Stem Cells – What, Why, Wh

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Stem cells are a hot issue. The reason for this extreme interest is the promise of regeneration. They are presently making big waves in life sciences research conferences, in ethical discussions, and also, already, in clinical trials. Unfortunately they have also already featured in news items relating to falsification of scientific results[1]

Modern medical science has improved health in leaps and bounds when it comes to prevention of illness through sanitation and vaccination. It has also vastly improved global health with antimicrobial drugs for treating ongoing infections. It is also greatly improving obstetric care (though there is still a lot to do in developing countries).

In the parts of the world with financial resources and access to advanced hospital care, surgery and modern medicines have also achieved tremendous success in curing cancer, heart disease, obesity and other scourges of the modern world.

Such medicines have also allowed us to control to some extent the more chronic degenerative disorders of joints, kidney, lung, liver and brain to allow an acceptable quality of life to their sufferers.

However all of this is work on preventing death of cells and tissues and on controlling symptoms as one possibly can.

Regeneration, that is, re-establishing structure and function in organs which have irreversibly lost that function, is still largely a dream – a modern dream similar to the fabled elixir of everlasting life.

Medical successes in all the fields mentioned above, through increasing the longevity of patients have created a bigger market yet for regenerative medicine. This is in the population of older people who are not yet ready to die and who are keen to maintain their health and functionality for as long as they are to live.

Those of our patients, and of ourselves who have overcome heart attacks, angina and strokes all wish to continue living to the best of their ability. As do those patients continuing to struggle with diabetes or cirrhosis and coronary bypass graft patients and cancer survivors.

The present medical facilities for treating the degenerative disorders which accumulate in us as we get older are a mixed team of talented transplant surgeons, replacing joints, livers, kidneys and hearts with plastic and metal mock-ups or better still with donor organs.

Despite the great skills of these surgeons, their job is limited by the quality, durability and lack of plasticity/healing of artificial implants and also by the scarcity and immune rejection of natural organs for donation.

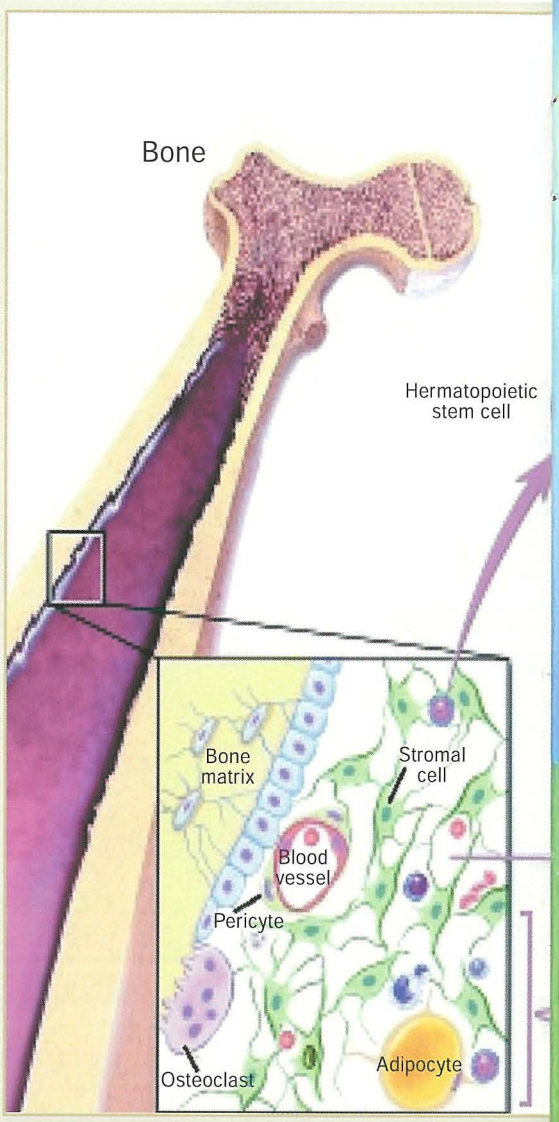
It is into this gap that the promise of stem cell therapy hopes to expand. Whilst the surgery mentioned above is a saving grace at present, I think we all hope for a day when it is largely irrelevant. As a comparison one can consider the relative obsoleteness of gastric ulcer surgery in the present milieu of endoscopy and the arsenal of anti-ulcer drugs.

Stem cells – basic definitions

So what are stem cells?

Stem cells can be broadly defined in terms of their two most salient features – the capability to self-replicate and the capability to differentiate into a wide range of derivative cell types. Both these features are necessary to make a stem cell and once a cell has these two features it shares the property of stem-ness. A cell of this nature must probably have the capability to perform a functionally polar or non-symmetric division where one daughter cell will produce another stem cell whilst the other daughter cell is programmed to differentiate into a number of more mature cell types. An easy framework in which to understand the stem cell function is in the bone marrow where a single stem cell can divide to produce a self-replica and another daughter cell which can divide to give rise to all the cell types found in blood.

Basic research on stem cells has been ongoing since the 60s when Till and McCulloch first identified colony forming units in the spleen of irradiated transplanted mice.



Different sources of Stem cells

Stem cells are usually defined by the range of cells they can differentiate into and/or according to their source of origin.

