Adventures in Stem Cell Land

By [Ricki Lewis, PhD](http://blogs.plos.org/dnascience/author/rlewis/) Posted: April 23, 2015

Two weeks ago a neurologist asked me to blog about a US-based company that is offering stem cell treatments, because it had raised hopes among some of his patients. Intrigued because I cover  [“stem cell tourism”](http://stm.sciencemag.org/content/7/278/278ps4.abstract) in my bioethics class and ask students to evaluate companies, I did a little poking around.

I’m questioning what appears to be a strategy to deceive desperate and vulnerable patients by offering stem cell treatments under the guise of participating in clinical trials. The company name isn’t important, because I suspect many others are doing worse. But their strategy, which may well be legal, is unethical.

REGISTERING A CLINICAL TRIAL
First, some basic information. The Food and Drug Administration (FDA) approves drugs and medical devices for marketing. The National Institutes of Health (NIH) funds basic research and clinical trials, which can be registered at[clinicaltrials.gov](http://www.clinicaltrials.gov/). Registering does not mean approval from either agency.

*From the FDA*: “At this time, there are no licensed stem cell treatments.” However, stem cells are the important parts of bone marrow and umbilical cord transplants to treat certain disorders.

*From the NIH*: A  registered trial may be observational, which means it doesn’t have to be randomized or controlled.

STEM CELLS IN FAT
The company sells a procedure that extracts mesenchymal stem cells (MSCs) from a patient’s fat, separates out the stem cells, and then injects them where they’re needed. These stem cells are pluripotent — capable of several fates — and are very well-studied. [Vet-Stem](http://www.vet-stem.com/) has been offering MSCs to treat injuries and degenerative conditions for dogs, cats, and horses for years.



Are patients receiving proven treatments, or are they guinea pigs in dubious clinical trials?

Key words on the website include “*superiority*,” “*advanced*,” “*excellence*,” and of course “*cutting edge*.” But no mention of “*experimental*” or “*investigational*,” and to their credit, “*cure*.” The connection to clinicaltrials.gov uses the word “*study*.” Testimonials are prominent, but I prefer the [dog and cat success stories”](http://www.vet-stem.com/testimonials_sdetail.php?id=51) at Vet-Stem.

A company rep explained that payment for treatment is separate from participating in the clinical trial. He said this three times so it must be important in how they manage to legitimize what they sell. Assessment consists of self-reporting. I was reassured repeatedly that a PhD in neuroscience reads PubMed to determine safety and efficacy of studies supporting the company’s offerings. The other staff members are the surgeons who actually transfer the fat.

I picked up all sorts of errors on the website:

1. The use of the phrase “registered through the NIH” reverberates throughout, and is the fourth sentence of the opening page. Said the neurologist who contacted me, “Anyone can register a trial.” He has conducted dozens of them, real ones that is.

2. The definition of stem cell makes the common oversimplification error: “These cells have the ability to change or ‘differentiate’ into other types of cells.” No. The primary characteristic of a stem cell is its ability to self-renew. If a stem cell didn’t replicate, it wouldn’t be a stem cell. It begets another stem cell and usually a progenitor cell, which typically spawns increasingly specialized cells that ultimately produce a differentiated cell type. But a stem cell is always perpetuated, and that’s why moving stem cells about the body willy-nilly could, theoretically, trigger cancer.

3. Grammar. You don’t have “amounts of stem cells.” *Numbers.*

4. Regenerative medicine is not new. It’s been going on for decades. (Well, so has personalized medicine. It’s called genetics.)

5. Why use a patient’s own stem cells? Yes, the body won’t reject them. But they might re-introduce genes that contribute to the condition in the first place.  The name of the company includes the word “gene,” suggesting that this is a possibility. Or, it uses “gene” just to sound techy.

6. Where is the evidence, in large-scale, random controlled clinical trials, for efficacy of the“treatment” or “therapy?”

7. The list of treatable conditions is odd. They aren’t single-gene disorders. One folder denotes “autoimmune,” yet other folders are for multiple sclerosis, diabetes, and rheumatoid arthritis – classic autoimmune conditions.

8. Assessment is dubious. Treatment for COPD (which doesn’t make any sense at all to me) is assessed with a “quality of life” questionnaire a year after treatment, and for rheumatoid arthritis treatment success is judged by “*participants’ assessment of their overall ability to be active*.” How about something objective and measurable?

It is thinly-veiled pseudoscience.



PLAYING THE PATIENT
I thought I’d investigate something I might one day have: osteoarthritis (OA) of the knee.

I already knew that dogs with OA of the hip had fared quite well with the very same treatment from Vet-Stem, in a randomized, blinded, controlled clinical trial. “*Dogs treated with adipose-derived stem cell therapy had significantly improved scores for lameness, pain, and range of motion compared to control dogs*,” the study found.

