

Pulmonary Hypertension Stem Cell Therapy Fact Sheet

What are stem cells?

- True stem cells are cells that can divide to replace themselves indefinitely (i.e. self renew), so unlike regular cells they do not age. They can also give rise to daughter cells, called “progenitor” cells, which are destined to become a number of different cell types, by a process called differentiation.
- Stem cells vary in their capacity to differentiate or mature.
 - Some can produce all the cell types of the body and these are called “totipotent”.
 - Some can produce multiple types of cells that are part of a specific organ or tissue and these are called “multipotent.”
- Progenitor cells cannot self renew and have a limited capacity to differentiate. Usually they produce mature cells of a single type.
- Embryonic stem cells are derived from the fertilized egg and have the capacity to produce all cells in the body (i.e. totipotent), but we are only just beginning to understand how to safely control and use these powerful cells.
- Stem cells are also found in the bone marrow and many other tissues of children and adults. These “adult stem cells” have a more limited capacity to produce different cell types (i.e. multipotent), often restricted to cells of a single organ or a small number of organs.

What are “autologous” cells?

- Cells harvested from an individual that are then returned back to the same person are called “autologous” – meaning from self.
- These can be stem cells, progenitor cells or regular cells; for example, many patients provide their own blood to be used during a major surgery as an “autologous” blood transfusion.
- Autologous cells have the advantage of being immunologically identical to the person that will receive them, since they were harvested from that person. Therefore the cells themselves will not cause a rejection reaction.
- Adult stem or progenitor cells are autologous when they are harvested from the same individual that will receive the cell therapy.
- Cells that come from another person are called “allogeneic” and these are susceptible to rejection when transplanted into a different individual (just like an organ transplantation).
- Embryonic stem cells by necessity are allogeneic and therefore are susceptible to rejection.

What are “endothelial progenitor cells”?

- Progenitor cell is the name that is given to the daughter cells of stem cells that will go on to differentiate into a specific cell-type.
- Thus, “endothelial progenitor cells” (or EPCs) are progenitor cells which can produce the cells lining the inner surface of all blood vessels, called the endothelium.
- EPCs are thought to be produced in the bone marrow and are released into the circulating blood. EPCs are believed to travel to damaged blood vessels or regions that have inadequate blood supply, and contribute to blood vessel repair and regeneration.

What do stem cells have to do with pulmonary hypertension?

- We don't yet know the answer to this important question but it is an area of great interest and much ongoing research.
- At present, there are two competing scientific views:
 - Some researchers believe that certain kinds of stem or progenitor cells may actually be contributing to blood vessel thickening (remodeling) and blockage in PAH.
 - Other scientists think that progenitor cells might be able to repair damaged blood vessels and restore more normal blood flow in the lung.
- Both schools of thought may be right since there are likely both "good" and "bad" progenitor cells (like good and bad cholesterol); in other words some cells may enhance healing, but others may contribute to abnormal growth.
- Clearly, more research is needed to define better the roles of different kinds of stem and progenitor cells in PAH and how to identify "good" from "bad" cells.

What is cell therapy?

- Cell therapy is a procedure in which living cells represent the "therapeutic" agent.
- Some "cell therapies" have been around for many years, like blood transfusions.
- The use of stem cells has also been a standard practice in the treatment of certain diseases; for example bone marrow transplantation is routinely used for leukemia.
 - However, the use of stem or progenitor cells to treat heart or lung disease is very new, still experimental, and very much an area of intense research.

What about stem cell therapy for PAH?

- This is perhaps one of the more recent applications of cell therapy and it is still very much in the early phases of human research.
- In animals, a number of groups have shown remarkable benefits using various kinds of stem or progenitor cells (most often EPCs) in experimental models of PAH.
- However, there is only very limited clinical experience with progenitor cell therapy in patients with PAH, and no definitive and rigorously designed trials (i.e. like we have done for all approved PAH treatments) have been performed so far.
- Therefore, the potential benefits and risks of progenitor cell therapy for PAH are largely unknown. Therefore, it is very important that this therapy be offered only in the context of a research study that will help provide these answers.
- Stem or progenitor cell transplantation is experimental and is not a proven therapy, and it is not approved in the US or Canada for the treatment of PAH.

How can stem cell therapy be offered to patients if it is not yet a proven treatment?

- There are countries that do not prohibit the use of this unproven treatment, and some companies have set up operations in these countries to provide this therapy at considerable cost to patients.
- It is understandable that many patients may be willing to undergo cell therapy even though the risks and benefits still remain to be determined.
 - However, it is important for patients to understand that there is no solid evidence to support the clinical use of cell therapy for PAH at this time, among the possible outcomes are that cell therapy might, in some patients, actually make the disease worse, instead of better. It should be only provided as part of a research study that will address the key issues of effectiveness and safety. Practitioners who may charge large amounts of money to administer unproven treatments raise serious ethical concerns among the PH community.