# From a Tube of Blood To Exosomes…The Stem Cell Therapy Story 2022

**Address By Walter P. Drake**
**To Our New Graduate Students**
**Panama College of Cell Science-January 1, 2022**

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Dear Future Stem Cell Scientists:

Thank you so much for your participation in our 3 year online Ph.D. program in Stem Cell Science.

When we first formed the **Panama College of Cell Science** in 2005 with a couple of retired professors and myself in Thailand, we were so excited about what was happening and so hopeful that this "New Medicine" would become the answer to our

most serious diseases.

As a backdrop to my address to you, please remember these two things:

> (1) When we talk about stem cell therapy, **we are ONLY talking about treatments involving Adult Stem Cells**, typically harvested from a patient; not Embryionic Stem Cells which have never in the last 20 years generated any cure or treatment of any kind; and
>
> (2) When I discuss therapies and treatment options, **I am ONLY talking about international developments, because stem cell therapy in the US has been blocked.** While we do have in the US some peripheral treatments going on, such as with Platelet Rich Plasma (PRP), the most useful therapies are only available outside of the United States, the best centers being in Thailand, Panama, Mexico, and Dubai.

Anyway, back to developments since 2005, when our College began sharing the world's knowledge with our students. David Granovsky captured the excitement of the times when he wrote:

**"In 2004 I worked for the first commercial stem cell treatment facility in the world. [ed. note: Thailand] I watched them as they treated congestive heart failure patients who were tired of being stuck on transplant lists for hearts that might never materialize. I watched these patients brought in on wheelchairs with gray complexions and oxygen canisters. I then saw them come back later on their own power with smiles on their faces and a bounce in their step. These were people who were doubling their ejection fractions (vol of blood pumped out of their hearts) and people who went from Level 3 or 4 congestive heart failure down to Level one. This is the difference between the rest of their short lives in a bed waiting for a heart transplant at Level 3 or 4 AND playing tennis, making love to their spouses, chasing their grandchildren around at Level 2."**

So moved by his experience, David became one of the world's foremost adult stem cell advocates for patients, and he still maintains an excellent stem cell blog at: repairstemcell.wordpress.com

Thailand really launched international stem cell therapy with their cardiac stem cell center which began treating cardiac patients with their own stem cells. The group was put together by Don Margolis (American) and a leading Thai cardiac surgeon, who trained for 20 years in the USA. They reported that stem cells from a patients blood were multipotent, and that they could derive angiogenic, myocardial, and neural cell lineages. They concluded that a small quantity of a patient's own blood contains many lineage-specific precursor cells so as to make this a potential source of autologous treatment "for a variety of diseases". Porat, Y et al., "Isolation of an Adult Blood-Derived Progenitor Cell Population Capable of Differentiation Into Angiogenic, Myocardial, and Neural Lineages", British Journal of Haematology, 135: 703-714 (Dec 2006).

**So, in summary, the stem cell revolution started out by using a tube of the patient's peripheral blood, and then expanding the number of cells in vitro prior to re-injecting to achieve a therapeutic result. This was how it all began. And it began in Thailand.**

The next amazing development was the explosive report in 2008 by Dr. Carlos Lima, of Portugal, of a protocol wherein neural stem cells obtained from a paralyzed patient's own nose and transplanted into the patient's backbone permitted some paraplegics to leave their wheel chairs and walk! The olfactory stem cell transplants were put into the spinal lesions of paraplegic and tetraplegic patients. Dr. Lima and his team in Portugal performed this surgery on over 100 patients with few adverse events and dramatic functional improvement when accompanied by appropriate physical rehabilitation regimes, and actually getting people walking with various degrees of success. [From the Charlotte Lozier Institute].

