



hours with coaches' hours: lifting weights, game-planning, preparing for practice, reviewing practice, visiting with the media, setting his team's tempo, then going home and diving into his man-cave to watch defenses until he fell asleep.

Once a loner in his study habits, Manning has in recent seasons tasked his backup to dissect defenses and, as he orders, "find something interesting." The backup, grateful for the opportunity, does what Peyton would do: He returns with pages of notes. Which gives Manning more to process, more to harness, more to try to control. Manning has turned the ultimate team game into something closer to golf: He doesn't compete against opponents as much as against his own limits. And, while he might be angry about his neck, and he might feel shortchanged by the lockout, he's not entering the twilight of his career in denial.

Unlike Brady, who says he wants to play until he's 40, Manning has never placed an arbitrary number on his career. It will end when his body no longer allows him to be great. His ego lies in his legacy, not in his longevity. His contract negotiations in July were proof. For once, he didn't sign a cap-buster. He insisted on a back-loaded, cap-friendly five-year, \$90 million contract, complete with a team opt-out for next year should Manning be unable to play.

Manning knows that if he's going to win a second Super Bowl—if he's going to silence critics who claim that only one represents potential unfulfilled—he can't do it alone anymore. Which is another reason why he'll probably remain sidelined unless the playoffs are in reach. He won't suit up at 70%, for a losing team, unable to make the plays that he once chided his teammates for not making. "He won't put himself in," Sorgi says. "He'll wait."

But will it be a different Peyton Manning who does eventually get back behind center? "I don't know," Archie Manning says. "This is a transition for Peyton. He's accepted it. He's going to do all he can do."

In other words, he's still Peyton. Injured or not, what makes Manning great is a reserve of ruthlessness, confidence and will that allows him to believe he can control the uncontrollable.

He will continue to believe it, until the end. **B**



SCIENCE

CHASING THE MIRACLE CURE

Peyton Manning won't be the last star to experiment with stem cells.

