**Colorado researchers use horse sense to innovate joint therapies**

**By Electa Draper *The Denver Post*** POSTED:   04/08/2015 12:01:00 AM MDT



Brenda Simmons hugs her horse Little Brother at her ranch in Granby late last month. Simmons and Little Brother have had stem cell therapy on their legs, preventing debilitating issues for both. (*Andy Cross, The Denver Post*)

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| When Little Brother came up lame six years ago at the age of 8, Brenda Simmons took her horse from one veterinarian specialist to another to find a fix.Injections of the horse's stem cells into a lower leg joint and tendons relieved his pain and returned full function to a horse that had been unridable."He was better than ever, and he's still going strong," the 58-year-old Granby resident said. "I asked the vet, 'Can you do that for me?' "She couldn't, but a physician in Edwards, Dr. Scott Brandt, did treat her with stem cells.After crippling pain had sidelined her for years, she said, injection of her own stem cells and other living cell products, taken from her bone marrow and fat tissue, has restored the former runner and skier to a more active life over the past year. She had already had one knee-replacement surgery, but she now believes she can avoid a second one.http://extras.mnginteractive.com/live/media/site36/2015/0408/20150408__CD0405REPLACEMENTS-01~p1_200.jpg( | )"It's not mainstream. It's still in development," Brandt said of treatment that can cost $8,000 to $12,000 and isn't covered by insurance. "But it will happen in our lifetimes. This will delay or prevent many surgeries."Many orthopedic specialists remain skeptical of these treatments — unsure where proven advancements end and experimentation begins in doctors' offices using people's stem cells along with other biological components.Yet leading researchers say there is real potential, especially if the Food and Drug Administration eases restrictions on culturing adult stem cells in labs for reinjection.Even as these alternatives to surgical fixes for knees, backs, hips, shoulders and elbows are being developed, joint surgeries are booming as Americans resist being stiff and sore.Adult stem cells, with their remarkable capacity to develop into different cell types and to serve as internal repair shops, are among the most promising areas of treatment, along with gene therapies. Yet surgical techniques also are advancing and making it easier than ever to retool body parts.Surgeons are making smaller and smaller incisions in such delicate procedures as repairing herniated discs in spines, and joint-replacement patients are recovering more quickly with new parts that are lasting longer.New territoryClose to home, horses are leading humans into new territory, inspiring not only patients such as Simmons but researchers in regenerative therapies at Colorado State University in Fort Collins and the University of Colorado Hospital in Denver. They seek the next big remedies for human musculoskeletal disease through application of established equine medicine."Horses have similar problems to humans, especially in their joints," Good rich said. "Most things working for a horse joint will work for a human."Horses have even more in common with human athletes in terms of injuries, Goodrich said, and she works with a top knee surgeon at Vail's Steadman Philippon Research Institute and The Steadman Clinic, a designated national medical center for Olympians.Horse lovers and philanthropists John and Leslie Malone — "fascinated by the healing power of stem cells," CSU officials say — recently committed the largest cash gift in university history: $42.5 million. It's dedicated for a center to investigate regenerative therapies to help animals and people. The donation launched the CSU Institute for Biological Translational Therapies, for which additional fundraising is briskly proceeding."Through this gift, we are really going to expand our knowledge of stem cell therapies," said veterinarian Laurie Goodrich, associate professor in equine surgery and lameness at CSU's College of Veterinary Medicine.http://extras.mnginteractive.com/live/media/site36/2015/0408/20150408__CD0408HIPKNEEPOPULATION-01~p1_200.jpg( | )For horses, researchers derive stem cells from bone marrow usually taken from the sternum or iliac crest. They get a small amount of stem cells, perhaps 100,000.Then they grow them in the lab, attaining 20 million to 30 million cells.That's the part the FDA doesn't allow in human therapies. You can't manipulate or multiply stem cells for injection into a joint or ligament. You can only inject into patients what you have taken out of their own marrow or other tissues."You get a much better result injecting more stem cells," Goodrich said.Brandt said he boosts stem cell numbers by also using adipose, or fat tissue. But Goodrich and CU researchers say cells from bone marrow are preferred because they are better at suppressing inflammation and forming matrix.Sending signalsStem cells heal. They aren't so much incorporated into joints in the form of new cartilage, tendon, ligament or bone, Goodrich said, as they are signals for these tissues to release regenerative proteins and other molecules.Dr. Cecilia Pascual-Garrido, orthopedic surgeon at the University of Colorado Hospital, said she spends a lot of time in the lab trying to regenerate