KESSLER FOUNDATION Podcast Transcript

Changing lives through regenerative rehabilitation research:
The Derfner-Lieberman at Kessler Foundation - Ep.28

Listen to the podcast here.

JOAN BANKS-SMITH: 00:07

[music] Welcome to a special edition of Fast Takes. In this episode, we discussed how lives are changed through regenerative rehabilitation research in our Derfner-Lieberman Laboratory. I'm Joan Banks-Smith, editor and producer of this podcast. Our host is CarolAnn Murphy. She's a senior writer at the foundation. For this roundtable, CarolAnn spoke with Drs. Trevor Dyson-Hudson, Gerard Malanga, and Nathan Hogaboom from the Derfner-Lieberman Laboratory. We'll explore the new interdisciplinary field of regenerative rehabilitation and the advances being made at Kessler Foundation in applying new approaches to the treatment of disabling musculoskeletal conditions in military and civilian populations.

CAROLANN MURPHY: 00:53

Welcome to our team of experts from the Derfner-Lieberman Laboratory for Regenerative Rehabilitation Research. This new laboratory at Kessler Foundation is in the forefront of a new interdisciplinary field that promises to revolutionize treatments for people with disabling injuries. Dr. Malanga, describe for our listeners how this field has evolved.

TREVOR DYSON-HUDSON: 01:17

It sort of evolved from two different fields kind of merging together, if you will. So for the past 10 to 15 years, this area of regenerative, quote-unquote, "treatments," or some people call it orthobiologics, has arisen first with the use of something called platelet-rich plasma, where blood is spun down to get to the platelet level. And on those platelets are a variety of growth factors that can facilitate tissue healing. And it has been found to be extraordinarily helpful for tendon problems and also for osteoarthritis. Over time, then procedures that involve various types of cells, cellular procedures, either bone marrow or adipose, that are commonly referred to as stem cell therapies has also occurred and has been applied to the, quote-unquote, "able-bodied population," so patients that have or people that have tendon tendinitis, tendon tears, whether it's the tennis elbow, the rotator cuff, and people that have osteoarthritis.

MURPHY: 02:17

To start your investigation, what types of patients did you choose to focus on?

DYSON-HUDSON: 02:22

Trevor and I explored this process in the spinal cord injury population several years ago, applying PRP to spinal cord injured patients that suffered from shoulder pain. Now, it is well recognized that, on top of having neurologic issues, the spinal cord population, because of their use of their upper extremities, develop significant musculoskeletal problems ranging from rotator cuff problems, elbow problems, carpal tunnel syndrome, and other issues. And the disabled population in general, whether it's spinal cord injury or head injury or post-CVA or stroke population, will also develop various things involving both the upper and lower extremities. And so in that initial study, we looked at PRP and see how well it did in that population because the traditional treatments are sometimes not very helpful, sometimes contraindicated, and sometimes really aren't reasonable, such as surgical procedures because they would result in immobilization and a lack of use of a limb that are vital for daily activities.

DYSON-HUDSON: 03:28 So in that initial study, the PRP proved to be very beneficial but kind of wore out after about six months. So we were looking for other methods of enhancing-- particularly, rotator cuff shoulder problem can be as high as 70% of the spinal cord injured population. Now we've been applying a procedure where we extract adipose tissue or fat from the lower abdomen or upper gluteal area using a device called Lipogems and taking the raw fat, cleaning it, breaking it down to smaller particles or micro-fragmenting it, and then under ultrasound guidance, injecting it into the areas of tissue pathology, whether it's the rotator cuff tendons, the biceps tendon, or the joint. And our initial study has demonstrated remarkable benefits both clinically and in terms of statistical benefit in probably over 75% of the pilot study. And now we're moving forward with a randomized control study.

MURPHY: 04:29 Thank you, Dr. Malanga, for this background on regenerative rehabilitation research and your initial work on overuse injuries of the shoulder in the population with spinal cord injury. Furthering this promising line of research depends on funding. Dr. Dyson-Hudson, how have you obtained the support needed for your initial and ongoing studies?

