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STEM CELLS

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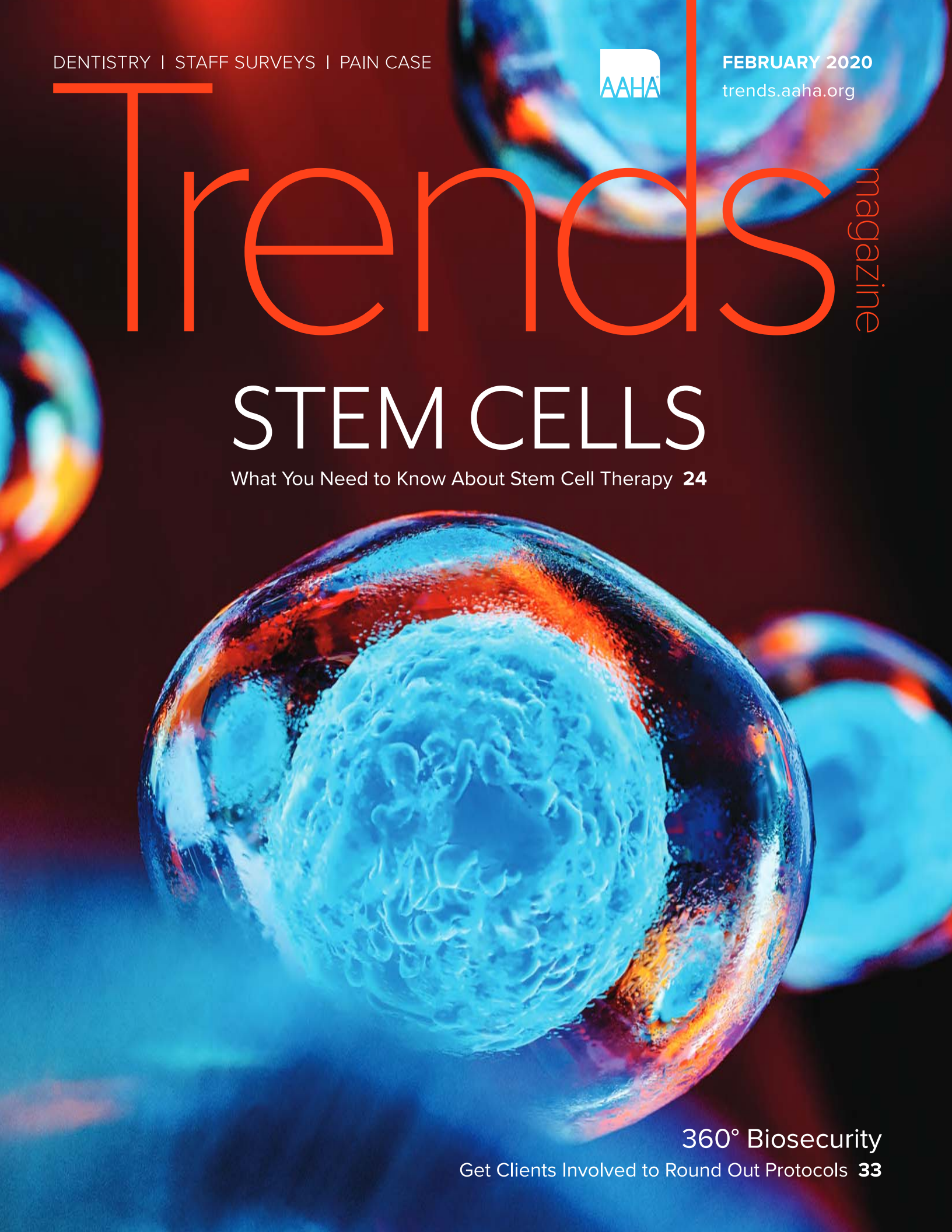