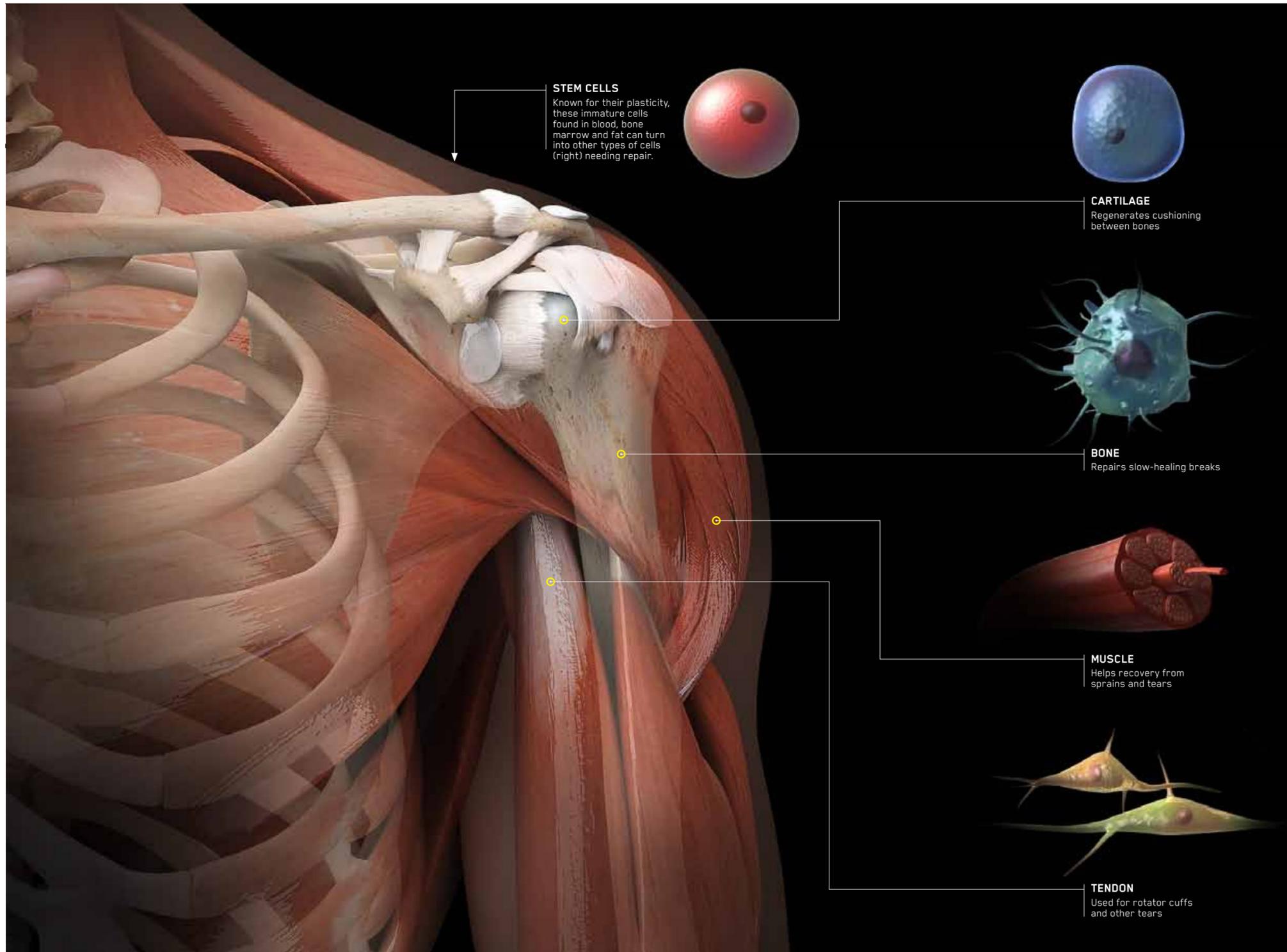
BY SHAUN ASSAEL

ILLUSTRATION BY VIKTOR KOEN



Jim Bradley understands the season-on-the-brink desperation that reportedly sent Peyton Manning and his ailing neck to Europe this summer, seeking the experimental promise of stem cells. For the past two decades as the Steelers orthopedist, Bradley has listened to injured athletes beg him to be creative in getting them back on the field. "In the last year, I've seen half a dozen guys go to South Korea, Japan, Germany, even Russia for stem cell procedures," says Bradley, a past president of the NFL Physician's Society. "And there's going to be plenty more."

In case you haven't logged long hours watching *House*, stem cells are immature cells with life-changing potential; scientists think they could possibly do everything from reverse the sinister effects of aging to fend off cancer and make hearts healthier. Doctors in athletic circles



→
Extracting marrow, as Purita does here for a stem cell treatment, is minimally invasive compared with traditional surgery.



are particularly optimistic about a specific line called mesenchymal stem cells, which they can extract in sizable numbers from fat and bone marrow. When properly cultivated and injected into an injured body part, they might be able to repair a banged-up jock's cartilage, bones, tendons and muscles dramatically faster than conventional surgical methods (see sidebar).

Clinics around the world report amazing results using these minimally invasive cellular procedures to repair torn ACLs. That's also part of the problem: The most exciting action is happening overseas.

Thanks to a mix of politics, bureaucratic foot-dragging and scientific caution, American doctors are prohibited from culturing stem cells, let alone culturing them into stages as advanced as their foreign counterparts. Hence Manning's trip abroad. Bradley, a former Penn State defensive end, doesn't mince words. "We're at least 10 years behind the rest of the world," he says.

The 57-year-old doctor should know. In January 2009, after Hines Ward left the AFC championship game with a torn MCL, Bradley administered a form of platelet-rich plasma (PRP) therapy, a strange and novel procedure back then. Placing a sample of Ward's blood in a centrifuge, Bradley isolated the plasma and platelets, which contain natural repair engines, then reinjected the serum into the receiver's injured knee. Ward returned to the field two weeks later for Super Bowl XLIII, a remarkable recovery he and Bradley credit to the procedure. Had the Steeler opted for rest and physical therapy instead, the two say Ward likely would have watched the big game from the sideline.

At the time, Bradley was hailed as a genius; weekend warriors everywhere started asking for the "Hines Ward treatment." But compared with the latest stem cell technologies, PRP looks about as revolutionary as leeches. Instead of relying on the relatively small number of stem cells that swim in blood, cellular scientists elsewhere in the world are extracting millions more out of bone and fat, then engineering them into injury-fighting miracle workers. In Europe, for example, healthy top-level soccer players are already having their stem cells harvested and grown into lines of bone, cartilage, muscle or tendon. "They're doing it so they'll have a ligament line ready if they get a tear during the season," Bradley says.

