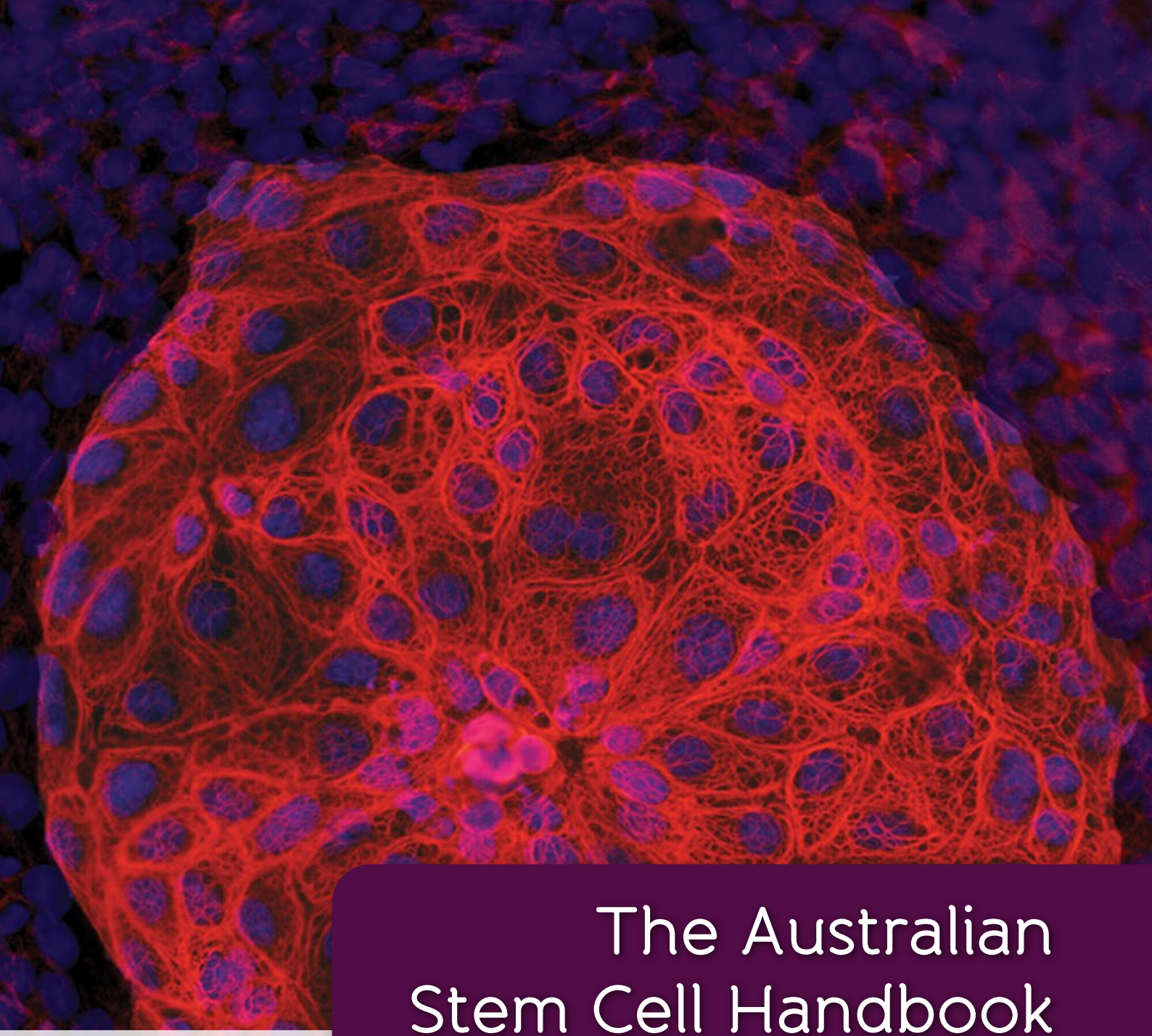

The Australian Stem Cell Handbook

What you should know about stem cell therapies: *now and in the future*

April 2015

National Stem Cell Foundation of Australia

STEMCELLS AUSTRALIA

The National Stem Cell Foundation of Australia

The National Stem Cell Foundation of Australia (NSCFA) is a not-for-profit company limited by guarantee (ABN: 84 152 713 098) and an Australian Tax Office endorsed charity. NSCFA was established in 2011 as the follow-on organisation from the Australian Stem Cell Centre. Our mission is to promote the study and use of stem cells in the prevention or control of disease in human beings and to enhance public education in this field. As a registered charity, all donations made to the Foundation are tax deductible and will be used to support stem cell research and enable us to continue our public education and outreach activities.

