mike Roberts
Which I think strategically works back to your original question. Rather than thinking about bracing angles, let's just think about, okay, let's condition ourselves.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
So in the event that we have an injury, we're going to be sort of primed to deal with it.

Dr. Andy Galpin
I'll tell you a little secret behind the scenes. When we have had athletes, and I had one very high-profile one this year, go through an incredibly traumatic injury, and he damn near blew up the Internet because people were going to assume he was going to be out for 10 to 11 months, and he almost made it back to play at the end of the season. I'll stop the story there. But what

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we always do prior to any surgery is have them train as hard as humanly possible in every other affected area that we can, and even in that area, if we can, as much, for this exact reason and plenty others. But that is a really, really, really good way to come back from surgery much faster, is getting as much muscle as you possibly can prior to going into it. For not the reasons people think, but for this included. So yeah, it works.

Dr. Mike Roberts
It does. And I think while you were in the brace, Matt Stock at UCF, he had done some work with one of his PhD students where they did action imagery, imagining the affected limb contracting-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... things like that. That can add a little bit of at least function. In addition to that, Darren Candow, creatine during-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... a bracing. Arnie Ferrando, high-dose essential amino acids.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
So let's put all these in the bucket-

Dr. Andy Galpin
Of course

Dr. Mike Roberts
... and say this is how we optimize.

Dr. Andy Galpin
We do all that stuff.

Dr. Mike Roberts
Yeah, exactly.

Dr. Andy Galpin
Because that's the way to go.

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Dr. Mike Roberts
Yeah, exactly. So Max, awesome study. He is now going to try to make sort of a career out of disuse atrophy.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
He did some really cool stuff showing that certain proteins, these are like nuclear proteins, they seem to be main players in terms of mechanisms that are involved with disuse atrophy. But long story short, to the point of priming the body, resistance training, right?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Is the answer in terms of maintaining the muscle bank. Because yes, you will lose muscle, but you will certainly have more muscle after the brace compared to someone who didn't train. Now, the retraining, the recovery resistance training, this is where it gets a little bit dicey. Relative, meaning body mass adjusted, muscle mass increases with eight weeks of recovery resistance training was actually more in those that didn't have any prior training experience.

Dr. Andy Galpin
More in those that did not.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So, newbie gains.

Dr. Mike Roberts
Newbie gains outpaced the recovery gains with people that had prior training experience, which I think is good news.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Ish. Which is to say that, look, if you are training for years and years and years, this works towards sort of that ceiling effect of adaptation. You are going to have newbie gains, which are almost like this exponential phase of hypertrophy and strength, and then we hit this putative ceiling.

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Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
If we then go disuse, we go here, and then if we retrain, we get close to ceiling again.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? If you're somebody that's a newbie and you have a bracing event and you have muscle atrophy, the good heartwarming story is when you're done, resistance train.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And you're still going to have gains.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
And you're going to set yourself up for a better outcome in the long run, right?

Dr. Andy Galpin
What's interesting about this, and if I was a reviewer on that paper, this is what I would ask you. Your two-week bracing model is a very short term.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
But it's full bracing. How much does that differ from a more traditional detraining, which is-

Dr. Mike Roberts
Oh, yeah

Dr. Andy Galpin
... I stopped exercising for six weeks.

Dr. Mike Roberts
Adam Sharples.

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Dr. Andy Galpin
Right. So, I wonder if this is just a classic, "You just didn't do it long enough." And so they maybe got a little bit of the training group. Right, of course. They kind of just recovered a little bit and then you get what I'm sort of-

Dr. Mike Roberts
I do, yeah. And I think, like Ricky Ogasawara, they did that. Him and Jeremy Leneke did like that six-month bench press training. Could you do three weeks on, one week off?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Or maybe even two weeks off versus-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... continuous. It's like, yeah, you can take one to two weeks off over six months.

Dr. Andy Galpin
Often.

Dr. Mike Roberts
It really doesn't-- Yeah, often. Exactly, yeah. Good question.

Dr. Andy Galpin
This entire detrain, retrain model stuff and muscle memory. If you are talking to a neuroscientist, muscle memory is a motor control thing.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Right? I remember how to ride my bike, so on and so forth. When you talk to a muscle physiologist, that's not muscle memory from our perspective. So maybe just start us right there. How do we think about us and our small group of dorky friends? How do we think about muscle memory? What is it? And what do we know about that in all levels, actually? Because this is a very interesting topic.

Dr. Mike Roberts
It is. So, yeah, to your point, when we think about muscle memory, we think about the spaghetti noodles. We don't think about the alpha motor neuron that innervates it-

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Dr. Andy Galpin
For sure

Dr. Mike Roberts
... or anything upstream.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? But there is evidence of muscle memory at that level-

Dr. Andy Galpin
Of course

Dr. Mike Roberts
... when you look at spaghetti noodles, which is to say, hey, look, we resistance train, we take these spaghetti noodles, and we make them larger. We put more dots with a Sharpie marker. Those would be myonuclei. If you then stop training for six months, a year, those spaghetti noodles will sort of retract and go back to their original size, putatively. Right? You won't see the loss of Sharpie marks. Those myonuclei that were glommed on typically like to hang around. Now, I know Kevin and Cory Dungan, they have this power model. There's a little bit of rodent evidence suggests maybe that's not the case. But by and large, most people would agree on this. Okay? So, myonuclear permanence is one of those theories.

Dr. Andy Galpin
This is the analogy I gave everyone earlier was the store manager.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
So, you opened up a bunch of new shops, you hired to make sure you have one manager per shop, and now you start closing down stores, but you keep the managers.

Dr. Mike Roberts
Yeah, you don't take them to the back and you know.

Dr. Andy Galpin
So, the store is not there, and this theoretically then should allow you to reopen that store.

Dr. Mike Roberts
Yeah.

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Dr. Andy Galpin
Because you already have a manager ready to go.

Dr. Mike Roberts
100%. Good analogy. Great analogy, yeah.

Dr. Andy Galpin
Okay, so keep going with-

Dr. Mike Roberts
So, there's that aspect of it, is that we have myonuclear permanence. We keep those, retain those, so that when we retrain, they are reinvigorated. Right? So, this manager that's hanging out in store A because store B was closed, well, now we're opening store C. He's going to store C and all the knowledge he had retained from running store B is kicking back up and business as usual. That's kind of what we think about in terms of.