Much like the steroids scandal a decade ago, this stem cell gold rush is testing sports' ethical boundaries—but this time the issue is about aiding recovery instead of enhancing performance. Anti-doping authorities and federal regulators find themselves in uncharted territory, raising questions about whether our own blood can be considered a drug. In this new reality, the cutting edge is no longer just what jocks are putting into their bodies. It's about what they're putting back into their bodies.

Christopher Centeno of Regenerative Sciences has paid the price for being on the front lines of this culture war. Until last year, Centeno was doing a booming business culturing mesenchymal stem cells at his Broomfield, Colo., clinic. When NFL defensive end Jarvis Green visited the doctor in 2010 after two failed knee surgeries, the player faced the end of an eight-year career with New England. Shortly after receiving his stem cell treatment, Green was back in the NFL. "Before, I couldn't walk up the stairs," he told *The Mag*. "Three weeks later, I went to an NFL training camp and didn't miss a day."

Green's recovery gave him one more season, with Houston, before he retired. But he had one of the last seats on Centeno's cultured stem cell miracle train. In August 2010, the U.S. Food and Drug Administration brought the hammer down on Regenerative Sciences, filing a federal injunction to prevent Centeno from culturing. The FDA claims he was "adulterating" blood in a way that turned it into an unapproved new drug. Centeno, who still provides same-day stem cell procedures, has spent \$500,000 fighting the agency's controversial opinion and even more money moving his culturing operation to a new clinic offshore in the

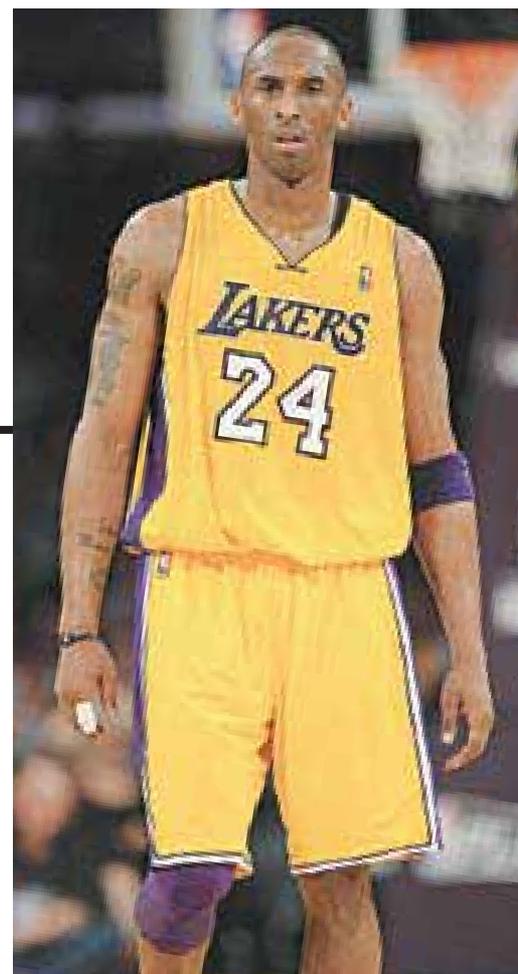
THE MAGIC WITHIN

Stem cells have the potential to help us heal from torn ACLs, sprains, broken bones and more. Under U.S. law, doctors can isolate these cells—usually from fat or bone marrow—for re-injection to an injured area but must do so in a single visit without manipulating or adulterating them. Culturing cells, the FDA argues, would turn them into new, unapproved drugs. Abroad, however, doctors culture them for weeks and increase cells more than 100 fold, using chemicals to create specific lines of bone, cartilage, tendon and muscle cells.—S.A.

THE KOBE CONNECTION

Peyton Manning isn't the only creaking athlete on a global quest for a pain-relieving, career-extending miracle.

The Mag has learned from a doctor with knowledge of the procedure that Lakers guard **Kobe Bryant** traveled to Düsseldorf, Germany, this past June to have his troubled right knee treated by Peter Wehling, a doctor at the forefront of blood-healing science. Wehling, who would neither confirm nor deny seeing Bryant, claims to cultivate and incubate blood cells to produce high levels of growth factors, which are then reinjected into the joint or spine. "I am the only one to have found a way to cure arthritis," the former physician for Pope John Paul II told *The Mag*. According to another source, Bryant found Wehling through Tracy McGrady. The Pistons guard declined to comment, but his spokesperson confirmed that "he has great respect for Dr. Wehling and had a wonderful experience there." Bryant's agent did not respond to repeated inquiries about his trip. —S.A.