Up until the time of his passing in 2012, Dr. Lima continued to develop and study his protocol, finding and reporting that the success in the use of neural stem cells to treat a patient suffering from Paraplegia or quadriplegia, seemed to vary inversely with the time to treatment. Patients treated with stem cells shortly after injury or within 1-2 years of injury certainly do much better than those whose injury is more time distant. The postulate for this finding was that while the spinal cord is repaired in the more time-distant injuries, the patient's muscle mass and the nerve-muscle feedback mechanism has been degraded to a substantial extent, that it can take a long time for recovery to occur, if at all, even though the spinal cord nerve trunk is largely repaired. [You can read

more about Dr. Lima and the early history of stem cell medicine Here:

https://drakebiomedicalinstitute.wordpress.com/history-of-stem-cell-treatments-2/

**So, in summary, as of around 2012, we had the approach of injecting a patient's own stem cells into this or that organ to repair function from disease of injury.**

The next development was the critical finding by Dr. Neil Riordan, that umbilical cord blood collected from the placenta and umbilical cord of normal term babies was immune privileged, and hence that the stem cells and could be transplanted to ANY patient without any negative immune consequences. So big was this finding that Dr. Riordan went to Panama and opened the **Stem Cell Institute-Panama** where he continues to treat our most serious diseases with Umbilical Cord Stem Cells (UCB's). Other centers have followed suit as well.

**Dr. Riordan's contribution to the field was the finding of a stem cell source that was not from a patient, and the importance of this finding cannot be under-appreciated. Many older patients have poor numbers of stem cells and inactive stem cells, making therapy using very robust UCB stem cells much more effective**.

While all of the work and achievements using Adult Stem Cells was occurring internationally, what was happening in the US? Billions and billions of taxpayer dollars were assigned to Embryonic Stem Cell research with almost none to adult stem cell therapy. But, despite no research funding of any kind, the next big development came, surprisingly, from within the United States. Although generally blocked and criticized at all levels of government, including the NIH, there was a brief period of several years wherein the FDA allowed the stem cell field in the US to develop, before shutting it down completely. And it was during this time that Dr. Steven Victor of New York came along and described the SVF…the Stromal Vascular Fraction…the Liquid Gold…of stem cell therapy. **This formulation has proven to be the most robust stem cell therapeutic still available today.** An elegant, yet relatively simple procedure, the Stomal Vascular Fraction is what is left over after 60 cc of fatty tissue is harvested from a patient's belly fat and the fat cells removed. Adipose tissue is the source, and Mesenchymal Stem Cells, endothelial cells, growth factors, cytokines and many other constituents are the product. You can see a complete definitive description here:

https://drakebiomedicalinstitute.wordpress.com/2015/03/31/better-late-than-never-to-stem-cell-party/

**From Dr. Victor's immense contribution in 2015, the modern field of Autologous Stem Cell Therapy was born and still thrives overseas, as many centers changed over from using peripheral blood to using adipose derived SVF as their source of patient specific stem cells for therapy.**

Dr. Victor currently treats his patients in Dubai UAE, not able to do so freely in the US.

And then along came Kristin Comella. No one moved the needle of progress in Autologous Stem Cell Therapy farther or faster than Dr. Comella. If Dr. Victor was the inventor of the SVF procedure, Dr. Comella grabbed on to it with tenacity only seen in a very top scientist…she was going to take this Autologous Stem Cell Therapy using SVF and start curing patients.

With hundreds of registered Clinical Trial studies under her belt, her team in Florida successfully treated many kinds of conditions and diseases with collaborating physicians and health care providers. Her team made use of legal, patient-specific FDA guidelines, including studies permitted by Institutional Review Boards, patient-specific stem cell clinical trials, and direct treatments using the patients own stem cells that are harvested and re-injected for therapeutic purposes.

In 2017, Dr. Comella published a paper detailing the successful autologous stem cell therapy on 676 patients using SVF. Her paper was the FIRST of its kind in the US. On peer review, this paper not only passed without objection but was earmarked for immediate fast track publication in one of America's most prestigious journals, the ***Journal of Clinical Medical Research***. You can read more about this amazing stem cell therapy pioneer here:
https://panamacollegeofcellscience.org/2019/01/23/kristin-comella-phd-leading-the-way-to-adult-stem-cell-therapy/

**And so it was that using the SVF from a patient's belly fat became the dominating format for successful Autologous Stem Cell Therapy, still used worldwide today.**

Following her blockbuster peer-reviewed research report, the FDA finally had enough of stem cell progress. After all, you had individual practitioners such as Dr. Victor, Dr. Comella's team, and other physicians in private practice, treating patients and leading the development of this new treatment modality…without Big Pharma getting anything out of it, and without FDA participation. It was embarrassing wasn't it? Plus Big Pharma, the major pharmaceutical houses, do not seemingly want to see advances in adult stem cell therapy either, because that means a reduction in their sales as patients use their own repair stem cells to control many diseases rather than pills. Adult stem cells in your own body cannot be patented like an embryonic stem cell can be. The idea of patient-specific adult stem cell therapy using the patient's own stem cells and administered by a patient's physician was abhorrent to many people in power.