Dr. Andy Galpin
Do we have a sense of how long that permanence stays for? Is that six years, 12 years, 60 years?

Dr. Mike Roberts
So, if anybody has this, it'd be Lex Verdik. I think they did sort of population-wise, looking at across the age spectrum. I'd have to go look in the literature, to be quite honest with you.

Dr. Andy Galpin
It's certainly dependent upon how long you train.

Dr. Mike Roberts
Initial stimulus.

Dr. Andy Galpin
Exactly.

Dr. Mike Roberts
There's a lot of caveat. With that being stated, though, I would be surprised if you don't retain those, if you train consistently, be it on and off, if you don't retain those until sort of, we'll call it, age 50 and beyond. Boy, I'm shooting from the hip.

Dr. Andy Galpin
Yeah. Sure.

Dr. Mike Roberts
And then at that point, now there's debate with age-related muscle atrophy, whether the drivers of why the muscle tissue can't grow in response to training or taking a lot of protein in. This

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would be the classical term of anabolic resistance.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Still an active sort of area of research right now. But with that being stated, I think if you're young, you're healthy, the good example would be train from the age of eight until senior year of high school, intense travel ball, did the conditioning.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
Sort of partied around in college. But then junior year reengages Those myonuclei gains are not going away-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... in my opinion.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We have zero data to support that but-

Dr. Andy Galpin
Well, you're not stretching that far, though, from what I think most people that do this research would say.

Dr. Mike Roberts
Yeah. That's fair.

Dr. Andy Galpin
I don't think you'd get a lot of pushback-

Dr. Mike Roberts
Yeah, that's fair

Dr. Andy Galpin
... on that. It certainly is a situation where that retention is not going to go away in two weeks.

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So if we look at-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... your model, even with a full disuse, I would struggle to think that you're going to have back to baseline accretion. They're just not going to have that.

Dr. Mike Roberts
And we measured that in our study, and we did not see a retraction in the number of myonuclei per fiber in the trained group. So that speaks to your point.

Dr. Andy Galpin
So that is two weeks, but it's full.

Dr. Mike Roberts
It's almost full disuse.

Dr. Andy Galpin
It's full lockdown.

Dr. Mike Roberts
Yes, full lockdown.

Dr. Andy Galpin
So if you take this into a quadricep muscle or group of muscles rather, that are-- Maybe you're not lifting weights-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... but you're still walking and standing and squatting and moving around. There's enough stimulus there to probably keep those around for many months to years. I would think after a number of decades, you've probably seen some return to baseline, but where that line is, I don't know. Maybe, again, Kevin might have a better opinion on this. But okay. So we know that. Point is, you can take some amount of time off, and then when you get back to training, what happens?

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Dr. Mike Roberts
So Adam Sharples, again, go read his papers, because his initial work here would indicate that, look, if you train for a period of seven weeks, resistance train, you see hypertrophy. You then take a seven-week period off, and then you retrain for seven weeks. You not only will get to that initial hypertrophy during the first block pretty rapidly-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... but you actually exceed that level. Right? So the conferred advantage aspect there is that be it myonuclear number increases and retention, be it three-dimensional changes in the chromatin within the nuclei, which leads to this sort of modeling of genetic material so that when you retrain, you can express those-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... exercise responsive genes very efficiently. That's what we're talking about. It all hinges on the myonuclei, the number, and then the dynamics in terms of how your genes are expressed, is what we talk about when we talk about muscle memory.

Dr. Andy Galpin
So we have an ability to gain some muscle initially.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Lose it.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
But we conserve that ability to gain muscle so that the second time we go after it, it's actually easier.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
In fact, there might even be an advantage where you can go past-

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Dr. Mike Roberts
Yes

Dr. Andy Galpin
... where you were. And there genuinely might not be, but is there anything that Adam or anyone else in this field would say we can then take that to enhance our training programming strategies?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
What could we conclude at this point from that information?

Dr. Mike Roberts
There is a one-off paper. It was in older participants, and what they did was they trained them for a, we'll call it, a typical 12-week. It could've been actually longer. It may have been like a six-month training period. It was either 80% one-arm training, generally speaking, or it was something to the tune of like 55% one-arm training. Six months of that, okay? Clearly, both groups are gaining strength. I think the 80% is probably getting a little bit stronger, et cetera. Then they had this one-year hiatus, and then they tested at the end. Guess who was stronger above baseline after the one-year hiatus? It was the high-load group.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? Which is remarkable. Now, the hypertrophy, they actually didn't do any imaging. I think it was all circumference tape measure stuff, so they didn't have sophisticated methods. But I looked at that paper thinking, "Wow, that's crazy."

Dr. Andy Galpin
Uh-huh.

Dr. Mike Roberts
Which speaks to the sort of the neuromuscular neural aspects of that could be at play as well with-- There's some sort of retention of motor drive, central motor drive to the muscle or whatever, and that seems to be manifested better with higher load training, if that makes sense.

Dr. Andy Galpin
Yeah. No, it totally does.

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
What about for aging muscle?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Anything we can learn from this understanding of detrain, retrain for folks? Does the story change? Do we have any information that, hey, maybe that is true when you're college age-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... but not true of our 50-plus-year-olds. Do we have any data on that?

Dr. Mike Roberts
So to the best of my knowledge, there have been more sort of subchronic studies looking at the effects of proteostasis and muscle protein synthesis, decrements therein, with younger and older pops. We put, Matt and I, with a colleague that Matt had in Orlando, we actually put in an NIH proposal. We thought we were going to get funded. Didn't. Boo-hoo.

Dr. Andy Galpin
Story of every one of them.

Dr. Mike Roberts
Yeah. But we wanted to do the study that we did, but we wanted to do a younger and older pop with the notion that the retrain in the older pop would probably be impaired because-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... generally speaking-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... the adaptability response in somebody average age of being 55 in our hands is not as good. When you start talking above the age of 80, like some of the Scott Trappe stuff. You've worked

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with Scott. There seems to be strength adaptation, but debatable as to whether or not you have hypertrophy with resistance training. Look at single fiber level stuff, right?