DYSON-HUDSON: 04:50 Gerry had a lot of the different projects over the years. As he said, it really started with the platelet-rich plasma. And that was funded through a pilot program through Kessler Foundation and Dr. DeLuca. We were kind of looking for the next step, and I was thinking, "Well, let's do a multicenter study with PRP." That's when he was saying, "You know what? I'm seeing a lot of great results with the micro-fragmented adipose tissue." So in essence, we were kind of starting over again because there really wasn't much in the literature about this, especially in spinal cord injury people with shoulder pain. And that's when Michele Pignatello approached us about the Derfner Foundation. We were able to get funding through them, and they really kind of helped us take it to the next level. They provided the initial funding for our first pilot project, a micro-fragmented adipose tissue, and then they subsequently started providing funding to assist with training. Because of all of this, we have been able to continue growing and start to establish ourselves. I mean, Gerry was already a leader in the field, I mean, in his own right, but it was an opportunity now for Kessler Foundation and our background of postdoctoral training and research training to start to get involved and start to develop Postdoctoral Fellowship Program here.

MURPHY: 06:23 The establishment of the Derfner-Lieberman Laboratory is clearly a really important step not just for Kessler Foundation but for the field as a whole. Dr. Dyson-Hudson, with a pilot study in wheelchair users with spinal cord injury, you found remarkable improvements in shoulder pain and function after the injection of micro-fragmented adipose tissue. How were you able to leverage those findings to expand this line of research at the laboratory?

DYSON-HUDSON: 06:53 With some pilot research at least showing that we could do this safely in people with spinal cord injury, it showed that we could take the next step. And so that provided us with some pilot data that we then went to the New Jersey Commission for Spinal Cord Research to fund the next level. Because our first study, everybody got the micro-fragmented adipose tissue. There was no comparative group. So we don't know if

people's shoulder pain just improved with time, which can sometimes happen, or if that, in fact, as Gerry pointed out-- how would it compare? How was its longevity in terms of treatment effect when compared with another group that received the treatment? Would it last longer than something else? And so with this pilot data, we were able to secure funding from, as I said, New Jersey Commission for Spinal Cord Injury Research. And that's where we are now with the micro-fragmented adipose tissue for rotator cuff disease and manual wheelchair users with spinal cord injury.

MURPHY: 08:08 So an important aspect that you mentioned is the postdoctoral training at Kessler Foundation. That's really where the potential for advancing the field comes from is training a new generation of scientists in these new technologies and techniques. Trevor, could you speak about the postdoctoral fellowship and regenerative rehabilitation research that was established at the foundation?

DYSON-HUDSON: 08:32 Thanks to funding from Derfner Foundation, it allowed us to bring a postdoc, somebody young who can help us build this field, kind of next generation. And so it allowed us to bring Nathan Hogaboom, who joined us a number of years ago. And he was able to start to, one, take over some of these projects as well as work more closely with Gerry to start to work on potential other research projects. So Gerry was doing a number of things clinically, but he really wanted to develop research evidence to support the type of clinical treatments that he's providing. And so Nathan kind of provided that avenue, somebody who can work closely with him to conduct research studies. And then through this process, Nathan would learn himself and allow us to kind of continue and expand our program.

MURPHY: 09:38 The Derfner Foundation Fellowship was established to bridge clinical care and rehabilitation research, enabling the team at the Derfner-Lieberman Laboratory to define research questions and develop regenerative strategies to answer those questions. Dr. Hogaboom, as the inaugural Derfner Foundation fellow, please share your experience with the fellowship and your subsequent appointment as co-director of the Derfner-Lieberman Laboratory.

