

Stem Cells: Current Usage and Future Potentials

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In recent years, the term “haematopoietic stem cell transplantation” has replaced “bone marrow transplantation”. It is more precise and emphasises the “haematopoietic stem cell” as the key element. Haematopoietic stem cells (HSCs) are the earliest, most immature, cells that possess the greatest potential for self-renewal and long-term marrow repopulating capacity. These cells can be harvested from the bone marrow, peripheral blood, umbilical cord, and even the fetal liver. The sources of HSCs may be a compatible family member or an unrelated donor (allogeneic transplantation), an identical twin (syngeneic), or the patient’s own cells previously collected and suitably stored (autologous).

HSC transplantation sprang to life in the late 1960s, when 3 patients¹⁻³ with congenital immunodeficiency disorders were successfully transplanted with bone marrow cells from their siblings. In the early 1970s, Donnell Thomas and colleagues⁴⁻⁶ showed that some patients with refractory leukaemias could achieve long-term disease free survival with a marrow transplant. Later it was shown that better outcome could be achieved in patients transplanted in the early stages of disease. By the mid-1980s, allogeneic bone marrow transplant was widely accepted for the treatment of congenital immunodeficiency diseases, severe aplastic anaemias, and acute and chronic leukaemias.

Unrelated donor marrow transplant became a reality in the early 1980s. By the mid-1980s, volunteer marrow donor registries were set up in several countries, beginning with the National Marrow Donor Programme of the USA, which now has 6 million registered donors. These registries consisted of panels of HLA-typed volunteers who agreed to serve as donors for unrelated patients. The establishment of large donor panels dramatically increased the use of unrelated donor transplants.

Elaine Gluckman⁷ carried out the first cord-blood HSC transplantation in October 1988 for a young boy suffering from Fanconi’s anaemia. Stem cells from umbilical cord blood may be a good source of allogeneic stem cells for persons without a related marrow donor. However, a large supply of cord blood units must be readily available. Several cord blood banks have been set up worldwide, with a total of about 100,000 units of cord blood.

The use of HSCs has come a long way and its use is now fairly well established. However, more work is needed to reduce the risk of the transplant and to increase its effectiveness.

We are now beginning to see the use and the potential of non-haematopoietic stem cells,^{8,9} particularly in organ regeneration. It may soon be possible for a person to use a sample of his or her own stem cells to regenerate tissue, which would reduce or even eliminate the danger of rejection. How might this be done? Some possibilities include:

- ◆ Collecting healthy adult stem cells from a patient and manipulating them in the laboratory to create new tissue. The tissue would be re-transplanted back into the patient to restore a lost function.
- ◆ Therapeutic cloning may create embryonic stem cells (ESCs) that are genetically identical to the patient.
- ◆ One less invasive way to achieve this goal would be to manipulate existing stem cells within the body to perform therapeutic tasks. For example, scientists could design a drug that would direct a certain type of stem cell to restore a lost function in the patient’s body. This approach would eliminate the need for invasive surgical procedures to harvest and transplant stem cells.

On the surface, the possibilities for stem cell therapy seem limitless. However, the true potential and limitations of stem cells will need to be defined. Some questions being addressed include:

- ◆ How long will a stem cell therapy last? The reason we age is because our cells do. If adult stem cells are used in disease treatment, will the tissues created from those cells age and malfunction more quickly? Scientists do not yet know how long different stem cell treatments might last.
- ◆ Can we ensure that stem cell therapies will not form tumours in the body? Embryonic stem cells are naturally programmed to divide continuously and remain undifferentiated. To be used successfully in treatment, ESCs must be directed to

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differentiate into the desired type of tissue and ultimately to stop dividing. Any undifferentiated ESCs that are placed in the body might continue to divide in an uncontrolled manner, forming tumours.

Avoiding tumour growth is crucial to the success of stem cell treatments. In both embryonic and adult stem cells, the improper regulation of genes can lead to uncontrolled cell division and tumour formation. This is a special concern with cells that have been cultured in the laboratory for a period of time, because they may regulate their genes differently to the way they normally would in the body.

Why does this happen? Because most cells in our bodies are not meant to divide indefinitely, and none of them are meant to grow in laboratory dishes. Many tissues, such as the blood and skin, rely on a renewal process that directs cells to stop dividing, to differentiate, and even to die after a period of time. Proper direction comes in the form of signals from neighbouring cells and the environment in which the cells live.

To make cells grow indefinitely in laboratory dishes, this process must somehow be put on hold. This objective is accomplished by feeding the cells with a liquid medium containing nutrients and growth factor proteins, which together cause the cells to activate genes which promote cell division. In most cases, all the regular signals provided by the cells' normal environment are not present.

Not all cells respond well to this new living situation. Some will die, leaving only the ones that are better suited to an environment in which indefinite growth is encouraged. After many rounds of division in a laboratory dish, the surviving cells may have changed so much that they are unable to respond to the signals in the body's normal environment. They may even have permanent changes in their DNA. Putting these cells back into the body is a risky proposal, because they are conditioned to continue growing rather than differentiating, thus possibly forming tumours.

Successfully simulating the body's normal environment in the laboratory is one of the major challenges in stem cell research, and it is the focus of intensive research efforts around the world. Future therapies will rely on our ability to manipulate stem cells in a way that will be accepted as normal by the body.

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