Dr. Andy Galpin
There's some insights I can share with you offline about that-

Dr. Mike Roberts
Okay

Dr. Andy Galpin
... paper.

Dr. Mike Roberts
Okay. All right. All good. But there is a general anabolic resistance. People ask, what is the magical age? So recent Stanford paper, I think Michael Snyder's group-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... and they looked across the gut microbiome, the-

Dr. Andy Galpin
Sure

Dr. Mike Roberts
... PMBCs in the blood, the blood markers, and they showed that when you look at all these multi-omics, so how genes are expressed in tissue How the gut microbiome is altered, what happens to these proteins in the blood that are linked to this SASP phenotype, et cetera. Just the whole body, we're getting this molecular snapshot. We have two critical ages at which things start to sort of turn on us. One is the age of, bingo, 44.

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
This is me. The other is at the age of 60. I think the age of 60 is really that inflection point at which, okay, now we're going to have a diminished response-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... to training, be it endurance, resistance, whatever, because that is a primary effect of aging,

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especially at the muscle. I think we just have something that triggers, be it three-dimensional changes in the chromatin, be it ribosome function, be it the sensing of nutrients and the proteins that were responsible for that. But some switch all of a sudden goes awry, right? And that's a scary thought. But long story short, the good news is if you do train, even at that age, you still will see adaptation. You will get stronger, and you will hypertrophy. In our hands, compared to college-age cohort, the gain in muscle mass is about 50%, which you would see as an older individual.

Dr. Andy Galpin
You've published some stuff on this, and I actually just read a paper probably two weeks ago that came out. Post-menopausal women. And why I think this is of interest to what you just said is, I don't know why, but there's a narrative that because of the known hormonal changes that happen post-menopause, that therefore is a reduced, blunted, or completely ablated ability to grow muscle, when in fact, I don't know where you stand on this, but my indication, my reading of the literature is that is as dead wrong as one could be on that topic. So, first of all, do you agree, disagree on the simple question of women have the ability to grow muscle post-menopause?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
At the same rate as they were pre-menopause.

Dr. Mike Roberts
Ugh.

Dr. Andy Galpin
Okay, tell me more.

Dr. Mike Roberts
Yeah. And that's because with the current analysis we're doing, we're taking a molecular approach, albeit it was a 12-week study. But we've trained a lot of older and younger individuals, and the summary is we just don't, with our two-day per week training program, which typically tries to target around 12 to 16 sets per exercise-

Dr. Andy Galpin
It's a very reasonable program for a normal human being

Dr. Mike Roberts
... gym pop.

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Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? This is something that you would program as a Gold's Gym personal trainer.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
You name it, right?

Dr. Andy Galpin
Quality, yep.

Dr. Mike Roberts
Yeah. So long story short, we just don't see the same magnitude of hypertrophy when we look at our more nuanced methods of ultrasound or changes in DEXA lean mass, et cetera.

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
In our hands.

Dr. Andy Galpin
Yeah, tell me more.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So what you're saying, assumption is, when you get a better view of the muscle, then you actually start to see nuance.

Dr. Mike Roberts
There is nuance there, but that's for men and women alike.

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
So again, whether you're post-menopausal or you're a male that's starting to really feel the andropause-

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Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... of effects and test is going down, your gains are about 50% that which would be seen in the college-age cohort.

Dr. Andy Galpin
Assuming the same training volume and the same-

Dr. Mike Roberts
Relative, yeah. Relative training volume

Dr. Andy Galpin
... corrected for as many things as reasonable-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... one can be corrected for.

Dr. Mike Roberts
100%, yes.

Dr. Andy Galpin
But that happens independent of hormonal changes.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
In the sense that-

Dr. Mike Roberts
We don't think that it's the testosterone, and we don't think that it's the estrogen that's the primary driver there. We think that, again, it's-

Dr. Andy Galpin
And it's not the receptors either.

Dr. Mike Roberts
I don't think so, to be fair.

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Dr. Andy Galpin
It could be the ribosomal stuff.

Dr. Mike Roberts
It could be the ribosomal stuff. It could be things that we're currently unaware of. And to give you a spoiler alert on this topic, okay, here's where I'm going. Our study, we have an older cohort, we have a younger cohort. This is not published yet. So Dustin Lewis is doing this analysis right now. But what we're seeing is with 12 weeks of training, be it the imaging of the VL with an ultrasound, be it DEXA lean body mass changes, we have a 50% reduction in hypertrophy. There's still hypertrophy, but a 50% reduction in the older group, okay?

Dr. Andy Galpin
It's attenuated. Yeah.

Dr. Mike Roberts
Yeah, attenuated hypertrophy. We took pre and post biopsies in all these individuals, and we ran global proteomics, which, in my opinion, is what you ought to do, especially with chronic training paradigms. When you get into omics, this is a whole different episode. You can do genomics. You can do deep sequencing, microarrays, et cetera. You can do transcriptomics, which is all of the mRNAs in a tissue. You can do proteomics, which is all the proteins in a tissue. Ultimately, proteomics-

Dr. Andy Galpin
Genomics is all the genes.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Yeah. Metabolomics and all of the omics.

Dr. Mike Roberts
Exactly. A lot of people have done transcriptomics because they've been intrigued with the notion that when we have mechanical tension with resistance training, we see a huge sledgehammer effect on the gene changes at the mRNA level. And so that's just naturally where the field has gravitated. Hardly anyone was doing proteomic work, and so I really wanted to sort of pound that drum hard because I said, "Well, this is a knowledge gap, a opportunity. And oh, by the way, we have a really nice collaborator on campus that does this work."

Dr. Andy Galpin
Okay.

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Dr. Mike Roberts
"And she's excited that we give her human muscle." What we are seeing, Andy, is this. The young cohort, on average, apologies if I misquote this when you see the publication, but the muscle proteome is changing robustly in the young cohort, which coincides with the enhanced hypertrophy.

Dr. Andy Galpin
This is more turnover, right? This is-

Dr. Mike Roberts
Yeah. Turnover of proteins, expression of new mRNAs where you have the production of new proteins at a higher level that weren't there prior to training, okay? That coincides-

Dr. Andy Galpin
You're getting more people in the restaurant and getting them out-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... faster, right? Like it's a much bigger turnover of positive, negative, the whole thing. The ship is just moving really quickly.