NATHAN HOGABOOM: 10:05 When I first started, I really had not heard of regenerative rehab, even though my former advisor at the University of Pittsburgh, Mike Boninger, was the head of the Regenerative Rehab Institute with NIH. Upon arriving, I was able to be exposed to a brand new field that is not only brand new to me but, really, brand new to research and to clinical practice. And it really allowed me to learn a lot about the field, learn about what's being done both clinically and in research, and allowed me to think of possibilities for where do we want the research to go, where do we want clinical practice to go, identifying the gaps in clinical practice and kind of where the evidence is lacking so that we can, essentially, generate that evidence. And so the fellowship, it offered me the opportunity to enter into this field, fairly unique crossroads where a lot of the research is being done in animals or kind of more basic science. And here we are, really trying to expand the clinical translational aspect. So I was able to kind of merge my doctoral training, which was more in measurements and kind of quantitative approaches to understanding responses to different interventions or stimuli in human subjects. And I was able to apply that to what we're doing here. And

so the goal, really, is to use quantitative methods and qualitative methods to assess responses to these treatments in order to build a foundation of evidence that would advance the field.

MURPHY: 11:57 Dr. Dyson-Hudson, would you care to comment?

DYSON-HUDSON: 11:59 Nathan mentioned the Alliance for Regenerative Rehabilitation Research, which is at the University of Pittsburgh, headed by Mike Boninger as well as some other investigators across the country. And it was almost a perfect storm because Nathan joined us as a postdoctoral fellow in regenerative rehabilitation. We didn't give it that term, I think, at the time. We were just calling it regenerative medicine. However, his involvement with us made us more aware of these other things that were out there, and they were very interested in supporting the field of regenerative rehabilitation at a number of different-- one, they host an annual meeting, which is an opportunity for people to get together and discuss both basic science and clinical research and to just advance the field of regenerative rehabilitation, and they also provide a lot of travel scholarships. And so I just think Nathan's joining our organization and their desire to help spread and educate the field about regenerative rehabilitation really happened at a perfect time.

MURPHY: 13:23 To complement the research fellowship, there is a clinical fellowship. Dr. Malanga, you host the clinical fellowship in regenerative orthopedics and musculoskeletal medicine. Could you tell us about the role of that fellow in the research being done at the Derfner-Lieberman Laboratory?

DYSON-HUDSON: 13:40 In addition to the generosity of initiating a postdoc PhD person to facilitate research, the Derfner Foundation has also facilitated me to have a clinical fellow. So this is a clinical fellow who spends a year with me learning the nuances of the evaluation and treatment of patients suffering from a variety of musculoskeletal injuries, and the proper application of these various regenerative procedures, how to assess and how to understand the basic science, and then how to perform these procedures, and also to facilitate post-procedural rehabilitation. So we now have our second fellow, and he's been remarkable. He will be going down to the [Fast DC?] area, continuing this type of activity in the future. And we have a new fellow just starting last week.

MURPHY: 14:37 Thank you, Dr. Malanga. Are the fellows applying any new technologies to document the findings of this new research?

DYSON-HUDSON: 14:45 One of the funding sources facilitated the purchasing of equipment. One of the things that we've purchased is this ultrasound device that can measure the elasticity of tendons, something called elastography, which is in its infancy, in terms of trying to figure out how to apply it. But we now are looking at documenting improvement in the tendon integrity of the treatments that we're using by using elastography as a method of documenting changes within this one study of rotator cuff, and we've also studied Achilles' tendon, to see the value of using elastography. So again, that equipment has been invaluable for us to continue to facilitate research in this area. That is really important for researchers around the world, quite frankly, because elastography is a little bit tricky to apply. In addition to that, we have a serial MRI

evaluation of our rotator cuff patients, seeing what happens every several months, of that tendon to demonstrate objectively changes in the tendon. And Nathan has developed a quantification technique to quantify objectively improvements and changes in the tendon.

HOGABOOM: 16:08 And in our case, we're using these two noninvasive imaging methods to measure responses to the interventions. And so the goal of kind of this avenue of research is we want to assess clinical importance, so looking at how does the subject or the patient feel after being treated with these different modalities. But also, we want to look at what's occurring on the tissue level. I guess one of the premises is that you're using these techniques to regenerate tissue, and, at least in humans, that has not really been proven. And so the way you would prove that, essentially, noninvasively is using imaging methods. So if we see that people have clinical improvement, they're reporting less pain and better function, and we are also seeing changes at the tissue level showing healing, we have just a better understanding of what's going on behind the scenes after these different treatments. We've recently purchased an ultralow freezer, a minus-80-degree freezer. And the future of that is to potentially establish a biorepository, so all these treatments that we're doing, collect blood samples, tissue samples to examine what's happening on the molecular or cellular level as opposed to the tissue level. And so the whole goal of all these approaches to this is to generate a very holistic understanding of what is happening to these tissues after you treat them so that we can figure out are we actually regenerating tissue or what exactly are we seeing.