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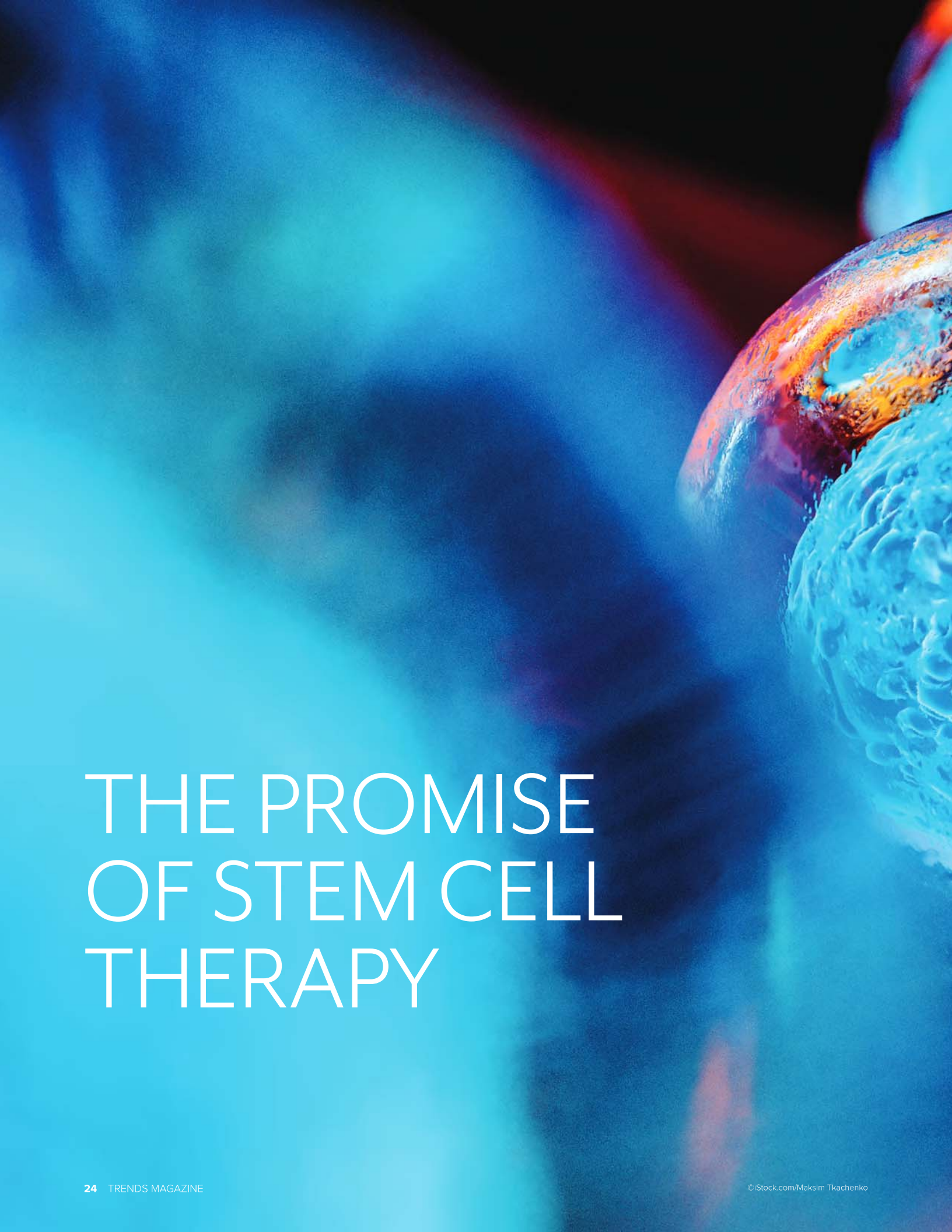