cartilage. She has performed cartilage cells transplantation and other surgical cartilage procedures."We are trying to regenerate a tissue that is hard to regenerate," she said of collaborators such as CSU's Goodrich."Horses are having excellent results with stem cells," Pascual-Garrido said. "The FDA is making it a lot harder to get more for humans and to advance the research."But the FDA is concerned that cells manufactured or multiplied outside the body could become ineffective or could develop unwanted characteristics, such as tumor production, so the agency is developing methods to predict how adult stem cells will behave in patients.As promising as stem cell therapy appears, Pascual-Garrido said, it has limited application for patients — those with less severe osteoarthritis."It will never work for advanced osteoarthritis," she said. "I think the future is in identifying these patients very early."There won't be a shortage.Joint disease, or osteoarthritis, is the degeneration of joint lining and cartilage and the underlying bone, which causes stiffness and pain. The Centers for Disease Control and Prevention estimates that osteoarthritis affects almost 14 percent of U.S. adults age 25 and older. And the estimate from the CDC that the disease bothers more than a third of adults 65 and older is "conservative."The 78 million Americans born between 1946 and 1964, the baby boomers, are aging and slowing, but not going gently into their rocking chairs. They want to remain as active as ever, Brandt said.By 2010, U.S. adults were undergoing 719,000 total knee replacements annually and 332,000 total hip replacements, according to the National Hospital Discharge Survey.But that is just a preview of the surgeries yet to come for joint replacements, cartilage and ligament repair, stress fractures and shoulders' torn rotator cuffs."We also see more elderly patients who are living longer, doing well otherwise and want to stay active into their mid-80 and 90s," said UCH spine surgeon Jens-Peter Witt. "We're doing more surgeries on them."Demand on the riseAnd demand is increasing for procedures by younger patients, in Generation X, who want them done earlier, according to Steven Kurtz, director of the Implant Research Center at Drexel University in Philadelphia.Kurtz and fellow researchers had forecast an increase in demand for hip replacement surgery of 174 percent and an increase of knee replacements of 673 percent through 2030. He found, however, that it has become evident that younger patients [will drive demand even higher](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2745453/).Dr. Douglas Dennis, a nationally ranked knee surgeon at Porter Adventist Hospital, said regenerative therapies for hard-to-grow cartilage help when there are repairs needed for small defects in cartilage."I don't think we're moving away from knee-replacement surgery," Dennis said. "Right now there is no good long-term data for injections of stem cells, platelet-rich plasma and other biologicals."Surgical techniques also have evolved. When Dennis started doing knee replacements 29 years ago, patients' hospital stays could run to 17 days. Now he sends about half his patients home the next day, which greatly lowers the risk of hospital-acquired infections.In joint-replacement surgery, bones are capped with metal alloys, Dennis said. But the disc-shaped polyethylene material implanted between the metals in knees has continually improved — staying supple longer — resisting oxidation and infection.New entry points into hip joints are used. The size of incisions has shrunk over decades from 16 inches to 4 inches.To repair herniated discs in spines, surgical incisions and instruments have downsized even more. If a surgeon doesn't have to implant relatively large items such as metal caps and plastic liners used in joint replacement, things can get really tiny.Endoscopic spine surgery — using small tubes with progressively better optics — has reduced incisions from more than 3 inches to about .20 inches, Witt said."We're trying to get there with less trauma," Witt said of surgery on herniated discs. "High-precision optics let us operate with smaller instruments, allow us to look at a particular nerve root, visualizing it live on a high-definition screen."The patient experiences a lot less post-operative pain, he said.Two days after his March 25 surgery for a herniated disc, 34-year-old Dean Hogsett of Lakewood was out and about."I'm impressed," Hogsett said. "I had trouble for two years. For the last three months, I was miserable. I had surgery. I walked out the same afternoon. The next day, the nerve pain was gone. I'm surprisingly well."But while the arc of the healing arts is toward minimally invasive surgeries, Witt said, it requires retraining more surgeons, and so far, the newer technologies aren't supported by either the insurance system or research funding."A lot of new development will come out of molecular biology and less from the procedural and surgical side," Witt said. "Preventing the breakdown of these tissues will replace repairing them."Electa Draper: 303-954-1276, edraper@denverpost.com or twitter.com/electadraperBrenda Simmons takes Little Brother for a ride near her home in Granby.Brenda Simmons takes Little Brother for a ride near her home in Granby. (*Andy Cross, The Denver Post*) |

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