And so, a federal lawsuit was filed in 2019 against Dr. Comella to stop her treatment of patients and to slow the progress of adult stem cell therapy. The case was **United States of America v. US Stem Cell Clinic, US Stem Cell and Kristin C. Comella.**

**"…the Court agrees with the FDA that the SVF is a drug".**

And that was the end of stem cell therapy in the United States of America (June 3, 2019).

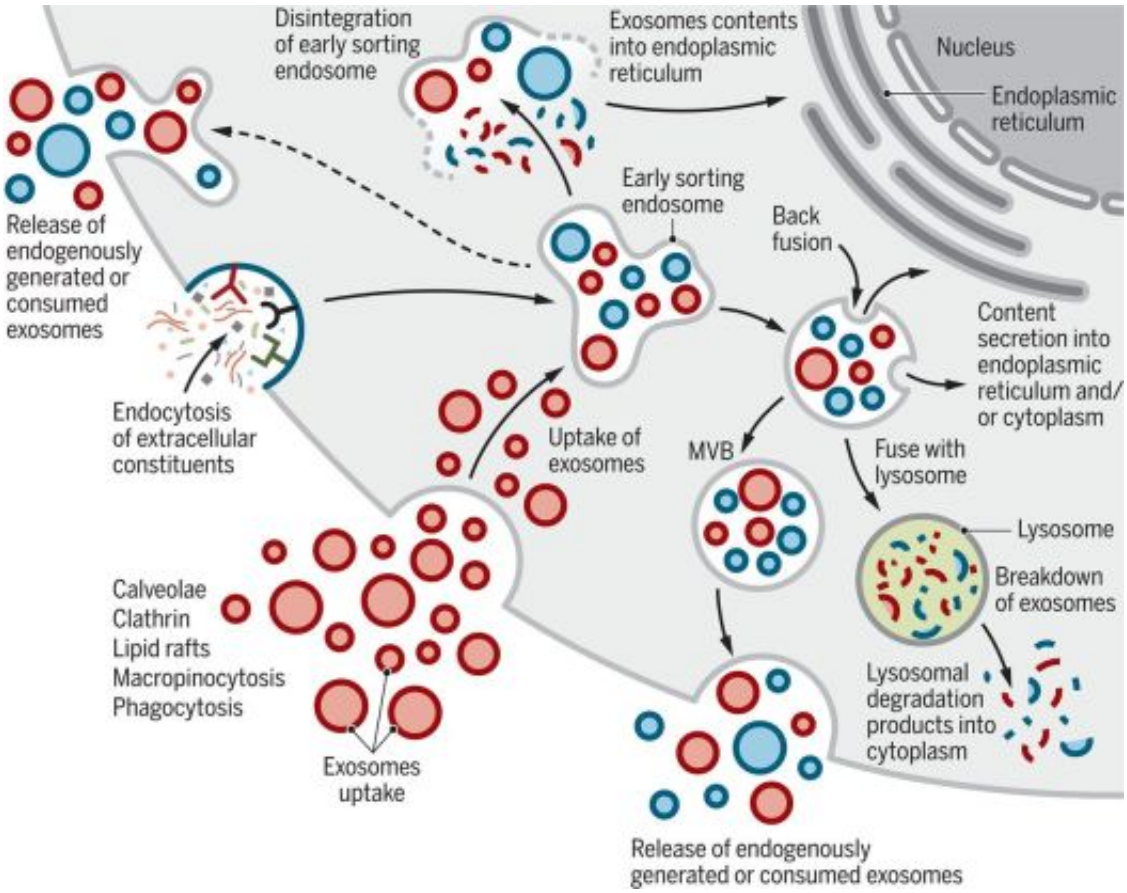
But while these advances using autologous stem cells for therapy were ongoing worldwide, **a cloud began to appear at the Panama College of Cell Science.** And that cloud was what we refer to as the "Paired Mice Experiments". In the paired mice experiments, the circulatory system of an old mouse was joined to a young mouse in such a way that their circulatory systems are mixed, and blood, plasma, and serum flows between them. The question asked was whether muscle repair in the aged mouse could be boosted by circulating stem cells from the younger mouse. But in a surprising turn of events, it was discovered that indeed there was improvement in muscle regeneration in the aged mouse, but that this was NOT due to stem cells from the young mouse, but rather due to circulating blood factors from the young mouse. Continuing experiments took place between 2005 and 2015, which went on to identify certain effective growth factors transmitted from the young mouse. The experiment showing improved muscle repair in the aged mouse was replicated to show also improved neuron growth as well. Finally the researchers blurted out: **"Plasma alone had the same effects. "We didn't**