Cayman Islands. "The FDA has pushed this therapy out of the U.S.," he says.

A spokesperson for the FDA declined to comment, saying only that U.S. policy is to allow the injection of stem cells that are treated with "minimal manipulation," which federal regulations define as "processing that does not alter the relevant biological characteristics of cells or tissues."

Yankees starter Bartolo Colon was treated using stem cells in March 2010, when he was still unsigned and struggling to throw 80 mph after rotator cuff surgery. Orthopedist Joseph Purita, who runs the austere named Institute of Regenerative & Molecular Orthopaedics in Boca Raton, Fla., traveled to the Dominican Republic to perform the procedure, at Colon's request. There Purita harvested marrow from the then 37-year-old pitcher's pelvis and spun it in a high-speed centrifuge to procure a syringe full of thick, mesenchymal-rich serum. But instead of waiting weeks for those cells to multiply and grow as cultures, Purita stayed within FDA guidelines and injected Colon's cells directly into his right shoulder and elbow. The process took about an hour.

Skeptics say that minimally manipulated stem cells are a crapshoot because they're so unpredictable. Maybe they'll turn into ligaments or cartilage. Or maybe they won't. "There's very little evidence that bone marrow stem cells taken from one site and injected into another will do anything," says Theodore Friedmann, a University of California at San Diego geneticist who heads the World Anti-Doping Agency's gene doping panel and is charged with advising WADA on stem cell policy. "The most likely outcome is that if you put stem cells in places that are unfamiliar to them, like a knee or shoulder, most of them will just die."

Colon's impressive start this season—he compiled a 6-4 record with a 3.20 ERA before the All-Star break—caught MLB's attention, and league investigators asked for the records of his treatment, wondering whether something other

than stem cells deserved credit in his recovery. When two MLB representatives visited Purita in June, he acknowledged using small amounts of human growth hormone when performing the same procedure on his everyday patients in Florida. But he also said that he did not give the banned substance to the pitcher. "I don't make the rules, but I follow them," he says. "I'm not here to create a controversy."

MLB continues to look into the treatment, but the league's medical director, Gary Green, isn't exactly sure what to make of this new sports medicine frontier. "There's always a fine line between what's a performance-enhancing drug and a therapeutic one," he says. "It's what all the leagues have to struggle with."

Similarly, WADA, which was built to police substances that athletes put into their bodies, seems unsure what, if anything, should be done about these latest advancements. When the agency first started looking at what it terms blood-spinning therapies, it banned all of them. Then, in 2010, after studies failed to show that athletes were getting the kind of gains from PRP that come from steroids, WADA did an about-face and lifted all its restrictions.

Now the anti-doping cops are struggling with what they should do about stem cells. Friedmann favors WADA's doing nothing—at least at the moment—because of his skepticism about whether the treatments work. "I have no doubt that this science will become feasible," he says. "I just don't think it is now."

Yet the gold rush continues, with ambitious physicians using the rich, powerful and desperate as guinea pigs. Manning went to Europe hoping his neck would respond the same way as Green's knee and Colon's shoulder and elbow. It was a stretch. Stem cells have not been widely used to address nerve issues, as Manning is thought to have pursued, the way they have muscle, bone, tendons and cartilage. Few papers have been published on the procedure, and no one in the field knows of any credible clinical trials. "Safety is an issue," says John Gearhart, the director of

the University of Pennsylvania's Institute for Regenerative Medicine and one of the nation's foremost experts. "You can't predict what will happen when you put a stem cell in a place where you don't normally find it."

But technology is driven by Darwinism and by capitalism, evolving quickest where there's a financial interest. And there's even talk among stem cell experts about Chinese labs genetically engineering human stem cells from enzymes and nutrients. If that advance ever becomes a reality, it likely would make the plates and screws used in modern orthopedics look like medieval bone saws and hot irons.

That's one day. Stem cell treatments are still a work in progress, as evidenced by a certain Super Bowl MVP's turning to traditional orthopedic surgery when his medical Hail Mary fell short. Manning likely will miss the rest of the season, and his time on the bench is exactly what Bradley says will continue to push the quarterback and his peers to the corners of the world for any chance to extend their careers.

"When I got into this, I thought these treatments—not plates and screws—were the next big things in orthopedics," he says. "And I still do. This is just beginning. Guys like Peyton are part of the first wave." **E**