MURPHY: 17:54 The Alliance for Regenerative Rehabilitation Research and Training does incredible work and encourages the dissemination of all this new knowledge that's being gained. There were a number of rising stars featured at their 2020 conference, and Dr. Hogaboom was one of them. Dr. Hogaboom, tell us about the award-winning research that you presented at that conference.

HOGABOOM: 18:16 I presented on the work that I did as postdoc and some of the kind of foundational work. We did the pilot studies, one of which Trevor mentioned was the micro-fragmented adipose tissue for shoulder pain in wheelchair users as well as the-- we used micro-fragmented adipose tissue, also called MFAT, and did a small pilot study through NJRI and Dr. Malanga's clinic, testing MFAT as a treatment for meniscus tears. And the results were similar to the shoulder study, where most people had positive findings. Both of these projects, the shoulder study and meniscus study, we leveraged the results from these pilot studies, and we were able to receive funding for larger clinical trials. And so my presentation was on both the results of the pilot studies as well as transitioning from a pilot to an actual randomized controlled trial.

MURPHY: 19:15 The scope of this research is expanding at Kessler Foundation. Dr. Dyson-Hudson, can you expand on the different patient populations that you're looking at and some of the other types of musculoskeletal conditions that you're targeting?

DYSON-HUDSON: 19:28 We have several ongoing studies happening here at Kessler Foundation and New Jersey Regenerative Institute, some that have been mentioned. But the two primary ones are the micro-fragmented adipose tissue for rotator cuff disease in wheelchair-

using individuals with spinal cord injury. And then the other is the micro-fragmented adipose tissue for the treatment of meniscal tears in active-duty personnel. The first one, as was mentioned, so the one for shoulder pain in people with spinal cord injury, that's funded through the New Jersey Commission for Spinal Cord Research. And then the one for the treatment of meniscal tears is funded through the Department of Defense. Nathan and Gerry have been working very hard with our collaborators. The one that's for meniscal tears in active-duty military personnel is part one of a multitude of projects that is through Uniformed Services University and MIRROR, which is an acronym standing for Musculoskeletal Injury Rehabilitation Research for Operational Readiness. And so this was a large funded project that would then support other projects. And so one of the projects that was supported by that was the mentioned micro-fragmented-adipose-tissue one for the meniscal tears. But it has gone on to also fund two other studies that Nathan is leading along with Gerry, that Nathan could speak better to.

MURPHY: 21:09 Dr. Hogaboom, please tell us the details of these projects that focus on chronic musculoskeletal conditions in military populations.

HOGABOOM: 21:17 We have two different additional projects, both in active-duty military populations, looking at the different injuries. So the one we have is for neck injuries, which are very common in the military, in different segments of the military and different populations. And so a collaborator of ours developed a particular device that is potentially beneficial in reducing neck pain caused by forward head posture. And so we received a funding on the order of 200 or so thousand dollars to essentially do a small-scale clinical trial testing this device. We're collecting self-report measures such as asking people how their neck pain is as well as looking at more quantitative objective measures of X-rays and measuring the angle of the neck curvature. And so that's a two-year study that began about a year ago, and we're starting to ramp up testing right now, [currently?].

HOGABOOM: 22:24 The second study is more based on the basic science spectrum as opposed to the others that we have been doing. We are looking at what's called a hemarthrosis of the knee, which is essentially a spilling or an accumulation of fluid after an acute knee injury. And so we're looking at that particular fluid. We're going to be analyzing it for various inflammatory cytokines as well as this cellular content to look at what exactly is within those hemarthroses. And so we're partnering with investigators up at West Point, at the United States Military Academy to essentially recruit 10 people, active-duty military members who injured their knees and have an hemarthrosis, and analyze those samples. And ultimately, what we'd like to do is see if there's a way to essentially harness the body's own regenerative and healing capacity within those hemarthroses to essentially provide a treatment for knee injuries.

