STEM CELLS

Stem cells are cells not yet specialized to perform a particular function. They have the potential to differentiate into blood cells, muscle cells, neurons and many other types of cells that perform a specific function. Stem cells have two possible fates: they can divide repeatedly or they can differentiate to produce the cells needed for growing tissues through self-renewal. The most versatile form of stem cells are those found in the blastocyst of an embryo four to five days after fertilization. These are totipotent or pluripotent stem cells, meaning they can differentiate into all or nearly all types of cells in the body. Embryonic stem cells can be isolated and grown in a laboratory where they can grow more or less indefinitely and may provide an almost endless supply of new cells for transplantation; however, there are numerous ethical concerns about using them for potential therapeutic purposes. “Adult”, multi-potent stem cells are more specialized stem cells. They are less able to multiply and are already specialized such that the number of cell types they can give rise to may be limited to cells in the same family or “lineage”. These are cells that work throughout our lives to renew tissues.

Focusing on the nervous system, the conventional view of non-neural adult stem cells is that they are already too specialized but other scientists dispute this view, saying that these cells could nourish or protect neurons in some way. Some neural stem cells can be found in the adult nervous system, but there are few and their activity is limited. Scientists are looking at ways to “kick start” these stem cells with growth factors, so they could develop into neurons and neural support cells called glial cells (or glia). Following a breakthrough discovery in 2006, a new source of stem cells was identified. These cells are called induced pluripotent stem (iPS) cells. iPS cells are reprogrammed adult cells most commonly taken from a patient’s own skin but muscle, liver, as well as other tissue types can also be sources.

Scientists found a way to “turn back the clock” on skin cells, such that they will have a pluripotent potential believed to be equivalent to embryonic stem cells. This new source of stem cells circumvents the most serious ethical concerns; however, there are concerns about their use as they involve the use of viruses and the cells are genetically modified in such a way that they have potential to give rise to cancers. An advantage to the use of iPS cells is that they come from the patient, eliminating the rejection problems that come with transplantation of donor cells.

CELL PROTECTION

Neural stem cells secrete neurotrophic factors that nourish and protect neurons which could help protect existing motor neurons and slow progression.

HOW IT COULD HELP

To benefit patients living with ALS, stem cells would ideally support neuroregeneration, replacing damaged neurons and spurring functional recovery, but also could serve a secondary role by protecting neurons from injury.

CELL REPLACEMENT

Glial cells, that help support and protect neurons, are also affected by ALS; replacement glial cells might slow the progress of the disease. In theory, these glial cells could be manipulated to enhance their protective properties and scientists are currently testing approaches to make this happen with transplanted neural stem cells.

NEURON REPLACEMENT

This type of treatment is challenging in the setting of current knowledge and technology. The environment in the areas studied in the nervous system seems to encourage stem cells to develop into glial cells, rather than into neurons. Even if neural precursor cells receive signal to become motor neurons, they then need to grow processes (axons and dendrites) to make the right connections in the complicated wiring of the nervous system.

STEM CELLS

The ALS Society of Alberta

A DRUG DELIVERY SYSTEM

Some stem cells are naturally able to "hone in" on damaged areas. It may be possible to take advantage of this property and to genetically alter these cells to express specific beneficial molecules to prevent side effects that may result from a less targeted approach. In some animal models, injection of stem cells has shown some positive results. Stem cells injected into mice with SOD1 variant familial ALS have extended the life span of the mice, but did not prevent death. Clinical trials of stem cells in humans with ALS are taking place in the United States; however, they are in early stages where the safety and tolerability of therapies are still being studied.

CURRENT CHALLENGES

There are many hurdles to overcome before stem cell treatments would be viable, such as the determination of:

- The right type of stem cell for treating ALS must be determined.
- The correct site and method of transplantation.
- The chemicals that will encourage growth and differentiation of stem cells.
- Therapies that will prevent rejection and establish the safety of transplantation.

WHAT TO BE CAUTIOUS OF

- Claims based on testimonials rather than evaluated clinical research.
- Claims of multiple disease being treated with the same cells.
- If it is not clearly documented, the source of the cells or how the treatment will be done.
- Claims that there are no risks or dangers.
- High cost of treatment or hidden costs. Note that it is not customary for someone to pay to be part of a clinical trail.

ALS affects a large number of areas, requiring neural regeneration in multiple regions in the brain and throughout the spinal cord. Some of the stem cell treatments being carried out overseas involve injecting stem cells into the bloodstream and allowing the body to direct their use. This type of treatment may not be useful for ALS, as it is not known if cells from the blood readily enter the nervous system. Even assuming an available treatment could successfully transplant stem cells into the nervous system, restoring function following motor neuron loss would require that a stem cell differentiated into a motor neuron and grow along the same route as the defunct motor neuron to connect the muscle it served to the very specific part of the brain that controlled that muscle. While the few millimetres of growth seen in animal models takes months to achieve, some motor neurons would need to grow a metre in length. Even if nerves regenerate with such a hypothetical treatment, it does not mean that proper neuromuscular function will be restored. It is not known how to control stem cell growth within the nervous system, how to encourage normal development, differentiation, proper muscle innervations by the neurons, how to prevent them from making "bad connections", or to what extent the development of inappropriate or cancerous cell types will occur. Unlike drugs, stem cells cannot necessarily be made and tested in large quantities and treatments may need to be specific to each patient. At present, some scientists believe that the use of stem cells to provide support and therapy to motor neurons that are still surviving is the approach that will yield the earliest success. The most important question to ask about stem cell treatment for ALS is when we will understand enough about using stem cells to make an impact on the disease. When considering a stem cell therapy, look for preclinical studies that have been published, reviewed and repeated by other experts. The providers should have approval from independent committees and national or regional regulatory agencies to ensure the risks are as low as possible and that the potential benefits are worth the risk.