Dr. Mike Roberts
Yes. And oh, by the way, when you run that protein list of what changed in the young people A lot of those proteins are related to proteostasis, which-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... that works to that mechanism that you just spoke of. There is a lack of proteome plasticity in older people, which coincided with the diminished hypertrophy. So that is going to be probably, if not the title of the paper, we need to pay attention to this. We're not seeing enzymatic changes with resistance training. We're not seeing much by way of proteins that are ribosomal proteins, for instance, with resistance training. Stuff that we're seeing in the younger people, we're not seeing in the older people. Why is that? Don't know, except to say perhaps that there's altered proteostatic mechanisms which let some proteins hang around. They could be damaged in an older person. They're not getting cleared through proteolytic mechanisms. You have ribosome deficiencies which don't produce the new proteins needed for growth, et cetera. All this could be happening with aging, but not in the younger college-age.

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Dr. Andy Galpin
In this instance, you're defining older as 55 plus.

Dr. Mike Roberts
55 was the average age.

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
But it was between the ages of, we'll call it 50 to 70, lower 70s.

Dr. Andy Galpin
Well, this is really interesting. I don't know if folks listening will get the full appreciation of what you just said, but that's really interesting because traditionally, when we've looked at the molecular aspect of muscle growth in humans, skeletal muscle, we've hedged towards muscle protein synthesis.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
This is this direct marker right now-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... how much protein are you building? Again, skipping some steps there. What you're looking at, though, is miles above that, which is all the proteins in the entire thing. How are they working? And I say that as a distinction because some people have done this, but I don't know, 90-plus percent of the papers that have ever been done on protein synthesis don't account for protein breakdown. It's really hard to measure. It's a giant pain, and so we kind of just say, "Well, how much was synthesized?" And the assumption is then if you built more, you have more. Of course, the down part of that assumption is you're not accounting for how many you broke down, which you have to turn over. Right? Turnover meaning you kind of have to some damaged stuff, get that cleared out. I'll use the restaurant analogy. I don't know how long this is going to last or how well it's going to work, but you have enough people coming in your restaurant, some tables will break, and you want a nice restaurant, you got to clean out the garbage. If all you're ever looking at is how many new things you're buying, but you're not accounting for how many things you're taking out, you don't actually know the net. Right? This net protein balance is how we described it. What you're talking about is all of that combined with everything else in the

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equation, and you're simply saying, we have just way more activity. We have the entire protein side of the equation is moving, so this encompasses so many layers besides just protein growth.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Protein addition.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Which is very compelling.

Dr. Mike Roberts
Can I take your analogy? I think it was a great one. I'm just going to add onto it.

Dr. Andy Galpin
Okay.

Dr. Mike Roberts
This is what we do in science.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Like, "Oh, Andy had a great paper. I'm going to see if he-"

Dr. Andy Galpin
We make analogies and we make acronyms. We're very good at acronyms.

Dr. Mike Roberts
Very good at acronyms. So if you had a restaurant and you said, "I want to grow the restaurant. I want to become a competitor with these high-end restaurants." So what's the goal there? Getting clients in, and you got to get them out. If they just came, loitered, you're not making money. You're not growing. All right? So the turnover of clientele would be sort of what we're talking about when you talk about synthesis and when you talk about breakdown. All right? What we are doing with proteomics is saying, who are all the clients in there? What are they buying? High-ticket items, low-ticket items. How do they function? How can we refine the blueprint of our restaurant to better serve the clients?

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Dr. Andy Galpin
How long are they staying? How did they find us?

Dr. Mike Roberts
That's proteomics.

Dr. Andy Galpin
What are they wearing?

Dr. Mike Roberts
Looking at all these different proteins.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And then you take advanced bioinformatics and say, "Oh, wow, this bucket of proteins, these bucket of clients here, they themselves work for a company. This is important for our business to grow. We need to serve them better." That's what we're doing with bioinformatics and these protein lists saying, in the young participants, we're seeing a lot of proteins related to turning over clients. They are totally populating the list of what adapted to training, whereas you did not see that in the older population.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? Along with that, there's other just list of things that we can predict are going on because of these protein changes in the younger individuals, and we just saw the lack of proteome alterations, and therefore, no predicted pathways that are changing in the older population. Right?

Dr. Andy Galpin
That's really compelling stuff. It does highlight something that we talked about, geez, a couple of hours ago-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... at this point, which is the magic here is still in the muscle.

Dr. Mike Roberts
Yes.

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Dr. Andy Galpin
It's not at this point, and I will acknowledge, we are muscle physiologists, so we're going to be quite biased on this approach.

Dr. Mike Roberts
That's fair.

Dr. Andy Galpin
Fair distinction.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But it's not necessarily all driven by something outside. Hormones, endocrine system. Not to say that there's zero, but it looks like if there is a reduction in ability to grow muscle post-menopause or post-age, andropause for the male side of the equation, it's probably something happening inside the muscle or a collection of things that are mainly driving it. Is that a fair caveat?

Dr. Mike Roberts
I think that's a fair assessment, yes. Again, we need more-

Dr. Andy Galpin
So if we're going to solve this problem, if we're going to improve it, we need to continue to do work in there to figure out what's going on.

Dr. Mike Roberts
Agreed.

Dr. Andy Galpin
One more big topic for as long as I know exercise physiology programs have been around, we've all been indoctrinated to our classic interference.

Dr. Mike Roberts
Ah, yes.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
Bob Hickman's stuff, and you probably share the paper in all your classes and-

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Dr. Mike Roberts
Yes, the classical week-by-week changes with the concurrent versus the strength-only, endurance-only. Yeah

Dr. Andy Galpin
So the interference effect is effectively the idea that endurance exercise, aerobic exercise, potentially interferes with the ability to grow muscle.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
However, strength training muscle hypertrophy does not interfere with the ability to enhance aerobic capacity. So that paper, I think that first paper was 1980.

Dr. Mike Roberts
It was, yeah.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And then it went about, I don't know, maybe, help me here, 20 years or so before we started to get the molecular mechanisms?

