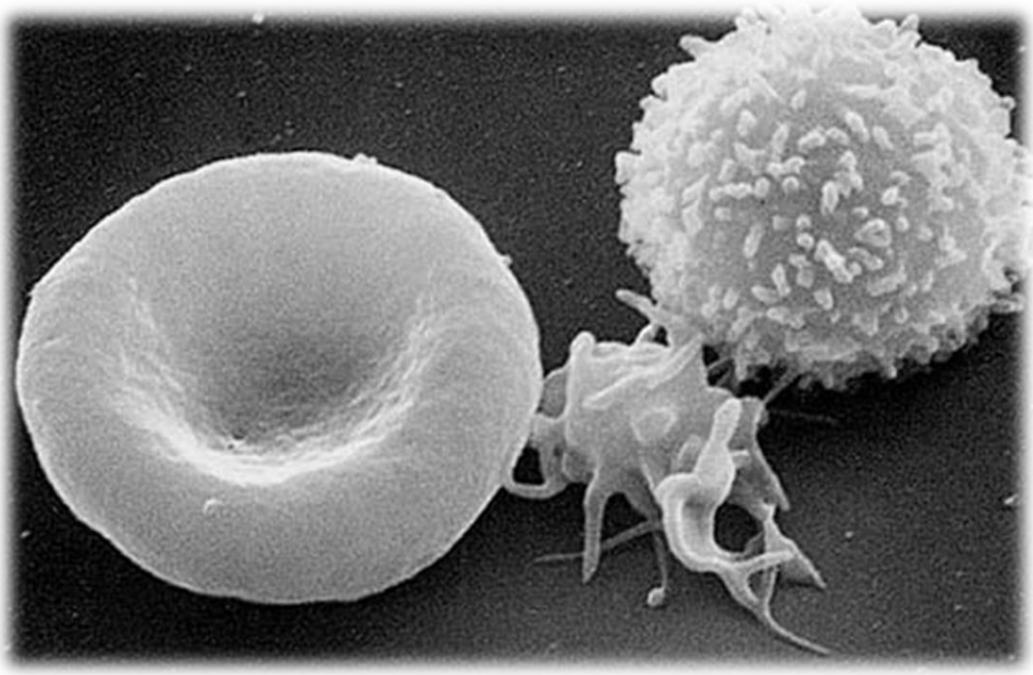
STEM CELL THERAPY, SCIENCE OR BUSINESS?



Platelets, erythrocytes and leukocytes

How have hundreds of clinics offering stem cell treatment for almost any illness, from trauma, arthritis, osteoarthritis, muscular dystrophy, amyotrophic lateral sclerosis and even stroke, cerebral palsy, cancer or autism emerged? (3).

Let us go back in time about ten years:

The concept of stem cells is not easy to explain. Stem cells are not distinguished by their appearance, but their behaviour. The most versatile are of embryonic origin. Initially they were isolated from mice more than three decades ago. This type of cell comes from embryos in their early stages of development (the blastocyst phase or, at the latest, the gastrula phase). They are cells with the potential to turn into virtually any cell line, so we also refer to them as “trunk cells”. Generally, they are extracted from the surplus embryos of *in vitro* fertilization techniques. Even from frozen, they can be thawed out and cultivated *in vitro*. However, the differentiation of these cells in a culture is not uniform.

Stem cells taken from embryos can be divided into an array of different cell types. This diversity can be exploited by modifying the characteristics of the culture medium, such as the addition of exogenous factors. It is vital to avoid the uncontrolled differentiation of these cells as there could be a risk of *teratoma*. This situation has often arisen during research. There is also the risk of antigenic panel stem cells triggering an immune response in patients. This second problem could be overcome by removing the patient's own cells and subsequently cloning them.

Cloning is a way of returning adult cells to their embryonic stage. Our bodies contain more than 200 cell lines. The differentiation of stem cells is an irreversible process. However, when the nucleus of an unfertilised ovum is removed and replaced with the nucleus of a somatic cell, it begins to divide as if it were a normal embryo. In this way the somatic cell can be reprogrammed and thus turned into a stem cell capable of regenerating any tissue or organ.

At this point researchers raised ethical questions. Experiments with stem cells which sought to clone animals using somatic cell cloning largely failed because of the high rate of deformities and high mortality involved. While reproductive cloning is unpredictable in humans, cloning cells to therapeutic purposes is, at least conceptually, very interesting.

Parthenogenesis, which occurs in nature in relatively simple animals, is able to produce embryonic stem cells without nuclear transfer. Conceptually it involves a chemical "deception" of an unfertilized egg so that it starts dividing as if it had been fertilized. The pseudo-embryos obtained are more easily cultivated than those obtained by nuclear transfer.