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ETHICAL CONCERNS

There are numerous ethical issues surrounding the use of embryonic stem cells. Gathering embryonic stem cells result in the destruction of the blastocysts. Sources of embryonic stem cells include aborted embryos and unwanted embryos from in vitro fertilization (IVF) procedures. Donations of human eggs are in short supply and altruistic donation is an invasive and potentially harmful procedure.

One alternative, therapeutic cloning, as a source of embryonic stem cells, presents concerns as well, as scientists have not perfected the process of somatic cell nuclear transfer. As a result, many eggs could be wasted in failed attempts before stem cells could be successfully obtained. To get around this, researchers could use animal eggs for somatic cell nuclear transfer; however, this involves creating an animal/human hybrid embryo, a process that is considered unacceptable for both medical and ethical reasons. Bill C6, the Assisted Human Reproduction Act, became law in Canada in March 2004. This bill regulates in vitro fertilization and prohibits human cloning. This bill provides balance between respect for human life and potential for modern science. ALS Canada funds peer-reviewed research (which goes through a rigorous peer review process by researchers in the Canadian scientific community) and funds research that is evaluated at a high level using international evaluation methods adopted by the Canadian Institutes of Health Research.

The ALS Society of Canada does not fund any research employing totipotent cells which are derived from intact or modified human embryos and will not do so until there are federally established guidelines. ALS Canada encourages researchers to apply revolutionary methods that create stem cells from a patient's own body to find treatments and cures for ALS.

OVERSEAS TREATMENT

Many clinics overseas are capitalizing on the hope of stem cell treatments, and are marketing directly to the consumer over the internet. However, these clinics are uncontrolled, non-approved and their "treatments" are not based on scientific evidence or accepted clinical practices. Many clinics offering stem cell treatments are located in developing countries, where this type of procedure is unregulated. There is no evidence verifying that overseas stem cell "treatment" is safe. No ALS patient has yet been known to recover from the disease as a result of a commercially available stem cell treatment - although many have paid out of their own pocket for such treatments. Clinics may also be contributing to public expectations that exceed what the field can reasonable achieve. Most of the websites advertising stem cell treatments do not mention the risks or side effects. The practices promoted in these websites have not undergone proper clinical trials to prove their efficacy and may pose serious risks. For example, some of these companies offer stem cells taken from umbilical cords of aborted fetuses, despite no clear evidence that this could benefit an ALS patient, or that the source is safe and disease-free. Given the limited abilities of sorting out cell populations, it is possible that these "stem cell therapies" contain numerous other types of cells. Characterizations of the types of cells being given to patients are not provided to the public or the scientific community. Rarely is follow-up provided and placebos are not tested. Examples of routine follow-up clinical assessments include muscle strength testing and EMG. Measurement of forced vital capacity (FVC) could be used to prove whether these therapies are effective; however, the average cost of a course of these therapies among the sites mentioned costs approximately $21,500, excluding travel. ALS Society of Alberta supports the individual's right to choose what treatment they wish to undertake but strongly recommends that anyone considering alternative treatment discuss the issues surrounding such a treatment with their physician before making a final decision.

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ALS professionals represent a close-knit community dedicated to understanding and finding a cure for this disease. People living with ALS should be assured they will not miss out on meaningful therapy, as long as they maintain membership of or contact with a recognized ALS clinic, association or society.

ONLINE RESOURCES

The ALS Society of Alberta Web Site: www.alsab.ca

The ALS Society of Canada Web Site: www.als.ca

Aligning universities, industry, government and non-governmental organizations, the stem cell network is devoted to pursuing Canadian leadership in stem cell research:
www.stemcellnetwork.ca

Canadian Institute for Health Research's guidelines for stem cell research:
www.cihr-irsc.gc.ca/e/15255.html

International Society for Stem Cell research:
www.isscr.orgg

Australian Stem Cell Centre: www.stemcellcentre.edu.au

List of ALS-related clinical trials occurring in the United States:
www.clinicaltrial.gov/ct2/results?term=ALS

The ISSCR patient handbook on stem cell therapies:
www.isscr.org/clinical_trans/pdfs/ISSCRPatientHandbook.pdf

Stem Cells and MND (ALS) from the MND Association of Great Britain:
www.mndassociation.org/research/research_explained/stem_cells_and_mnd/index.html

A Guide to "Stem Cell Tourism":
www.treat-nmd.eu/patients/stem-cells/stemcelltourism

BBC article about clinic offering false treatments:
www.news.bbc.co.uk/2/hi/health/4985230.stm

BBC article about the risks of stem cell treatments:
www.news.bbc.co/uk/1/hi/health/4561933.stm

Episode of 60 Minutes, featuring an expose of a clinic in Mexico offering fraudulent stem cell treatments for ALS:
www.cbsnews.com/video/watch/?id=6408512n&gtag=cbsnewsMainColumnArea.2