Podcast Episode 5: current status of stem cell treatments

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Potential of stem-cell treatments for regenerative medicine

In this episode I have done some research on the status of stem cell treatments. Many of us are not that familiar with cell biology. So let me start with reminding everyone of how organisms develop through cell division, the potential of stem cells, what type of stem cells there are, and what they do. Afterwards I'll talk about the current status of stem cell treatments. What is available right now, what is in the pipeline, and what are the opportunities to benefit from this.

All body tissues are built from cells. Cells divide, age, and die. When cell division capability declines over time and not enough new healthy cells are recreated, our tissues and organs age. The root cause of many diseases lies in the aging process of our cells. For this reason, there are no cures for age-related diseases. We usually say that an aged person died of heart disease, cancer, or had Parkinson' disease. In reality he died of aged cells. Now stem cells are different from normal cells. In a fully developed organism stem cells mostly don't do very much. But in times of crisis, like injury, they spring into action. Differently from normal cells, they can not only create specialized daughter cells, but also renew themselves. This characteristic of stem cells is explored by the field of regenerative medicine hoping to recreate diseased cells in the body or grow new tissues for transplantation. That could be nerve cells, heart tissue, bones, teeth, etc. Stem cells are really considered the best option to respond to needs for tissue and organ transplantation through their ability to differentiate into the specific cell types that are required for repair.

Researchers, the general media, as well as start-up entrepreneurs and investors are generating a flow of exciting news about the potential of stem cell therapies, and we actually do witness exponential advancement in clinical trials revolving around stem cell-based therapies. There clearly is the prospect of stem-cell-based therapies making a huge impact on slowing down, stopping or even healing some of the most debilitating age-related diseases, for which conventional drug-based therapies are not really effective.

Types of stem-cell

Depending on country and culture, stem cell research is subject to ethical concerns. To understand those concerns as well as the nature of stem cell research we should remember that stem cells exist in a developmental hierarchy with stem cell types evolving into other, more specialized types – a bit like a tree.

At first there is the fertilized egg. This is the first stem cell of an organism. It has the capability to differentiate into any possible body cell, and is therefore called totipotent. After several cell division cycles we enter into the embryonic stage, when stem cells become pluripotent. At this stage they are still capable to differentiate into almost all other body cells. Stem cells would be most useful for the development of treatments at this stage. However, ethical concerns start to kick in because the

extraction of embryonic stem cells involves the destruction of human embryos. And as a result, many countries put strict limitations on the use of embryonic stem cells for scientific research or medical treatments. Limitations tend to be even more restrictive when the foetus has already been formed. The next developmental stage of stem cells are multipotent, or also called adult stem cells. They are the most common, occur in all body tissues, and are capable to make a limited range of differentiated cells within the same tissue, like blood, gut, brain, or skin. At this level, there are no ethical concerns. The same is valid for unipotent stem cells, which can make only single kind of cell, e.g. sperm cells or muscle cells.

A new type of stem cells, called induced pluripotent stem cells, or iPSC, can be artificially created in the laboratory by reprograming adult stem cells into their previous pluripotent stage. There are still challenges though, but once this technology is fully mastered, they will be able to replace embryonic stem cells for the purpose of developing treatments without any ethical concerns. For this reason, iPSCs are a very important turning point in stem cell research.

Stem cells are already there. The challenge for scientists is to gradually learn how to manipulate molecular pathways to enhance the function of aged stem cells, or to build and control the processes of extracting, growing, and transplanting stem cells to recreate aged tissues and organs without any side-effects.

Targeted diseases

Many of the most debilitating diseases are targeted by stem-cell treatments. Among them are neuro-degenerative diseases like Parkinson's, Alzheimer's, ALS, and MS. Therapies aim to generate fresh neural cells from stem cells, which would take over the function of diseased neural cells in the body. Similarly stem cell treatments are developed for conditions like diabetes, repair of heart tissues after stroke, bone and tooth replacement, spinal injuries, or to replace the retina to heal degenerative macula and to restore vision. In fact it is hoped that ultimately stem cell treatments could help to rebuild or replace any type of aged body tissue.

Status of stem-cell treatment

The current status of stem cell treatments involves good and bad news. Worldwide there are many clinical trials running, involving stem cell therapies at various stages. And that number is increasing by the day. I found various numbers between a few hundred up to 6000 clinical trials being registered worldwide. Those numbers mostly depend on stem cell type and trial phase. E.g according to one research paper only 131 studies could be classified as clinical trials involving PSCs. Definitely, treatments against a number of diseases are already tested not only in the laboratory, but also in various animals and human patients. A relatively high number of those trials are concentrated on macula degeneration. Another high proportion is focusing on neurodegenerative diseases like Parkinson's, as well as diabetes, and heart conditions.

