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**DONALD YEALY:** This next story explores the promising field of regenerative rehabilitation. This science is still in its infancy, but it's asking vital questions about new ways to stimulate tissue regeneration. The answers may guide the development of tools and technology that provide hope for patients with previously untreatable injuries and disease.

**FABRISIA AMBROSIO:** So how have the constructs been looking?

**MALE SPEAKER:** Pretty good.

**FABRISIA AMBROSIO:** Are you getting good contraction?

**MALE SPEAKER:** I believe so, yeah.

**FEMALE SPEAKER:** At Dr. Fabrisia Ambrosio's lab, the focus is on skeletal muscle damaged by disease, trauma, and aging, and on finding ways to harness and accelerate the body's innate healing process.

**FABRISIA AMBROSIO:** So these are young muscles?

**MALE SPEAKER:** Yes.

**FABRISIA AMBROSIO:** And uninjured?

**MALE SPEAKER:** Yes.

**FEMALE SPEAKER:** This multidisciplinary team believes exciting discoveries sit at the intersection of regenerative medicine and rehabilitation science.

**FABRISIA AMBROSIO:** For a long time, regenerative medicine existed. Of course, rehabilitation existed. But the two fields really just didn't have a means to interact. So they were progressing in parallel.

**FEMALE SPEAKER:** But with the increase in the translation of stem cell transplantation therapeutics into the clinic, the two fields finally have the chance to connect. It's a discipline known as regenerative rehabilitation.

**FABRISIA AMBROSIO:** It was a logical partnership and a logical synergy. When an injury is too severe or when the extent of disease is too great, what we know is that rehabilitation alone is not sufficient, because there's simply not enough tissue remaining and not enough stem cells at that injury or disease site to actually promote sufficient repair, such that we can get full recovery.

**FEMALE SPEAKER:** By combining both disciplines, new and regenerated tissue is formed at the implantation site. And then, rehabilitation strategies accelerate tissue healing. The outcome can maximize new functional engineered tissue. Dr. Ambrosio's research focuses on severe soft tissue injuries involving volumetric muscle loss. In those cases, the team is investigating ways to bridge the tissue gap by promoting electric field generation and through the application of mechanical stimuli.

**FABRISIA AMBROSIO:** We know that stem cells are exquisitely mechanosensitive. So essentially, with regenerative rehabilitation, we're trying to tap into some of that mechanosensitivity of our stem cells, such that we can dictate how they behave.

**FEMALE SPEAKER:** They are developing and validating a novel smart biomaterial. It's an electroactive scaffold for skeletal muscle repair and regeneration.

**FABRISIA AMBROSIO:** We have been generating muscle constructs in the laboratory, small muscle contracts that are essentially comprised of a hydrogel polymer. And within this hydrogel, then, we are embedding boron nanotubes, which essentially are piezoelectric material.

**FEMALE SPEAKER:** Piezoelectric material can generate an electric charge in response to mechanical stimulation. The field of rehabilitation has long recognized the importance of electric fields for healing. But the use of piezoelectricity is a novel approach for skeletal muscle.

**FABRISIA AMBROSIO:** Our idea is if we can implant a scaffold that has this piezoelectric property, with mechanical stimulation, then, our hope is that we can generate an electrical field and promote stem cell regeneration and migration at that injury site.

**FEMALE SPEAKER:** The research is comprehensive in terms of evaluating how well the scaffold is working, including conducting a number of in vivo studies in mouse models. The mechanical stimulus used here is ultrasound. The mouse is anesthetized for a short time to ensure it does not move during this painless treatment.

**FABRISIA AMBROSIO:** We've chosen ultrasound, because we know in the case of a very severe muscle injury, it's just not clinically likely that we would be able to ask individuals to jump up and do a more aggressive exercise regime. So our idea is to start off with this low intensity ultrasound to stimulate the piezoelectric material scaffold. And then, as the individual progresses, and as we start to see the formation of some myofibers, then we would probably extend that to an exercise model, such as muscle loading, maybe even resistance exercise.

**FEMALE SPEAKER:** The exercise gives researchers an opportunity to look at the whole tissue functioning.

**FEMALE SPEAKER:** The mice, they love to run. So this is a way to really get that muscle contracting to stimulate the scaffold.

**FABRISIA AMBROSIO:** And so we're interested in looking at in the presence of this scaffold with the ultrasound and eventually exercise, how does the force look of these animals that have received the scaffold as compared to control counterparts?

**FEMALE SPEAKER:** The research is yielding exciting data.

**FEMALE SPEAKER:** And I'm currently extending these out to two and three months and seeing the same trend.

**FABRISIA AMBROSIO:** Probably most importantly, what we care about is the strength recovery after injury. That's the biggest thing that will affect the physical mobility of our patients.

**FEMALE SPEAKER:** In addition to strength and functionality, they're also measuring fatigue resistance.

**FABRISIA AMBROSIO:** If you think about something like walking or biking, for example, that ability to maintain force production over time is really important. So we have ways to look at that. Both in our animals and then even in our muscle constructs, we have ways to measure the strength of our muscle constructs under the different conditions and also fatigue resistance.

**FEMALE SPEAKER:** There is no prediction for when clinical trials in humans may begin.

**FABRISIA AMBROSIO:** At this point, I think we're really focused on trying to be very rigorous in our preclinical studies, so that we can make that transition to the clinic more seamless. The truth is that the standard of care for volumetric muscle loss is just insufficient, and it's inadequate. That's why tissue engineering approaches really represent an exciting area that we're hoping can really be a game changer.

**FEMALE SPEAKER:** Which brings us back to the discoveries that sit at the intersection of regenerative medicine and rehabilitation science.

**FABRISIA AMBROSIO:** To be honest, I would say that most people say that that makes sense. And we've had the experience of people coming to our symposium and being surprised, saying, wow, I've been doing regenerative rehab all along. I just didn't realize there was a community. I didn't realize that it was a formalized field. So I think it really is a logical partnership.

**FEMALE SPEAKER:** Here's some of what's new and notable in clinical at UPMC. Doctors William Welch and Taylor Abel at the Epilepsy Center at UPMC Children's Hospital have begun using responsive neurostimulation, or RNS, to treat children with epilepsy. RNS has been used to treat epilepsy in adults but is only now making its way into pediatric care. The neurostimulator device is implanted under the scalp to monitor brain waves and to prevent seizures when abnormal activity is detected. Until now, only a handful of RNS procedures have been performed in children worldwide.

The UPMC Heart and Vascular Institute and UPMC Magee-Womens Hospital are partnering to focus on postpartum care for women with hypertensive disorders of pregnancy. Doctors Malamo Countouris and Alisse Hauspurg created the UPMC Magee-Womens postpartum hypertension program. New mothers are followed by both a cardiologist and maternal fetal medicine specialist. Untreated postpartum hypertension can lead to heart attack, stroke, and heart failure even 10 to 15 years after delivery.

And finally, the UPMC Hillman Cancer Trials Finder is a mobile app that helps patients and physicians learn more about clinical trials happening throughout the Hillman network. Hillman currently offers more than 440 clinical trials. Users can filter trials by location and get a customized list of trials available in their area. UPMC Hillman Cancer Trials Finder is available to download both on Android and iOS platforms. And that's some of what's new and notable in clinical at UPMC.

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