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And this launched what I still see all the time of this idea that AMPK is somehow turned off when mTOR is turned on, which is the prevailing. You mentioned it as mTORC, that's the-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... more appropriate way, but in the popular sphere, you might hear this as mTOR.

Dr. Mike Roberts
mTOR, sure.

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Dr. Andy Galpin
Right.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But the basic idea is the same as it was in 1980. If you do strength training, you activate, in fact, we mentioned the primary way of phosphorylation as one of the big things, but you turn on mTOR.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
mTOR then turns on muscle growth. Okay, I'm cutting two hours of conversation-

Dr. Mike Roberts
That's fair

Dr. Andy Galpin
... down. If you do endurance exercise, it activates something else called AMPK-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... which then turns on and activates mitochondrial biogenesis.

Dr. Mike Roberts
100%.

Dr. Andy Galpin
I got more citrate synthase. I can utilize aerobic, whether I'm using fat or carbohydrate as a fuel, doesn't matter at this point.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
I've got more mitochondria. I'm almost done, and then I'm going to let you take over.

Dr. Mike Roberts
No, this all sounds great. This is good.

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Dr. Andy Galpin
Here's the issue. We've also been taught for 30-plus years that because of that, two things are important distinctions. One, if you then do aerobic exercise, this will block or blunt or eliminate your ability to grow muscle. So that's a set of questions I'm going to ask you. The other side of the equation is, if that is then therefore true, the only way for me to build mitochondria, which is one of the most popular things in the whole health wellness field right now is-

Dr. Mike Roberts
Oh, yeah

Dr. Andy Galpin
... mitochondria, mitochondria.

Dr. Mike Roberts
Especially with aging. Yes.

Dr. Andy Galpin
All of it, right?

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
And if you ask the wrong person on Instagram or on X, the whole world, I guess, comes down to mitochondria. Every health ailment ever is mitochondria's function. Great. If that is the case then, the only way to get that from an exercise via pathway is aerobic exercise, endurance exercise.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So I want to ask the interference-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... question, and then I want to ask you about where do we really stand? What has your lab done? Where do you see the data on the ability to increase the amount of mitochondria we have, the effectiveness of them, the size of them, whatever variable is relevant there? What do we need to know? And what do we know about the exercise stuff? And we'll save supplements, pharmacology, and all that, and drugs for another discussion. So big topic.

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Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
But start me there with the interference effect.

Dr. Mike Roberts
I think the interference effect holds true. You can also expand the reticulum of the mitochondrion muscle cells with resistance exercise, especially in the older population. Especially in the older population that's deconditioned. We see mitochondrial biogenesis all of the time, be it an acute bout, and we're looking for markers like PGC-1alpha is a famous one, TFAM. These all drive mitochondrial biogenesis.

Dr. Andy Galpin
Precursor up the chain, right?

Dr. Mike Roberts
Yes. We published one of the-- And this was an accidental paper. This was done with Robbie Seburn and Adam Sharples. We had a bunch of epigenetic pyrosequencing data from a six-week training study in older participants, and we said, "Hey, guys. Y'all know how to deal with this data. We don't."

Dr. Andy Galpin
Mm-hmm.

Dr. Mike Roberts
"Can we collaborate?" They said, "Sure." Robbie comes back and says, "Well, we didn't see across the entire genome much in terms of methylation changes based on the depth of sequencing, but what we saw consistently in all these older individuals was the demethylation at the region of the mitochondrial genome, which is responsible for biogenesis."

Dr. Andy Galpin
This is epigenetics.

Dr. Mike Roberts
This is epigenetics. So if you demethylate that region of mitochondrial DNA, which by the way is mutually exclusive in terms of location in the cell, this mitochondrial DNA's in the mitochondria. If you replicate that, that is a sign that you're making more mitochondria. If you demethylate the region that we looked at, that indicates that you're going to make more mitochondrial DNA. This was with resistance training, 12 sessions, older, deconditioned people.

Dr. Andy Galpin
So all you longevity people, hopefully you just paid attention to what Mike just said.

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Dr. Mike Roberts
Resistance train for mitochondrial health, especially if you're an older individual. I will stand by that statement, yes.

Dr. Andy Galpin
Amazing.

Dr. Mike Roberts
Amazing. So people have talked about the hormetic effect if you take-

Dr. Andy Galpin
Yep

Dr. Mike Roberts
... antioxidants. Ugh, that's a mess. I think exercise first, and then we can start talking about other things in terms of antioxidants. Megadose vitamin C and E, and this, that, and the other. There does seem to be an interference effect there-

Dr. Andy Galpin
Uh-huh

Dr. Mike Roberts
... that was reported.

Dr. Andy Galpin
Especially C and E together.

Dr. Mike Roberts
Yeah, C and E together. And Neil Schwartz, I think, did something at South Alabama with green tea catechins-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which is an antioxidant, showing that with endurance training, that interfered with mitochondrial biogenesis. So my answer is just bolster the endogenous muscle cell redox systems with-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... exercise while also stimulating mitochondrial biogenesis with exercise. Supplementation has

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its place, and we can talk about this later. We talked about this in the car ride. I believe in supplements. It's improved health outcomes at the society level when we fortified certain foods that are on our store shelves, right? That is not a bad thing. It's not a four-letter word. There are certain supplements that have a time and place. But long story short, I haven't been a big proponent of antioxidants, right?

Dr. Andy Galpin
As a prophylactic supplement.

Dr. Mike Roberts
Yeah. Now, I've seen stuff with ultra-endurance athletes, for instance, looking at expired methane, like whatever methane exhalation. Looking at-- There's some sort of lipid peroxidation marker in the blood that is sort of reduced peri-exercise with mega-dosing. That's all fine and good. So you're seeing biomarkers change, but some people would argue on the other side of that coin, you need the oxidative stress to then promote the adaptation in muscle.

Dr. Andy Galpin
Yeah. That's your signal.

Dr. Mike Roberts
If you blunt it. Yeah, if you blunt the signal, it won't happen. So anyways. Okay. Let me go back to the full stop period on interference effect. So we did a study, Paulo Mosquita, in collaboration with Andreas Kavazis. He had a very interesting, intriguing question. He said, "Look, if we took two groups of people," it's always two groups of people, "walk into the lab." This sounds like a bad bar joke, right? So one group of individuals, all they did for 14 weeks was endurance train. They did SIT training, which is like the Marty Jabala-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... FitMaster protocol. Right?