Paradigmatic adult stem cells are hematopoietic cells. There are more than half a dozen of these specialized cells, and some produce elements such as erythrocytes, and do this at an impressive rate: 350 million every minute. Other organs are also renewed quite quickly. This also happens in the case of the skin, and the liver can regenerate 50% of its weight (1,5Kg) in about a week. For reasons yet to be discovered, other organs, such as the brain and the heart cannot regenerate themselves despite containing stem cells, as showed by histological studies.

There is a vital issue: trans-differentiation, which is when a stem cell from one tissue can produce a different tissue. This issue was raised during bone marrow transplants. Donor cells were found in a wide variety of the recipient's tissues. It was considered possible that, under certain circumstances, stem cells from bone marrow could regenerate any part of the body. This strategy has not yielded the expected results.

There has been some success that gives hope of greater achievements in the future. The German TOPCARE-AMI project was a study conducted on patients who had suffered a myocardial infarction. The patient's own heart cells were injected into a damaged artery which had been the cause of the infarction, and after four months, the extension of necrotic tissue was reduced by 36%, and heart function improved by 10%.

The main problem with this type of study is the difficulty of isolating stem cells in tissues, given their scarcity and the lack of specific markers which indicate that they are, in fact, stem cells. These factors have led to a reprogramming of the research. Now, a search for substances that cause stem cells to migrate to the damaged tissue has been investigated. One of these substances is IGF1 (Insulin Growth Factor type 1). Antonio Musarò, La Sapienza University, Rome,

has shown that IGF1 attracts stem cells to the site of injury. And not only that: it also promotes the reversal of damaged cells to their primordial stage. The process of *de-differentiation* is the aim of regenerative medicine.

It is difficult to explain, then, the rise of clinics that offer "therapeutic" treatment which is not scientifically guaranteed.

The website of one orthopaedic clinic offers treatment using stem cells to restore degenerated tissue, claiming to relieve pain at the same time, which could easily be a fallacy. On another website, stem cells are offered to patients with neuro-degenerative diseases postulating the following argument: "the regenerative nature of stem cell adipose tissue can help relieve symptoms associated with the disease." Many scientists associated with stem cell research have expressed their displeasure with the rapid proliferation of these clinics that pretentiously offer cutting-edge therapies without any scientific evidence to back them up.

The Food and Drug Administration (FDA) allows these clinics to inject their own stem cells, or the tissue extracts thereof, into patients after only a minimal *in vitro* manipulation. It is assumed that these re-grafted cells will behave normally once injected (4).

These clinics operate on the fringes of illegality, offering amniotic fluid cells which are not subject to any regulation by the FDA. In other cases, they even offer stem cells derived from blood or fat tissue to treat neurological diseases such as Parkinson's disease or multiple sclerosis; another slightly dubious practice. It is highly unlikely that these cells will behave like normal cells when applied to brain tissue.

Moreover, many of these clinics are not legally registered, so it is unknown how many patients have been treated, or the consequences of these therapies which lack scientific endorsement.

These clinics say that they adhere to the regulations set by the FDA. They also tend to have online promotional videos on their websites which include patients who report dramatic improvements in their serious disease when treated with stem cell therapy.

On the other hand, Corporate Medical Societies exist. Thus, Insoo Hyun, professor of ethics at Case Western Reserve University, and former head of Ethics at the International Society for Stem Cell Research, said that "these clinics have a medical team, and the Deontology Codex requires them to use only those treatments based on medical evidence". Medical Societies can advise, but lack executive power. This is the opinion of George Q. Daley, a researcher at Mother School of Medicine at Harvard University, and current head of the International Society for Stem Cell Research. The dispute between scientific societies and clinics is like a game of “cat and mouse”.

While scientific studies searching for evidence after laborious and time-consuming clinical trials, some clinics try to lure patients by means of attractive advertising.

One thing that keeps clinical stem cell therapy in business is that many patients come to spend significant sums of money on treatment without questioning the validity of it. If the results are not as they had expected, patients prefer to remain anonymous, sometimes due to shame, others because of confidentiality clauses signed before commencing treatment.

The litigation that may result is extremely costly, and often patients have already spent too much money to allow them to initiate judicial proceedings whose results may extremely unpredictable.

The authors of this article recommend reading “Handbook of Stem Cells” [5].

Dr. Knoepfler has a blog that receives queries from many patients who have been treated these clinics. For the reasons stated above, they are reluctant to give their names and recount their personal cases. They simply want to “get things off their chests”.

Many people who go to these clinics overstate the alleged success of the therapy they have undergone while spurning any stories of failure, despite the precautionary warnings given by the academic medical community.

As pharmacists, we cannot ignore these dubious therapeutic practices which only seek to obtain immediate profits.

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Zaragoza, September 29th 2016

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