**have to exchange the whole blood," says Wyss-Coray. 'It acts like a drug.' "**

And we have been teaching about this over the last 10 years, that it is serum factors, not stem cells, that are going to be the future of therapy. And that future has arrived?

## Exosomes as the new Stem Cell Therapy…
## or Are They Just Snowflakes?

This image depicts how Exosomes serves as messenger molecules, moving "cargo" in and out of cells, as well as participating as extracellular messengers that control cell-cell interactions. Click on picture to make bigger:




Over the last 3 years, "exosomes" have become the new buzz word, a word not mentioned previously in any serious context. A new word…and a NEW stem cell therapy.

One might well ask: While SVF is such a terrific therapeutic modality, are stem cells included therein of any use? We have taught at the College that the controlling factor on what a stem cell becomes is the cellular environment it is placed in. **So BOTH parts-**

**stem cells as well as the very important serum factors are required.** But one thing is for sure. Purified, bare-bones stem cells with no associated serum factors don't do anything. **The recent observation that FDA approved UCB stem cells, that are now manufactured by some pharmaceutical companies for therapy, have No Therapeutic Effect whatsoever certainly suggests that bare bones cells with no supportive growth factors, cytokines, messenger molecules, endothelial cells, and exosomes…in short…the SVF soup…are devoid of stimulatory or repair function.** So we can thank the FDA for proving that.

Exosomes are messengers, that carry messages both intracellular and extracellular. Without these messengers, nothing gets done, cells don't do anything. BUT, they are not the only messenger molecules. There are hundreds of cytokines, proteins, enzymes, growth factors and other messengers, some identified and most not, that regulate cell-cell interaction, differentiation, growth, repair and so forth.

So, I now see some centers advertising treatments with exosomes. The idea is of course to treat with "serum factors" per the paired mice experiments. But exosomes have to come from some place, and that someplace is from Amniotic Fluids collected from normal C-section childbirth; and/or from placental tissues harvested from a normal delivery. This will prove to be a limited source.

There are various methods of harvesting and concentrating the exosomes. **Just as pure umbilical cord derived stem cells approved by the FDA have never been shown to have any beneficial effect in any treatment, so will "exosomes" prove to be equally ineffective in my view.**

And here is why I think exosomes will never have any therapeutic value. **I liken harvesting exosomes to the collection of snowflakes.** You see them, you grab for them, and they are gone. Can you capture a snowflake and keep it? Not easily if at all. There are many protocols for isolating exosomes from amniotic fluid, cord blood and other sources. There are test kits for testing for exosomes and modified automated cell counting equipment that can count them. But in my mind…after all this and that…they are gone…they disappear…they break into useless parts.

An exosome is a **very fragile** cell type, or I should say, circular body that can contain

RNA, enzymes, other triggering molecules. **The job of an exosome is to carry a message, and once that message is transmitted, it disintegrates. After all, the cells do not want "old" messages hanging around and interfering with the next round of messages. So they are not meant to exist for other than a fleeting moment!!!!** Keep exosomes in a test tube on ice for an hour and the degradation will begin destroying them. Many researchers are already reporting that exosomes are damaged by the very techniques used to isolate them, such as high speed ultracentrifugation, ultrafiltration, and lyophilization.

