

New insights on pelvic floor damage after vaginal birth, and new directions for treatment

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In the August 02, 2023 issue of *Science Translational Medicine*, University of California San Diego researchers lead a team that has

published new insights on pelvic floor muscle (PFM) dysfunction, which is one of the key risk factors for pelvic floor disorders, a set of morbid conditions that include pelvic organ prolapse and urinary and fecal incontinence, that impact close to a quarter of women in the U.S. and have a strong association with vaginal childbirth.

The work is part of a larger effort to advance understanding, treatment and prevention of [pelvic floor muscle](#) dysfunction in humans.

The big collaborative question the team is making progress on is the following: As bioengineers, clinicians, and basic scientists working together, can we move the needle when it comes to reducing damage to the female pelvic floor that occurs during vaginal childbirth?

In the short term, the UC San Diego team has just published new findings that advance this big challenge, though much work is still required.

Summary of the key findings

First, new tissue-level research demonstrates that for cis-women who have given [birth](#) vaginally and have symptoms of pelvic organ prolapse, their pelvic floor muscles show the damage signs of atrophy and fibrosis (which includes the excess buildup of collagen). This new direct evidence of both atrophy and fibrosis in the skeletal muscles of the pelvic floor of women with symptoms of pelvic organ prolapse is an important step toward developing strategies to either prevent damage or aid recovery after damage occurs.

This tissue-level research included samples from age-matched human cadavers as well as women undergoing surgery for [pelvic organ prolapse](#).

Next, the team showed that in a well-established rat model for vaginal

birth injury in humans, the pelvic floor muscles of the female rats sustained the same kinds of negative muscle transformations—atrophy and fibrosis—seen in the pelvic floor muscle biopsies of the women (referenced in point one) who have given birth and went on to develop pelvic floor prolapse.

This finding serves to validate that additional research using this rat model of birth injury will be relevant for understanding and potentially finding better ways to treat or even prevent pelvic floor dysfunction and the associated [pelvic floor disorders](#) in women.

Finally, the team showed that a tissue-specific cell-free pro-regenerative biomaterial, similar to the material invented at UC San Diego that is [currently in clinical trials](#) for helping to improve healing of heart tissue after [heart attack](#), could serve as a new approach for helping to prevent or heal pelvic floor muscles injured during childbirth. In particular, the UC San Diego team treated rats subjected to simulated birth injuries with an acellular injectable skeletal muscle extracellular matrix (ECM) hydrogel either at the time of or four weeks after simulated birth injury.

They found that the administration of the hydrogel reduced the negative impact of the simulated birth injury on the rat pelvic floor muscles. This new work highlights the need for further investigations of this promising biomaterial for the prevention of pelvic floor muscle dysfunction after birth injury.

"Understanding the natural pelvic floor muscle response after birth injury is crucial for developing and applying regenerative medicine approaches. Based on this, we first investigated the pelvic skeletal muscles' short- and long-term responses after birth injury using a rat preclinical model," said Pamela Duran, Ph.D., the first author on the paper who recently completed her Ph.D. in bioengineering at the University of California San Diego Jacobs School of Engineering. Duran

is currently a postdoctoral researcher at the University of Michigan.

"With these findings, we rationalized applying a cell-free biomaterial to prevent and treat the pathological changes of the pelvic floor muscle after simulated birth injury. The use of a low-cost and minimally invasive biomaterial is crucial for the clinical translation of this regenerative medicine approach to counteract the negative alterations of the pelvic floor muscles."

"Current clinical and preclinical strategies for treating damaged pelvic floor muscles have focused on late stage treatments that are suboptimal for patients and do not address the underlying causes of muscle damage. In this preclinical research, we have shown that injecting a hydrogel directly into muscle tissue of the pelvic floor offers a potential method for encouraging and accelerating the natural healing process. In particular, we see the possibility of muscle fiber restoration rather than the unhealthy buildup of collagen," said Karen L. Christman, a professor in the Shu Chien-Gen Lay Department of Bioengineering at the UC San Diego Jacobs School of Engineering.

Christman is also the Associate Dean for Faculty Affairs and Welfare at the UC San Diego Jacobs School of Engineering, where she holds the Pierre Galletti Endowed Chair for Bioengineering Innovation. Professor Christman is a cofounder, consultant, board member, and holds equity interest in Ventrix Bio Inc. and Kairos Technologies Inc.

These two companies [are working](#) to translate biomaterial technologies into the clinic for applications including efforts to encourage regeneration of heart tissue and improved heart functionality after a heart attack, and prevent adhesions after cardiothoracic surgery.

"Pelvic skeletal muscles' birth injury and subsequent degeneration is a key risk factor for pelvic floor disorders that negatively impact lives on

millions of women worldwide. Unfortunately, we know very little about tissue-level changes that take place in these important muscles as a result of maternal birth injury," said a corresponding author Marianna Alperin, M.D., M.S.

"The findings of our study are important because without understanding what goes wrong in [pelvic floor muscles](#), we can't develop effective strategies to treat these important components of the pelvic floor. As a result, currently available preventative or therapeutic strategies are extremely limited and do not include regenerative approaches."

"While cell-based therapies are promising in many areas of medicine, they are associated with many hurdles, including substantial costs. In contrast, the biomaterial tested in our study does not contain any cells and is therefore very safe and is low-cost. Investigating what goes wrong in the pelvic skeletal muscles and developing pragmatic approaches to overcome these negative changes is very important for improving women's health."

More information: Pamela Duran et al, Pro-regenerative extracellular matrix hydrogel mitigates pathological alterations of pelvic skeletal muscles after birth injury, *Science Translational Medicine* (2023). [DOI: 10.1126/scitranslmed.abj3138](https://doi.org/10.1126/scitranslmed.abj3138).
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