STEM CELL RESEARCH

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What is the main purpose of this whole area of stem cell research and somatic cell nuclear transfer, sometimes called therapeutic cloning?

If a person is suffering from a debilitating disease medical treatment strives to help that person recover from the disease so they no longer have to suffer from its symptoms and consequences. Modern medicine is able to bring relief to people suffering from many diseases, either with drugs or with more intrusive treatments. But where the disease results from the malfunction of cells, say in a particular organ of the body, as in type I diabetes, where the insulin forming cells of the pancreas fail to survive or lose their capability of making insulin, the hope is that stem cells capable of making the correct type of pancreatic cells will be able to be transferred to the affected pancrease and relieve the disease state of the person. Ideally the cells being transferred would be self cells, derived from the patient so immunological complications would be avoided.

This type of therapy may eventually be able to correct many different diseases including ones that are quite frequent in our society such as Heart Failure or Parkinson disease.

In laboratory experiments mouse embryonic stem cells have yielded neurons which could correct Parkinson disease in a diseased mouse. But in medicine, concerned with human diseases, this type of therapy is a long way off and currently there is a phase of intensive research aimed at accumulating the basic knowledge about how stem cells grow, how they can be induced to proceed along specific developmental pathways and how they can be kept in culture to produce the numbers of cells needed for any treatment.

Embryonic stem cells or early lineage stem cells, have the potential to enter differentiation pathways to produce the many different cell types occurring in our bodies. Adult stem cells, or late lineage stem cells, generally have a more restricted set of pathways of potential cell differentiation, mostly restricted to the cell types of the particular tissue of their origin. They also have a limited potential for multiplication, contrasting to the indefinite multiplication property of embryonic stem cells.

Both types of stem cells are subject to a great deal of research at present and are likely to be of complementary value both in research, providing increased knowledge, and in the future for the therapeutic correction of disease states.

In Australia the legislation permitting medical research with spare embryos, and embryonic stem cell lines, was put into place in 2002. It was made extremely clear in the legislation that there is a strict ban on any reproductive cloning and implantation of embryos is strictly prohibited.

What has happened since 2002, has there been any progress? Is there increased understanding?

There have been several thousand research papers published relating to human stem cell science since 2002. These papers have concerned both embryonic and adult stem cells. There are some important examples that I can cite relating to embryonic stem cells. Chang et al, PNAS January 2006, showed that it was possible to correct a common disease-causing mutation in embryonic stem cells which results in sickle cell anaemia. Single gene disorders such as Thalassemia and Cystic Fibrosis may ultimately be able to be corrected in this way.

Ludwig et al, Nature Biotechnology 2006, showed it was possible to grow human embryonic stem cell lines without using any animal cells or serum. This finding will be of importance if stem cells are to be used in human therapy.

Barberi et al, Nature Biotechnology October 2003, showed that culture conditions allowed mouse embryonic stem cells to proceed down the neuron cell differentiation pathway.

Blelloch et al, PNAS 2004, showed that mouse somatic cell nuclear transfer could be used to study why some stem cells can cause cancers while others do not. There have been hundreds of other advances in knowledge surrounding the isolation, culture and control of differentiation of stem cells.

A great deal more research is needed in order to achieve sufficient knowledge and expertise to demonstrate that cell lines derived from either embryonic or adult stem cells, will be able to be used in therapeutic treatment of a wide array of human disease states.

Embryonic stem cells are usually obtained from spare embryos from IVF procedures. These are donated either to other couples, they may be

discarded, or they are able to be used in research. Researchers must be licensed to carry out research and all experiments are under strict regulatory controls. The stem cells are isolated from these IVF obtained embryos after they have been cultured for a specified short period. The isolated stem cells can then be nurtured in cell culture conditions.

Another source of embryonic stem cells, proven many years ago in animal systems, is through the insertion of a nucleus from a somatic (body) cell into an enucleated egg cell. In humans the egg cells would be obtained by the same procedures used for IVF. In cases of diseases such as insulin dependent diabetes and motor neuron disease, it may be possible initially to use both somatic nuclei and egg cells from affected women because in this case the whole cellular environment would be identical to the cell environment of the person suffering from the disease.

In the Lockhart Review it was suggested that animal eggs could be used for some of the research so that fewer human eggs would be required. Many scientists think that using a nucleus and egg cell from different species complicates the research. Most scientists regard this particular recommendation to be of little importance.

All the processes of development of humans depend on the programmed actions of sets of genes working successively in a range of determined patterns. Each cell in our body has the same set of genes but different sub-sets of these genes are active in different cell types. Some housekeeping function genes may be active in more than one cell type but others are known to be specific to be particular cells. For example kidney cells have a set of genes which are active in coding for everything needed for kidney cell function and muscle cells or brain cells also have specified sets of genes programmed for action.

Stem cell research needs to learn how to deprogram cells which are committed to specific differentiated functions so that they return to an embryonic or totipotent state. The stimuli and conditions necessary to promote the gene programs needed for the development of specified cell types can then be provided. When this level of knowledge is achieved from the research process the great promise of cell-based therapies will be much closer to reality.