THE PROMISE OF STEM CELL THERAPY

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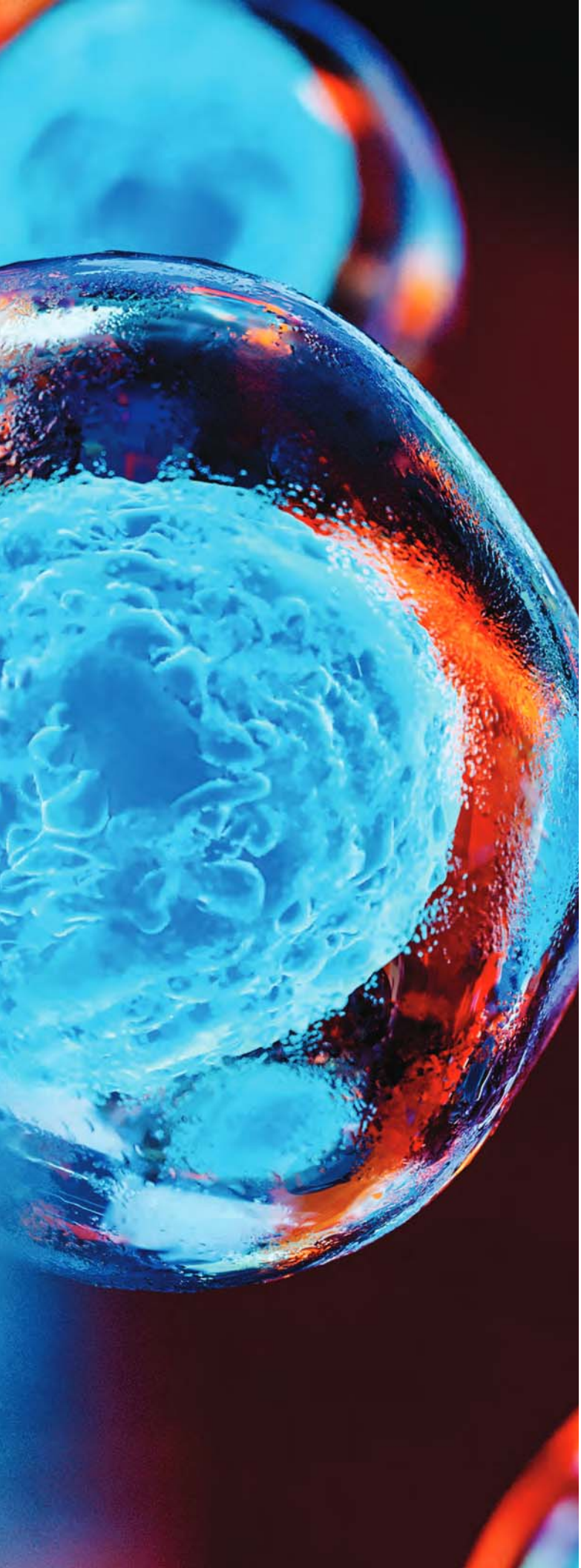

What We Know and Don't Know About These Exciting Cells

by Jen Reeder

WHEN LIZ LAGANA'S GOLDEN RETRIEVER WAS 11 YEARS OLD, he started having a "really hard time" with his osteoarthritis. Harley couldn't walk for very long, and stairs were a challenge. He'd been on pain medication for a long time, but it seemed to have stopped working.

"You don't want to put down an otherwise healthy dog just because he can't get around like he used to," she said. "But with an 85-pound dog, you can't just pick them up and carry them around, either."

So Lagana and her husband took Harley to AAHA-accredited Pharr Road Animal Hospital in Atlanta to see if stem cell therapy could help their dog.

It did.

"After the first treatment, it was amazing," she said. "His mobility was just so much better and he didn't look like he was in pain. It's a quality-of-life issue and I highly recommend it."

Success stories like Harley's, who lived to be 14½, are helping increase client interest in stem cell therapy for pets, particularly for osteoarthritis. The procedure is fairly simple: the veterinary team harvests mesenchymal stem cells (MSCs) from fat (adipose) tissue on the dog's or cat's belly while the pet is under anesthesia. The cells are typically processed by a lab, such as VetStem or MediVet Biologics, and a few days later, the hospital injects the MSCs into the pet's painful areas. Sometimes, platelet-rich plasma is also injected to increase success rates.

Results May Vary

Steve Winokur, DVM, CVA, is the owner of Pharr Road Animal Hospital, which has offered stem cell therapy since 2015 and treated Harley. He said seeing Harley's posture improve within a week of stem cell therapy was "one of those thunderclap experiences." He hoped all patients would respond as well.

"Unfortunately, not all patients have quite as good a response as you would hope for," he said. "Many do and some don't, as with any treatment modality."

Pet insurance companies such as Trupanion and Nationwide cover stem cell treatments when prescribed by a veterinarian. However, only a small percentage of Americans have pet insurance, and Winokur said clients often balk at the price (typically around $2,500, which includes pretreatment cancer screening). They'll opt instead for just platelet-rich plasma injections, which run about $600 and last around four months, as opposed to a year or more.