While the idea of treating with exogenous exosomes to stimulate innate stem cell activity sounds like a really good idea, the immense difficulty in the execution of the therapy will bar this idea from becoming useful in my opinion. I see some cosmetic manufacturers advertising "now containing exosomes". **These cellular bodies can't last an hour in a test tube on ice**, do you really believe there is anything whatsoever in that jar of cream? Same for "stem cell ingredients" for that matter.

## My View of the Future of Stem Cell Therapy

At the Panama College of Cell Science, we are emphasizing 2 lines of therapy that will continue to have major roles as we continue with this New Medicine:

**(1) Give me SVF!** There is still nothing that comes close to Dr. Victor's soup of mesenchymal stem cells and non-cell factors, per the following picture (click to make bigger):

**1. Autologous tissue and cells are used** [the patient's own bodily tissue and cells]. This eliminates all immunological issues of rejection or need for immunosuppressive drugs, eliminates risks of contamination with viruses, eliminates need for tissue matching or blood group matching.

**2. Fast preparation for immediate patient treatment**: They report that they can complete the processing of the stem cells in 1 hour, so that the patient can have the treatment same day. The patient receives very fresh cellular products, with little time for degradation to occur. Nothing better than fresh preps!!

**3. Adipose Tissue is the source**: Fatty tissue, generally obtained from the abdomen, contains 400 times more stem cells than peripheral blood of the same quantity. If you want a lot of stem cells, and you do need a high number to achieve a therapeutic result, then fatty tissue is where to go get some in high numbers. Their minimum number of cells used appears to be 100 million stem cells.

**4. A "soup" of cells including cytokines and growth factors** is used for therapy. We know that endothelial cells have been shown to work in harmony with stem cells to help grow them in large numbers. Endothelial cells are included. We also know that cytokines and unknown growth factors help in therapy, which , in other types of treatment centers, is why a soup of fetal tissue is so effective in therapy. Cytokines and growth factors are included. Many other beneficial cells are also included:

**Vascular Fraction Cellular Composition**

Adult autologous stem cells (Mesenchymal)
Endothelial Cells
Fibroblasts
Growth Factors
Pericytes
Preadipocytes cells
Smooth muscle cells

**Blood Cells from the capillaries supply including:**

B&T cells
Erythrocytes
Hematopoietic stem cells
Endothelial progenitor cells Macrophages
Mast Cells
Monocytes
Natural killer (NK) cells

**(2) Finding Supplements that stimulate innate stem cell activity** is going to be HUGELY important. Dr. Neil Riordan has developed the world's first and only supplement, called Stem-Kine, that increases your stem cell count. "Stem-Kine nourishes your bone marrow to release more of its own stem cells into circulation and protects those cells from oxidative stress. It does so through a "secret ingredient" – a cell wall extract of Lactobacillus fermentum – developed exclusively for Stem-Kine." as shown on his website:

https://www.stem-kine.com/stem-cell-supplement/

While the data only shows a mild increase of 2-fold, we will be able to do a lot better in the future. I mean, if you are already down 10-fold, boosting 2-fold will not not do much. Hopefully, different supplements for the targeted activation of a certain class of stem cells, or a certain location of stem cells can be developed. Not just as Stem-Kine does, generate a non-specific increase of stem cells for the stem cell highway (the blood system). **Dr. Riordan gave us a great start and a great idea!!**

This is my view of the future.

Thank you so much for joining with us in our online PhD program in Stem Cell Medicine, and we hope some of you will go on to advance the field in material ways…

## The Panama College of Cell Science
## The First and Still Only
## Online PhD Program in Stem Cell Biology

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**Key words so you can find us. Panama College of Cell Science teaches stem cell medicine,Panama College of Cell Science teaches stem cell biology,Panama College of Cell Science teaches stem cell science,where to go to learn about stem cell biology?,what colleges teach stem cell biology?,what university has a PhD program in stem cells,what university teaches stem cell biology,where can I find a PhD program in stem cell biology,where can I find an online PhD degree in stem cells,where can I find an online PhD degree in stem cell biology,which college of university has an online PhD degree in stem cells?,**

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