Dr. Andy Galpin
That's really short, high-intensity stuff, right?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Probably, I don't know, it was 30 on, a minute off, or some-

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Dr. Mike Roberts
Exactly.

Dr. Andy Galpin
Some version of that.

Dr. Mike Roberts
It was like a minute on, two minutes off, and they started with four sets. They worked all the way up to eight or 10 sets.

Dr. Andy Galpin
Yeah, so max intervals.

Dr. Mike Roberts
Yeah, max intervals, three days per week. They did this for 14 weeks, saw a clear increase in mitochondrial biogenesis with biopsy. They saw a clear increase in VO2 max. Great. The second group, all right, was why don't we exclusively resistance train them first in order to promote hypertrophy of the muscle cells, in order to increase the number of ribosomes, in order to increase the number of myonuclei per muscle cell?

Dr. Andy Galpin
This is six weeks of-

Dr. Mike Roberts
Seven.

Dr. Andy Galpin
Seven weeks of the strength training.

Dr. Mike Roberts
Seven, seven. Yeah.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
So we're going to prime the muscle cell with resistance training in order to make more machinery so that then when they endurance train during that second block, they have more myonuclei, more ribosomes. They can make more mitochondrial proteins, thereby enhancing the biogenesis response. We saw the opposite happen. Hampered response. And what is the hypothesis now? Well, the short answer is I'm not really sure. The long answer is I think what's happening when you resistance train or you endurance train, it's more complicated than mTORC and AMPK. What happens inside of the myonuclei, right, the store managers, you're sort of with one training

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stimulus, you're rearranging their thought process, the architecture of the DNA, to express genes needed for the adaptive response to resistance training.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
You then go to-

Dr. Andy Galpin
Prosperity

Dr. Mike Roberts
... exclusively endurance training, and yes, eventually, if it were longer than seven weeks, that diminished response would've dissipated. However, there is a lag time.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
We have primed the muscle to adapt to resistance training, right? So, interesting stuff there. Aside from that, the meta-analyses, I always like Jake Wilson's. I thought he did a really good job. This is like a 2012 JSCR paper, where they tried to take into account, okay, look, if you can currently train, if you want to just be the Matt Fraser of like I just want to walk around, be strong, be well-endured in terms of doing shorter endurance events or whatever, what are the variables that matter in terms of, okay, how much aerobic training with my resistance training is going to hamper things? What type of endurance training should I do? And it looked like according to that meta, that if you were to want to do endurance training while also trying to best maximize strength and growth, you need to do SIT training on a bike.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
Two days a week.

Dr. Andy Galpin
You hit three things right there. The exercise choice. That was not an accident.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Would love for you to share why that bike matters. You hit frequency.

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Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Again, not an accident there. And then you also had intensity. So if you wouldn't mind, why are those variables important to choose if that's the outcome you're looking for?

Dr. Mike Roberts
So less is more in terms of the interference effect. I think that's simple.

Dr. Andy Galpin
Right.

Dr. Mike Roberts
If you go out and you just crush, whether it's running or biking, whatever, seven days a week, and then you go lift three days a week, you probably will have a good physique and good health, albeit overuse injury. But if the goal is to maximize hypertrophy, good luck.

Dr. Andy Galpin
Yep. You just don't have enough specific signal-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... let alone metabolic and energetic capacity to grow.

Dr. Mike Roberts
Correct.

Dr. Andy Galpin
You're oh for two.

Dr. Mike Roberts
You're oh for two.

Dr. Andy Galpin
Got it.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
Makes a ton of sense. I think if you're running 100 miles a week, you could fill in the blank here. Not going to matter what you do-

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Dr. Mike Roberts
Yep

Dr. Andy Galpin
... from there. That makes sense. So from just a straight-up numbers, okay, I believe you. Viable story, Dr. Roberts. What's the next one?

Dr. Mike Roberts
Okay. The next one is intensity.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
I think this is a little bit more difficult to disentangle, and this is a little bit more evidence-led than evidence-based. But what I do believe is Marty Jabala did this study. I'm going to misquote the heck out of it. But the gist is this: they were interested as to whether or not long, slow-distance training versus SIT, sprint intervals, affected the ability to activate higher threshold motor units.

Dr. Andy Galpin
Yep.

Dr. Mike Roberts
And the answer is SIT is better.

Dr. Andy Galpin
You're drawing a clear distinction. You keep using S-I-T, SIT, as well, not H-I-T.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Because it's sprint.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
This is the key factor in that question-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... specifically.

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Dr. Mike Roberts
And I want to say when we talk about SIT, it's a spectrum, for crying out loud.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
You can do HIIT, which is two-minute intervals.

Dr. Andy Galpin
Sure.

Dr. Mike Roberts
Two on, four off, whatever. A SIT would be more of that 30-second Wingate type of stuff.

Dr. Andy Galpin
Real true velocity.

Dr. Mike Roberts
Oh, yeah. I don't like doing it. I like doing HIIT, and I like doing, I'm going to jog hard, jog hard. All my belly fat bouncing.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And then I'm going to jog soft. That's my HIIT training, right? So, but yeah, the idea there is that when you do SIT training, you can actually see a bump in power as well. And I think that speaks-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... to some of the neural adaptations.

Dr. Andy Galpin
Practicing going fast.

Dr. Mike Roberts
Yeah. Moving fast, sprinting fast. You're activating more higher threshold motor units. And those higher threshold motor units, they innervate a ton of type two muscle fibers, which basically means this: I think that's more favorable towards than translating to resistance training and sort of triangulating that to maximize growth, rather than doing long, slow training for 30 minutes, an hour, whatever. You're not activating high-threshold motor units, and then you're trying to adapt

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them with resistance training. Just seems out of whack, if that makes sense.

Dr. Andy Galpin
Why does the bike matter?

Dr. Mike Roberts
Ah.

Dr. Andy Galpin
From an exercise choice.