He's been disappointed that more people haven't proceeded with stem cell therapy—and he wishes clients would bring their dogs in during the early stages of osteoarthritis instead of as a last resort when the disease is advanced.

"The earlier we can start with them, the better the results," he said. "The big thing for me is trying to get information out to the owners to try and be more proactive."

John Peroni, DVM, MS, DACVS, codirector of the University of Georgia (UGA) Regenerative Bioscience Center, uses stem cell therapy to treat horses with ailments like torn tendons and ligaments, as well as joint disease, three to four times a month. He enjoys having the chance to treat them differently from 10–15 years ago.

"There's nothing better than seeing the reality of a clinical case improve with treatment that was not available and now it is," he said. "It really gets you excited about making a difference."

Peroni said one of the biggest misconceptions about stem cells is that they should be used as a "last-resort treatment" for end-stage problems like osteoarthritis, because that's probably not the way they'll be most effective.

"They should actually be used within the very early onset of injury," he said. "There's an inflammatory phase of wound healing that happens after all injuries, no matter what the tissue is like. [During] that phase is when the stem cells are going to be most helpful."

Success stories like Harley's, who lived to be 14½, are helping increase client interest in stem cell therapy for pets, particularly for osteoarthritis.

MSCs, which are typically harvested from fat or bone marrow, modulate immune responses and inflammation, so researchers like Peroni are investigating other potential applications. For instance, Peroni and his team collaborated with UGA veterinary surgeon Chad Schmiedt, DVM, when he performed two successful kidney transplants on cats and used MSCs as part of the immunosuppression protocol.

Recently they've been studying the use of platelet lysate as a substitute for fetal bovine serum when culturing stem cells—and they've found "phenomenal" biological properties in the platelet lysate itself, including anti-inflammatory effects.

"It actually kills bacteria in some cases better than antibiotics," he shared.

Every day in Peroni's clinical work at UGA, clients ask about stem cell therapy. He believes the demand is going to continue.

"If we don't stay at the forefront of this in veterinary medicine, we're missing the boat because clearly there's a lot of evidence to suggest that we can help tissues heal with stem cell treatments. The caveat is that basic science and the clinical applications have not quite yet met."

Photo courtesy of Liz Lagana

Know the Facts

Lisa Fortier, DVM, PhD, DACVS, principal investigator at the Fortier Comparative Orthopedics and Regenerative Medicine Research Laboratory at Cornell University, cautions veterinarians and medical doctors against being misled by stem cell products with very little science behind them. For instance, she said equine research has shown that true stem cells, which are isolated from bone marrow and have very strong regenerative capacities, can *prevent* arthritis in horses. But if companies don't isolate stem cells and just assume there must be some in the sample, it's obviously problematic.

She said the hot topic in stem cell research is secretome, both for university research institutions and for private companies.

"We used to think if you took a stem cell from wherever you wanted to and you put it into, let's say, a tendon, that that cell turned into a tendon cell and helped essentially regrow the tendon," she explained. "But we know that's not true now—that those transplanted stem cells don't live for very long, and it's really what they secrete: their secretome. They secrete trophic factors that recruit stem cells to the site and by lots of other mechanisms to enhance tissue repair."

Photo courtesy of Gallant

Fortier hopes secretome will be regulated like a drug and be available off the shelf in a sterile vial like a steroid. "It's much more controlled and will really be, I think, how the therapeutic promise of stem cells will be realized."

Lauren Schnabel, DVM, PhD, DACVS, DACVSMR, associate professor of equine orthopedic surgery at North Carolina State University and principal investigator of the Schnabel Equine Sports Medicine Laboratory, has shown that stem cells help tissue heal more normally, avoiding scarring. Tendons need to be highly elastic, so with a scar, horses are prone to reinjuring themselves, which can have devastating consequences.

"With the use of stem cells, equine veterinarians have been able to heal tendons with more normal tendon tissue and really, really significantly dropped their reinjury rate," she said. "It used to be up around 70%, especially for racehorses, and now it's all the way down to around 25% with stem cells."

A major focus of Schnabel's current research is manipulating stem cells so that they don't cause an immune response; they're basically hidden from the immune system. The goal is to be able to treat an animal with stem cells from a different animal of the same species, a process known as allogeneic stem cell therapy.