Thus one may talk about totipotent embryonal stem cells – these are the initial 8 cells in a morula (early embryo), each of which upon separation is theoretically capable of differentiating into a complete organism. In fact removal of one to two cells at this stage can be used to do genetic studies on an embryo pre-implantation[2] (as in certain

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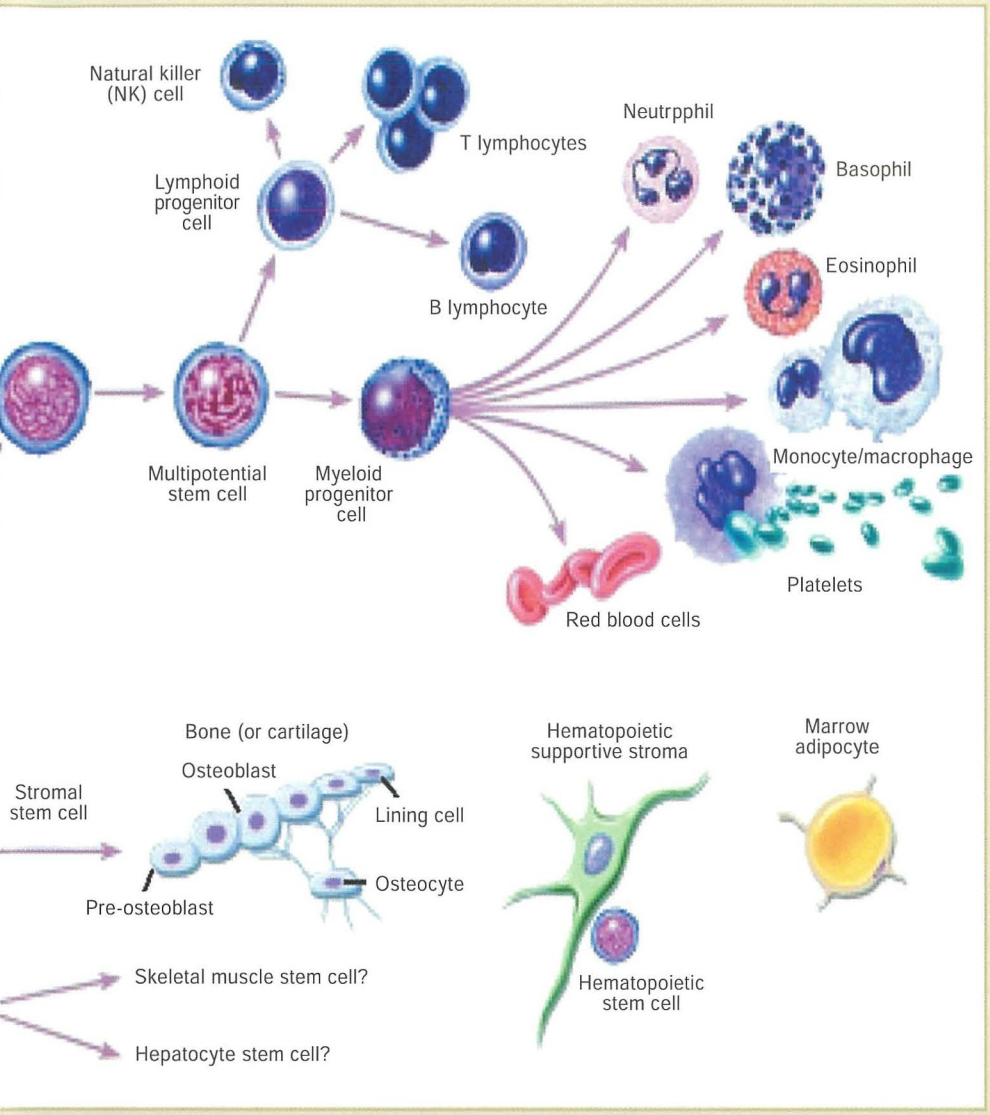

recent cases of designer babies produced with the aim of providing a bone marrow donor for ill siblings). The ability to remove such cells without destroying/perturbing the remnant group of 6-7 cells contribute to the discussion about the origins of personhood and the possibility of deriving human embryonic stem cell lines from very early embryos.

Following this, further cell divisions of the early embryo lead to a certain amount of differentiation with different cells forming the embryoblast which will give rise to the embryo and the trophoblast which will give rise to much of the placental tissue.

Cells derived from the embryoblast are usually referred to as pluripotent since they can produce almost all tissues but would not be capable inherently of producing a complete conceptus and resultant human being[3]. This is the usual source of human embryonic stem cells.

The more the embryo develops, the less the range of differentiation of its cells(with the exception of those cells destined to become germ cells); at this point, these cells are called multipotent stem cells and will differentiate into tissue specific stem cells. The natural function of these stem cells throughout embryonic development and adult life is to help replace cells lost by depletion or damage.

Embryonic stem cells are thus called because they are derived from the early embryo- the embryoblast. They can be kept proliferating in tissue culture without differentiation (usually under the influence of certain cytokines, particularly Leukaemia inhibitory factor)[4]. This 'immortality' raises the possibility of small numbers of human embryonic stem cell lines being used to treat large number of patients over long periods of years.

Stem cells with a limited pluripotency can be derived from human fetuses lost at different stages of pregnancy and may have been responsible for the partial success of fetal brain transplant surgery for Parkinsons'disease[5].

All other stem cell types commonly in discussion/study are known as adult stem cells, and here are usually named according to their source of origin – umbilical cord stem cells, bone marrow stem cells, neuronal stem cells, mesenchymal stem cells etc[6].

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