Dr. Mike Roberts
This is the hard one. This is just shooting from the hip, Andy.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Ground and pound, time under tension with grounding and pounding just doesn't seem to work well with then trying to grow muscle.

Dr. Andy Galpin
Yeah. If you look at Jimmy and Kevin's review paper on this topic, they walk through it pretty carefully. It holds up.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
It holds up. Why? I would have to jump from the hip as much as you did, but I would say the same thing you did, right? If you look at something like rowing and cycling versus running, I don't think it's a stretch for us to say, yeah, lots of that same amount of time is what we're saying. Same amount of energy output-

Dr. Mike Roberts
Yep

Dr. Andy Galpin
... same amount of miles, or however you're calculating it. If it's done on a bike or a rower, but more specifically a bike rather, there's no eccentric component.

Dr. Mike Roberts
Correct.

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Dr. Andy Galpin
There's not as nearly as much load on the body, physical load, gravity load. That probably takes some recovery resources away. It probably adds to maybe additional damage or injury or something like that. And then because when you actually look at the papers, the papers themselves show that.

Dr. Mike Roberts
Yep.

Dr. Andy Galpin
And so why, we're speculating, but the actual outcome is the part that we have pretty clear evidence on, which matters.

Dr. Mike Roberts
That's right.

Dr. Andy Galpin
So if you're going to do it, keep the volume reasonably low, make the intensity high, because if the volume is low and the intensity is low, then it's probably not enough to stimulate the mitochondria to do anything.

Dr. Mike Roberts
That's fair. Yeah.

Dr. Andy Galpin
But then do it on an exercise choice that doesn't zap all your recovery capacity, which a bike is probably a good route for it.

Dr. Mike Roberts
100%.

Dr. Andy Galpin
Makes a lot of sense, makes intuitive sense. So an interference effect does exist.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
It's there. It's probably a little bit more complicated than simply mTOR and AMPK.

Dr. Mike Roberts
And AMPK. Yeah. Agreed.

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Dr. Andy Galpin
Last thing I want to press you on is this relationship between ribosomes and mitochondria.

Dr. Mike Roberts
Sure.

Dr. Andy Galpin
If we were to just-- I'm sorry if I insult any mitochondria or ribosomes in the room, I apologize.

Dr. Mike Roberts
And they are distinct camps.

Dr. Andy Galpin
Yeah. This is not-

Dr. Mike Roberts
Holy war is about to be waged right here.

Dr. Andy Galpin
Sure. Roughly, we will say, as we've been talking about pretty consistently, the ribosomes play a large part in muscle growth.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
The mitochondria play a large part in energy.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So we will often then kind of bucket these. Ribosomes are our strength training stuff-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... muscle growth. Mitochondria are energy and endurance and things like that.

Dr. Mike Roberts
Can I add a wrinkle to that?

Dr. Andy Galpin
Please do.

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Dr. Mike Roberts
Okay. I have a student. His name is Nick Kontos, and I want to shout him out because he has found a way. So he is interested in cardiomyocytes, and he wants to elicit hypertrophy to mimic ventricular hypertrophy heart failure with phenylephrine. You can do this in a Petri dish. He found a way to get mitochondria into cardiomyocytes to see if that mitigated any of the bad response to hypertrophy. What we want to do, and I've told Nick this clearly, is what happens if we take muscle cells in a Petri dish, we transplant mitochondria into those muscle cells. We have another bucket of cells that we do, like a vehicle, so no transplant, and then we give them both an anabolic stimulus. Does that added mitochondria lead to enhanced hypertrophy? Because that is an unsolved question.

Dr. Andy Galpin
There has been a paper on, you mentioned earlier, pre-strength training prior to endurance training.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
There was a paper recently-

Dr. Mike Roberts
Opposite of that, Stu Phillips group.

Dr. Andy Galpin
Yes.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And I believe they found that that did in fact occur. Did they not see-

Dr. Mike Roberts
They did

Dr. Andy Galpin
... enhanced muscle growth after a period of four to five weeks of-

Dr. Mike Roberts
Endurance training

Dr. Andy Galpin
... I think it was low-intensity cardiovascular cycling, right?

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Dr. Mike Roberts
Yes. However, I will say this-

Dr. Andy Galpin
Well, there's two howevers here, but-

Dr. Mike Roberts
Yeah. One would be capillary, because enhanced capillarization or the enhancement of the network of capillaries with endurance training also occurs. We're not even touching that in this conversation, which leads to enhanced perfusion, et cetera. And then with that, the other hallmark adaptation is the reticulum expansion of the mitochondria. So in the human model, it's tough to disentangle, was it capillary? Was it mitochondria? Was it both? Was it something we didn't even look at? I hate writing just in vitro only papers, but I told Nick, "This would be the perfect one because we're clamping all that. We're removing that from the equation. Let's give these guys more mitochondria in the Petri dish versus not, and let's hit them with IGF-1."

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And if we see an enhancement in MPS, muscle protein synthesis, and an enhancement in cellular hypertrophy, then that's probably the best evidence-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... that we have that, hey, look-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... those older individuals I told you earlier in our conversation that are deconditioned and they see this robust increase in mitochondrial biogenesis with resistance exercise, that could be part of the driving force- That enhances hypertrophy in those older individuals. So anyways, people say, "Look, man, when you synthesize muscle proteins, how much ATP is that?"

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
Right? There's some modeling in the '70s with bacteria saying it's three or four ATP per peptide

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bond. And then you start thinking about-

Dr. Andy Galpin
That's a-

Dr. Mike Roberts
It's crazy.

Dr. Andy Galpin
That's a load.

Dr. Mike Roberts
A load. And then I told you, right? How many contractile proteins do we have in muscle?

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
It's 85% volumetrically filled with myofibrils, and then you look and you have all these-

Dr. Andy Galpin
Oof

Dr. Mike Roberts
... sarcomeric proteins, M line, Z line, et cetera.

Dr. Andy Galpin
That's a lot of ATP.

Dr. Mike Roberts
Yeah, bro.

Dr. Andy Galpin
The second caveat I'll add to that is I'm pretty sure a paper came out after that, that repeated the study or had a similar approach and did not-

Dr. Mike Roberts
Did not replicate. Correct.

Dr. Andy Galpin
So okay, I'm not making that second one up.