"When you're talking about a pure, cultured product, like we use, that takes two to three weeks to grow the cells. And sometimes you don't want to wait that long to treat an injury," she said. "Also, in older horses or dogs or cats—or us—they just don't grow as well as stem cells of a young, healthy patient. So we would love to have cells from young animals that we know are potent to use safely in other patients."

The experts interviewed for this article are intrigued by stem cell research involving feline stomatitis at the University of California, Davis. (In fact, UGA's Peroni encourages all veterinarians to read the published studies.)

Curative Properties

Boaz Arzi, DVM, DAVDC, DEVDC, Founding Fellow AVDC-OMFS, director of the Veterinary Institute for Regenerative Cures at the University of California, Davis, said stem cells are proven to cure—not just improve—feline gingivostomatitis, a chronic oral mucosal inflammation.

"We have a 70% response rate out of which much of it is a cure. You have a cat that's had this oral disease for several years. They come, and within three to six months they leave without the disease," he said. "That is, by all means, a cure."

Arzi's team has a project on spinal bifida, a congenital abnormality associated with the spinal cord, to work with stem cells to try to repair it, but it's mostly on a clinical trial basis. Much work in the veterinary world could have positive ramifications for humans, from helping regenerate tissue to modulating, or jump-starting, the immune system. But like other cutting-edge researchers, he's quick to note the importance of not letting applications get ahead of the science.

"I think more and more information is out there and people want more natural treatments."

—ALAN HOLTER, DVM

"My personal aim with stem cells is not to improve: I use it to cure. It's ambitious, but that's where we need to be," he said. "Stem cells do offer promise for many disorders that were previously not considered curable. But giving any regenerative therapy should be based on proper science and proper clinical trials. I think this is what we need to convey to the pet owner: not to be at full expectation, but also not to lose the excitement and the promise that it offers."

Still, it's hard to tamp down the growing public enthusiasm for stem cell therapy.

In October 2019, Aaron Hirschhorn launched Gallant, a biotech company that banks stems cells for pets and works to develop therapies, after stem cell therapy cured him of chronic pain from a back injury.

"It was completely life-changing," he said. "I went from not being able to carry my kids to playing football with them."

Gallant is promoting stem cell banking at the time of spay/neuter, when young animals are already under anesthesia, so they won't need to undergo anesthesia to harvest them later in life if they need them.

"All you're doing is taking something that you would have thrown away and putting it in our temperature-controlled kit," he said. "By marketing directly to consumers, a consumer can come in with the kit and make the veterinarian aware."

He said the Gallant team, led by Linda Black, DVM, PhD, president and chief scientific officer, is hoping to develop stem cell treatments for immune-mediated conditions like atopic dermatitis and dry eye in dogs and is working with the FDA along the way.

Alan Holter, DVM, medical director of AAHA-accredited Dodgeville Veterinary Service in Dodgeville, Wisconsin, said the practice began offering stem cell therapy in 2018 as a progression of offering pain management

Photo Courtesy of Dodgeville Veterinary Service

"Charlie is a different dog since this treatment. He is energetic, spunky, and so, so happy."

—EMILY SMITH

and orthopedic options. They've promoted the service through the website, social media, handouts, and an open house, but the main way is through one-on-one conversations with clients whose pets could benefit.

"I think more and more information is out there and people want more natural treatments," he said. "They don't want all the drugs. They're looking for other ways of treating their dog without medications."

However, the practice only treats an average of one such case every two to three months. His staff has embraced offering stem cell therapy; a veterinarian harvests the fat cells, a certified veterinary technician processes the samples in house with kits for about four hours, and then a veterinarian injects the joints—all in the same day.

"It's a very simple surgery and processing and a joint injection," he said. "Any veterinarian can do it."

Wisconsin resident Emily Smith took her chocolate Labrador retriever, Charlie Brown, to AAHA-accredited Dodgeville Veterinary Service for stem cell treatments after he fell on ice and fragmented his elbow. The pup was just one year and nine months old. He had a second treatment on both elbows about a year and a half later "to stay ahead of it."

"Charlie is a different dog since this treatment. He is energetic, spunky, and so, so happy," she said. "I am so glad we tried out stem cell therapy." ※

Award-winning journalist Jen Reeder scheduled stem cell therapy to treat her dog's osteoarthritis while researching this article.

Photo courtesy of Emily Smith