The news release from the human company about their new MSC treatment for OA announces collaboration with a Stem Cell Research Centre (SCRC). Nothing came up on Google. But it did appear at clinicaltrials.gov, on the very same entries, and from the very same city, as the stem cell company offering the treatments. Imagine that!

So I called.



Blubber harbors mesenchymal stem cells.

“*America’s leading resource for stem cell therapy*,” greeted me. I passed through layers of phone robots until a cheerful woman told me the cost for one injection of MSCs from my blubber into my knee: $14,900. I think I’d be better off at Vet-Stem.

Next I perused the medical literature since I, like the neuroscientist at the company, also have a PhD in a life science and enjoy reading a scintillating PubMed abstract now and then,

One recent study is from [Seoul National University](http://www.ncbi.nlm.nih.gov/pubmed/24449146). The proof-of-concept investigation was a phase 1 (safety) trial of 9 patients given a low dose (10 million), a medium dose (5 million), or a high dose (100 million) of MSCs, injected into the knee joint. A phase 2 trial (efficacy) injected an additional 9 patients with a high-dose preparation.

At 6 months, “*these results showed that intra-articular injection of [100 million adipose-derived] MSCs into the osteoarthritic knee improved function and pain of the knee joint without causing adverse events, and reduced cartilage defects by regeneration of hyaline-like articular cartilage,*” the researchers concluded. In addition to self-reporting on a rating scale, the study used “clinical, radiological, arthroscopic, and histological evaluations.”

That’s promising, but 18 patients? More telling was a [review article](http://www.ncbi.nlm.nih.gov/pubmed/23306713) from the Biomechanics Laboratory at the Rizzoli Orthopaedic Institute in Bologna, Italy. Those investigators searched PubMed for all uses of MSCs to regenerate cartilage since 2002: 72 preclinical papers and 18 clinical trials, only two of which used adipose-derived MSCs. None of the trials was randomized, five were comparative, six were case series, and seven were case reports.

The reviewers conclude, “*Despite the growing interest in this biological approach for cartilage regeneration, knowledge on this topic is still preliminary, as shown by the prevalence of preclinical studies and the presence of low-quality clinical studies*.”

Even the preclinical studies aren’t all that promising. One from March in [PLOS ONE](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0117945), on a rabbit model of corneal graft rejection to improve on a mouse model, found that adipose-derived MSCs actually made matters worse.

$14,900 for a shot of my fat into my knee, based on this? If I was a racehorse, maybe.



Liposuction aspirate.

OVERSIGHT?
Parts of the company’s offerings seem to add up to a legitimate whole.
• A surgeon can remove fat with mini-liposuction.
• A technician can separate stem cells or a soup containing them.
• A surgeon can inject stuff.
• The patient signs up for the procedure with quasi-informed consent and the self-report becomes part of a study registered at clinicaltrials.gov.

But how legitimate is it all?

Reading between the lines of the ClinicalTrials.gov [Protocol Data Element Definitions](http://prsinfo.clinicaltrials.gov/definitions.html), it appears that you can just make stuff up. It reminds me of when I registered my white Persian cat Angie and a friend’s llama many years ago as “Outstanding Young Women of America,”  for a newspaper column in the days before blogs. I can’t believe [Google found it](https://news.google.com/newspapers?nid=1917&dat=19860426&id=5wkhAAAAIBAJ&sjid=WXIFAAAAIBAJ&pg=2698,6170109&hl=en)!



Is offering stem cell treatments that have not shown efficacy but are registered in trials building a house of cards?

A study at clinicaltrials.gov requires a Human Subjects Review board, which includes an Institutional Review Board and an ethics committee. But “*A study may be submitted for registration prior to approval of the review board so long as the study is not yet recruiting patients.*”

The entries from the company at clinicaltrials.gov are dated 2015,  so patients might not have been recruited yet, enabling them to legitimately use the phrase on the opening webpage, “*IRB approved studies for stem cell treatments registered through The National Institutes of Health*.” But I’ve signed off as an IRB for local high school science projects just because I have a PhD.

The company’s autologous fat stem cell offerings would fall under “procedure/surgery” and “genetic (including gene transfer, stem cells, and recombinant DNA)” at clinicaltrials.gov. I do have a call in to the NIH to clarify oversight, so will update this post when I can.

I hope that one day, infusions of one’s own stem cells will indeed hold at bay Parkinson’s disease, multiple sclerosis, rheumatoid arthritis, and other conditions. But until that time, hiding behind the cloak of government “approval” by registering an observational study with clinical trials.gov is unconscionable.