Dr. Mike Roberts
I think you are correct.

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Dr. Andy Galpin
Okay.

Dr. Mike Roberts
And this is nothing against Stu, right?

Dr. Andy Galpin
Of course not.

Dr. Mike Roberts
When this happens to you and I-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... we'll come out with something and say, "Oh, wow, significant." But there are false positives like everything else in life.

Dr. Andy Galpin
And there's also, neither one of us are obviously very familiar with that second paper, so that could've been an inferior design or-

Dr. Mike Roberts
Yes

Dr. Andy Galpin
... a different design. A thousand things could've happened, but-

Dr. Mike Roberts
That's right

Dr. Andy Galpin
... I would say, I only brought it up to say I don't think it's a clear answer at this point-

Dr. Mike Roberts
Yes. That's right

Dr. Andy Galpin
... whether or not that happens. So I think your study still has legs to do.

Dr. Mike Roberts
Yeah.

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Dr. Andy Galpin
Because we don't know the answer.

Dr. Mike Roberts
Yeah. That's fair.

Dr. Andy Galpin
So that, really cool. Is there a competition in this cell? Does it have to choose? Does it have to choose which one it's going to do, support the ribosomes to grow, support the mitochondria, or are those independent? What's the mutual exclusivity here between this? Because this is the ultimate question, right?

Dr. Mike Roberts
This is.

Dr. Andy Galpin
If we know this answer-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... then we got no interference effect.

Dr. Mike Roberts
So we wrote this review article. Paulo Mosquita, who did that 14-week endurance training or resistance followed by endurance. He wrote a very nice review article trying to find all of the papers that have done resistance or endurance training or even concurrent training, looking at what happens with ribosome markers from biopsies and what happens with mitochondrial markers. And the short answer is, anything you can imagine happens, happens. Some studies-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... by and large, resistance training will increase more of the ribosome biogenesis than the mitochondrial biogenesis stuff. However-

Dr. Andy Galpin
Sure

Dr. Mike Roberts
... acutely, PGC alpha is activated in terms of mRNA expression, even phosphorylation of the protein with a bout of resistance exercise, dude.

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Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And then same could be said on the other end of the equation, where if you do this endurance exercise bout, albeit it's a little bit less-- There's less of an effect there with the ribosome stuff. If you do one bout of treadmill running and then, Andy, I get your biopsy pre and post, you're not going to see ribosome biogenesis-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... markers move the needle. We've shown that endurance exercise doesn't seem to stimulate ribosome biogenesis. Certainly does, though, increase capillarization, increases mitochondrial biogenesis.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
But resistance exercise is more complex.

Dr. Andy Galpin
Yeah.

Dr. Mike Roberts
And that's probably volume load dependent, which is to say, if you do a high volume training set, now you're sort of getting into this muscular endurance aspect that starts triggering some of those pathways-

Dr. Andy Galpin
Mm-hmm

Dr. Mike Roberts
... more so than just doing sets of three-

Dr. Andy Galpin
Yeah

Dr. Mike Roberts
... which probably doesn't touch those pathways, right?

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Dr. Andy Galpin
Right. Well, I think it's fair. You brought this up a while ago, and this is a great time to come back to it and finish that thought up. The idea that I don't think it would actually make any sense to grow a significant amount of noodle size radial increase and not touch mitochondria at all.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
If you look historically, what you and I were taught growing up was the fact that resistance exercise does nothing for mitochondria, and/or it's actually negative.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
Which I think was a really bad math problem.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
Right? You're looking at density, but you've increased the size. Okay. So even if I actually added more mitochondria, my density would've gone down.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
And this is how it was always described, right?

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So if you look at those early papers, mitochondrial density is lower after strength training, therefore-

Dr. Mike Roberts
Yeah

Dr. Andy Galpin
... you're less fit. You're out of shape more. It's like, well, time out. You still have more mitochondria-

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Dr. Mike Roberts
Yes. On an absolute scale

Dr. Andy Galpin
... probably bigger and function-- 100%.

Dr. Mike Roberts
Yes.

Dr. Andy Galpin
And you are an absolute being.

Dr. Mike Roberts
Yeah.

Dr. Andy Galpin
So the total amount of oxygen you can handle, and thus provide energy from there. So, I'm not exactly sure what the state of that literature is, but in my brain, that means we can now end that myth, the idea-

Dr. Mike Roberts
That resistance training is bad for mitochondria?

Dr. Andy Galpin
Right. Correct.

Dr. Mike Roberts
Oh, yes.

Dr. Andy Galpin
Gone.

Dr. Mike Roberts
Let's wipe that off the table. Absolutely not.

Dr. Andy Galpin
And we can even say it's potentially fairly beneficial.

Dr. Mike Roberts
For the deconditioned older population, for sure.

Dr. Andy Galpin
Not indicating at all you take a highly endurance-trained 25-year-old, have them lift some weights, and now their VO2 max goes up. Right?

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Dr. Mike Roberts
It's not going to happen.

Dr. Andy Galpin
This is not what we're saying.

Dr. Mike Roberts
Right.

Dr. Andy Galpin
But for those people, I think it's a great start. Okay, man. Well, this has been just remarkable. You're my absolute go-to source with muscle biology stuff. Anything I've ever put out, for the most part, is, I would say, 90% a quote of your work and your lab's work and-

Dr. Mike Roberts
Oh-

Dr. Andy Galpin
... all your folks

Dr. Mike Roberts
... making me blush. That means a lot. It really does, buddy. Thank you.

Dr. Andy Galpin
It's been great. So I learned a ton today.

Dr. Mike Roberts
And hey, look, I just want to give you thanks. I appreciate all the support over the years. You have been so generous, and every time we go to conferences, you give our work shout-outs, and my students are like, "You know Andy?" I'm like, "Yeah, I know Andy." They think I'm a rock star for knowing you, man.

Dr. Andy Galpin
There you go, man.

Dr. Mike Roberts
So I appreciate you, man.

Dr. Andy Galpin
Yeah, man. Appreciate you coming out here. I know it's a long trip, and taking the time out from the fam and the lab and all that, and yeah, this has been great.

Dr. Mike Roberts
Thanks.

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Dr. Andy Galpin

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