MURPHY: 23:39 Thank you, Dr. Hogaboom. I think it's important to emphasize that the work being done at the Derfner-Lieberman Laboratory focuses on minimally invasive types of interventions that may avoid the need for more aggressive interventions. Would you agree, Dr. Dyson-Hudson?

DYSON-HUDSON: 23:56 Yes, that is correct, at least in the spinal cord injury population. People who have a shoulder overuse injury, who have tried conventional treatments like physical therapy, medications and still are having shoulder pain, usually in these individuals, the next step is to do surgery. At least that's kind of what conventional wisdom says, that if physical therapy fails, then you may need surgery if you want to eliminate the pain. Unfortunately, for people with spinal cord injury who use wheelchairs, their arms are essentially their lower limbs. I mean, they rely on their upper limbs for all of their various activities of daily living, whether it be wheelchair propulsion, reaching, transferring, any of those things. And so usually, what would happen is after shoulder surgery, people are asked to rest their upper limbs. For a lot of people with spinal cord injury, that's not practical or very difficult to do.

DYSON-HUDSON: 25:06 The other challenge is, even if they do successfully rest their upper limb, will they be able to get to the level of activity they had prior to the surgery without somehow risking damaging the repair that was done by the surgeon? Really, what we're trying to do is identify alternate treatments that people can pursue before they go to that next step of surgery, things like-- when we first did the platelet-rich plasma study, that was a promising approach. We're looking at micro-fragmented adipose tissue now, and we're finding a lot of great results with that. So we're starting to explore some of these different kind of minimally invasive treatments as alternatives if more traditional methods fail and before that person goes to the next level of surgery.

MURPHY: 26:05 Dr. Malanga, would you like to add to Dr. Dyson-Hudson's comments?

DYSON-HUDSON: 26:09 Certainly, there are a lot of surgical procedures that are performed in the able-bodied population, and some of them have been called into question, number one, especially when compared to nonsurgical treatments. But patients are suffering from a variety of things, ranging from meniscal tears, rotator cuff tears, etc. And so this area of regenerative, quote-unquote, "treatments" has arisen. And while an able-bodied person might use the shoulder and perhaps they're involved in a sport activity such as baseball or volleyball that involves a lot of use of the shoulder, none of those folks put the same amount of load on the shoulder as somebody that's transferring or doing activities that is in a wheelchair situation, on top of the fact that, while rotator cuff pathology is common in the average wheelchair user, the sport wheelchair user has even higher incidence. So you have this process that gradually causes that person to become less active.

MURPHY: 27:15 Can regenerative approaches help overcome the challenges of treating shoulder injuries in wheelchair users?

DYSON-HUDSON: 27:22 And the surgical treatments, number one, have been poorly studied in the spinal cord injured population and, number two, are just not reasonable in terms of the normal spinal cord injured patient. So having success using these treatments where-- and there's this theoretical basis for using these treatments both on basic science, on an animal model, and some case series. So we need to demonstrate efficacy. But if these things can be effective in this highly demanding population, then the translation or transition to using these in able-bodied population becomes relatively a low bar. And so far, these things have been demonstrated to be extraordinarily safe with a level of

efficacy that's really becoming more and more visible, but we need to prove it using good science. And so just because it's less invasive or minimally invasive is okay, but it also has to be safe and effective.

MURPHY: 28:30 Given your funding sources, there's evidently interest in applying these approaches in the active-duty military population. Dr. Malanga, would you care to comment?

DYSON-HUDSON: 28:40 Yes. Well, the active-duty military population, again, is a population that is very demanding on a variety of their musculoskeletal areas, the knees, the shoulders, a lot of areas. So anything that you can do that, number one, minimizes the amount of surgical treatment and the downtime. So this concept exists in the military of readiness or preparedness of our military personnel. If they have injuries that knocked them out of participation, if you will, that's very costly and impairs our readiness in terms of a military operation. So again, having success in that area also allows for a very simple translation to the rest of the population. Because if we can have success in that military group, boy, we're serving our country, we're serving our men and women that are willing to serve us, and we can use that information for everyday people doing everyday activities.