However, the strong interest in stem cell research contrasts sharply with the number of actually approved stem cell treatments. So far these are limited to treatments using bone marrow and adult stem cells derived from blood. That includes treatments against leukemia and thallasemia. One stem-cell therapy has also been approved for spinal injury.

Numerous publications from the life-extension industry report on successful research and clinical trials involving transplanting cells and engineered tissues. A lot of progress has certainly been made, although we may still be many years away from stem cell treatments becoming off the shelf treatments, readily available in case of need. What kind of treatment might become the first to be approved? Probably against macula degeneration. Others will certainly follow. How long will it take? 5 to 10 years perhaps. But that will still be just the beginning. Too many challenges regarding safety and efficacy still need to be tackled in scientific research and clinical trials.

Nevertheless, stem cells derived from the blood or increasingly from adipose tissue (which means body fat) are being used by clinics to treat various orthopaedic, neurological, and other diseases without official approval, at the same time claiming that they constitute revolutionary treatments for such conditions (Marks). Many experts warn that clinical evidence of safety and efficacy is just not there yet. One expert related to the FDA wrote: “Outside the setting of hematopoietic reconstitution (tranl: blood production) and a few other well-established indications, the assertion that stem cells are intrinsically able to sense the environment into which they are introduced and address whatever functions require replacement or repair — whether injured knee cartilage or a neurologic deficit — is not based on scientifc evidence. Published data derived … from … trials … have not reliably demonstrated the effectiveness of stem-cell treatments ……. Claims that therapies are safe and effective must be based on evidence.” (Marks 2017)

In spite of the near complete lack of authorized stem cell treatments, a high number of stem cell clinics worldwide are found to already offer stem cell treatments.

I did a very short internet check on stem cell treatment providers and read the web sites of the first 3 clinics I found - 2 in Germany, and 1 in Switzerland. In fact none of them offers proper stem cell treatments in the sense of regenerating aged or diseased cells. They use stem cell therapy mainly as a teaser to attract patients, while promising them cures against all kind of illnesses. When reading more carefully through the technical jargon, one understands however that they are really selling different treatments, rather belonging to the anti-aging, aesthetics, and preventive medicine fields. These were then mislabelled as regenerative medicine. One clinic extracts actual stem cells from a patient’s body, then produces a cocktail of different possibly beneficial proteins through the help of those stem cell. Finally that cocktail without the stem cells is inserted into the body of the patient. Two of the clinics wrote that they also do administer stem cells after a health check and various other treatments, but did not explain any details. From my quick check I can only assume that patients may well obtain benefits from those clinics, but if they do, that would not be due to a stem cell treatment. They are likely spending money on so-called stem cell treatments, which may be harmless but useless. But may-be they

are also introduced to clinics in countries, where actual stem cell treatments have been already undertaken in clinical trials, but without having obtained authorization.

Another stem cell related area which is already now actively offering services to future patients is stem cell banking. The motivation behind stem cell banking is to store your own stem cells for later use.

For example there are companies offering to extract pluripotent stem cells from your baby's umbilical cord blood and freeze or cryopreserve them immediately after birth. One company I checked charges about 2700 EUR for 25 years of storage, and even offers prolongation if requested. Another possibility of stem cell banking lies in stem cells extracted from first teeth, or human exfoliated deciduous teeth in medical language.

Storing your child's stem cells into a stem cell bank offers it a ready source of high-quality stem cells for use in a possible future therapy, even it that therapy does not exist today.

Risks

As mentioned, regulatory authorities like the FDA from the US or the European EMO have issued strong warnings against most stem cell treatments currently offered to patients. Their concerns relate to safety and efficacity. There are reports of humans in clinical trials having developed tumors, or blindness as a result of treatments. Treatments may just not work in a fully predictable way. At this stage, offered treatments may be ineffective, they may even kill you, or they can save your life.

Now regulatory authorities are doing what they are supposed to do, meaning to ensure safety and efficacity for the greater patient population and the health care system. But science has already progressed further than regulation, although much may still exist at an experimental stage without mature processes. Taking the perspective of individuals who are seriously ill with age-related diseases, or close to becoming so, regulatory or even ethical concerns might take second stage. The stem cell therapy field is likely to balance regulatory and legal concerns with individual patients' needs and business opportunities.

Outlook

The future of stem cell therapies looks bright. In the framework of regenerative medicine, they will completely change the way how we look at age-related diseases. Massive challenges regarding safety and efficacity still need to be overcome until treatments will be officially authorized. But the desire for unauthorized treatments will increase, particularly for individuals who haven't much time left. For them potential gains may outweigh the risks. We can be sure that an important grey market is developing to offer unauthorized treatments of a variety of conditions. That may involve some creativity, perhaps travelling to another country to receive treatment. Treatments will also not always work as expected, and access to such clinics may not be straight-forward. But most importantly, as in the entire life-

extension industry, we should better learn to distinguish between the charlatan and the genuine treatment provider.

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