MURPHY: 29:47 Does the panel have any additional comments? Dr. Malanga?

DYSON-HUDSON: 29:51 I just want to add one thing regarding the military study that we're doing with the West Point Group. So Nathan outlined some of the things regarding that study regarding blood in a joint or hemarthrosis. But the main crux of the problem is that after a sport injury, the risk of developing arthritis in that knee is really profound over only a 10-year time frame. So if you take a 16- or 18- year-old and they have a ACL tear, a patella dislocation, or some sort of knee trauma, they're at risk for developing arthritis very high at a very early age. We know that having blood in a joint is not a very good thing. So we've developed a process or a program called PLAY, the Prevention of Long-term Arthritis after Youth Injury. And this initial study is to look at what are the components that are in that bloody or hemarthrosis effusion and seeing if there's any factors that we can then use to facilitate a healing or improvement of the inflammation and the joint breakdown so that these young military cadets, as well as, [using?] again, our youth can have a reduced risk of developing arthritis in the future. We are just about to initiate it.

DYSON-HUDSON: 31:14 So all these studies require a lot of due diligence, and I am so grateful and thankful to Jay Lieberman and the Derfner Foundation for facilitating what we're trying to do. We were so fortunate to have somebody like Nathan Hogaboom because you can find somebody, but if you have somebody that's special, is a deep thinker, can really help facilitate projects, then so many of these ideas then become realities and become true ongoing projects. There would be no way that I'd be able to do any of these projects without the facilitation of people like Trevor and Nathan and the rest of the Kessler Foundation staff and without the funding through the Derfner-Lieberman Laboratory, Derfner Fund. So that study now is finally at a phase where we've got all our ducks in line. Everybody's ready to go. We know what we're going to do, and we're going to start recruiting this fall. That will be easy to recruit because it's only an initial pilot of 10 subjects.

MURPHY: 32:17 Thank you to Doctors Malanga, Dyson-Hudson, and Hogaboom for today's engaging discussion. We look forward to following the advances of the Derfner-Lieberman Laboratory for Regenerative Rehabilitation Research.

DYSON-HUDSON: 32:29 I want to thank you for putting this together. And again, want to thank Jay Lieberman and the Derfner Foundation for the support of what we're trying to do. Want to thank Roger DeRose and his leadership in this area and his passion to facilitate what we're doing. And want to express my gratitude and thanks to Trevor and Nathan for their ongoing support and input and just really facilitating having these things move forward. The nicest part is just having people that have their lives improved by what we're trying to do. And if we can facilitate this to be something that's done across the country and maybe across the world, that would be really great.

DYSON-HUDSON: 33:12 This really would not have been possible without Gerry's leadership and guidance. I've known him since I first started here in 1997. He was then director of the Sports Medicine Program here and the Sports Medicine Fellowship Program. And one of the things that always impressed me about Gerry was just his desire for evidence and science and understanding why we do the things we do and really stress that when teaching and, also, just a great teacher. And so I think it's just been a relationship that has grown over the years. I think it really all started back in '97 or early years, and he's been supportive ever since. So thanks, Gerry, for all your support.

BANKS-SMITH: 34:08 [music] To learn more about the roundtable panel, the Postdoctoral Fellowship Program at Kessler Foundation, and the New Jersey Regenerative Institute, links are in the program notes as well as additional resource links. Tuned into our podcast series lately? Join our listeners in 90 countries who enjoy learning about the work of Kessler Foundation. Follow us on Facebook, Twitter, and Instagram. Listen to us on Apple Podcasts, Spotify, SoundCloud, or wherever you get your podcasts. This podcast was recorded on Thursday, August 18th, 2021, remotely and was edited and produced by me, Joan Banks-Smith, Creative Producer for Kessler Foundation. [music]