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Stem Cells Australia

Stem Cells Australia brings together experts in bioengineering, nanotechnology, stem cell biology, bioinformatics and clinical research to address the big challenges in stem cell science. Through a greater understanding of stem cell growth and development, this Australian Research Council-funded Special Research Initiative aims to develop innovative biotechnology and therapeutic applications. The Initiative also seeks to guide public debate about the important ethical, legal and societal issues associated with stem cell science. Stem Cells Australia was established in 2011 by The University of Melbourne, University of Queensland, Monash University, University of NSW, Walter and Eliza Hall Institute for Medical Research, The Florey Institute of Neuroscience and Mental Health, Victor Chang Cardiac Research Institute and Commonwealth Scientific and Industrial Research Organisation.

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The purpose of the Handbook

Stem cells are seen as a key tool in the future of medicine, for their abilities to regenerate damaged tissue, replace missing tissue and repair the effects of disease or injury. Experimental stem cell therapy is being developed for many common diseases, including blindness, stroke, arthritis, multiple sclerosis and heart attacks. Important research is being undertaken by reputable hospital, biotechnology and university groups in Australia and around the world. However, it is still early days, and some private non-academic organisations and individual practitioners are offering stem cell treatments that have not been shown to be effective and have not been proven to be safe.

We recognize that patients and families who are facing severe illness or injury may consider trying untested treatments, especially when there seem to be few other options. People in this situation may be at risk of harm, through lack of information or misinformation provided by less reputable practitioners who are not recognised specialists or experts in the diseases they are proposing to treat.

We recommend that you are very cautious before you agree to try an untested treatment, particularly if it costs a lot of money. Your regular hospital doctors and specialists, and your general practitioner, should be able to offer accurate advice on which treatments have been proven to work, and which are unproven, unlikely to help, and may even cause harm. If it sounds to be too good to be true, it is probably unlikely to help you. The best protection for patients and families in this situation is to be fully informed.

The Australian Stem Cell Handbook aims to provide you with answers to some common questions regarding stem cells, their use in medicine, and their promise for future therapies. It also aims to equip you to ask the right questions when researching stem cell treatments, to enable you to make the best choice for your health care.

About the Handbook

The Australian Stem Cell 2015 Handbook (the Handbook) is the second Edition of this resource which has been updated to reflect advances in stem cell science and clinical research, and the increasing number of unproven stem cell treatments being offered in Australia and overseas.

This Handbook has been written to help you gain a greater understanding of:

- Stem cells and what makes them so special
- Currently proven stem cell treatments
- The use of stem cells in research laboratories
- How experimental stem cell research becomes accepted and proven medical therapy
- How to recognise unproven stem cell treatments and why you should be careful pursuing them
- Current stem cell clinical trials and how to find out more

The Handbook aims to help you in your quest for information, and in critically analysing this information before making a decision to pursue stem cell treatment. As with all treatments, there are risks involved. We do not seek to advise you on what is appropriate treatment for you. We strongly advise you to take the information you gather back to your treating doctors and discuss with them what is most suitable for you. Importantly, we raise concerns about unproven stem cell treatments that are being offered in Australia and overseas. Please remember that just because a treatment is being offered in Australia does not make it a proven, safe and effective therapy.

Key signs that a stem cell treatment is likely to be unproven:

- **When the experimental treatment being offered is not part of a registered clinical trial**
- **Where many different diseases or conditions are treated with the same type of stem cell and procedure**
- **When patient testimonials are used to support claims of benefit with no independent verification, and no published scientific papers**
- **When the treatments are being advertised directly to you on the Internet, TV, radio or in newspaper articles and advertisements, rather than via referral from your treating doctor**
- **When it is claimed that there are no risks involved in the treatment**
- **When you are asked to pay for a treatment that is not yet an accepted medical practice**
- **When there is no Medicare or private insurance rebate for the treatment**

Authors: Associate Professor Megan Munsie PhD BAppSci from Stem Cells Australia has led the revisions of this version of the Handbook, with extensive input from members of the NSCFA Board's Scientific and Ethics Subcommittee Dr Chris Juttner MBBS BMedSci FRACP and Dr Karin Tiedemann MBBS FRACP, together with Dr Kirsten Herbert MBBS BMedSci FRACP PhD, Consultant Haematologist, Deputy Director Centre for Blood Cell Therapies, Peter MacCallum Cancer Centre. The authors are grateful for the additional contribution of our colleagues who were consulted during the preparation of the Handbook.

The Handbook was first published in 2013 by The National Stem Cell Foundation of Australia with the assistance of Stem Cells Australia and was based upon the 2009 'The Australian Stem Cell Centre Information Handbook'.

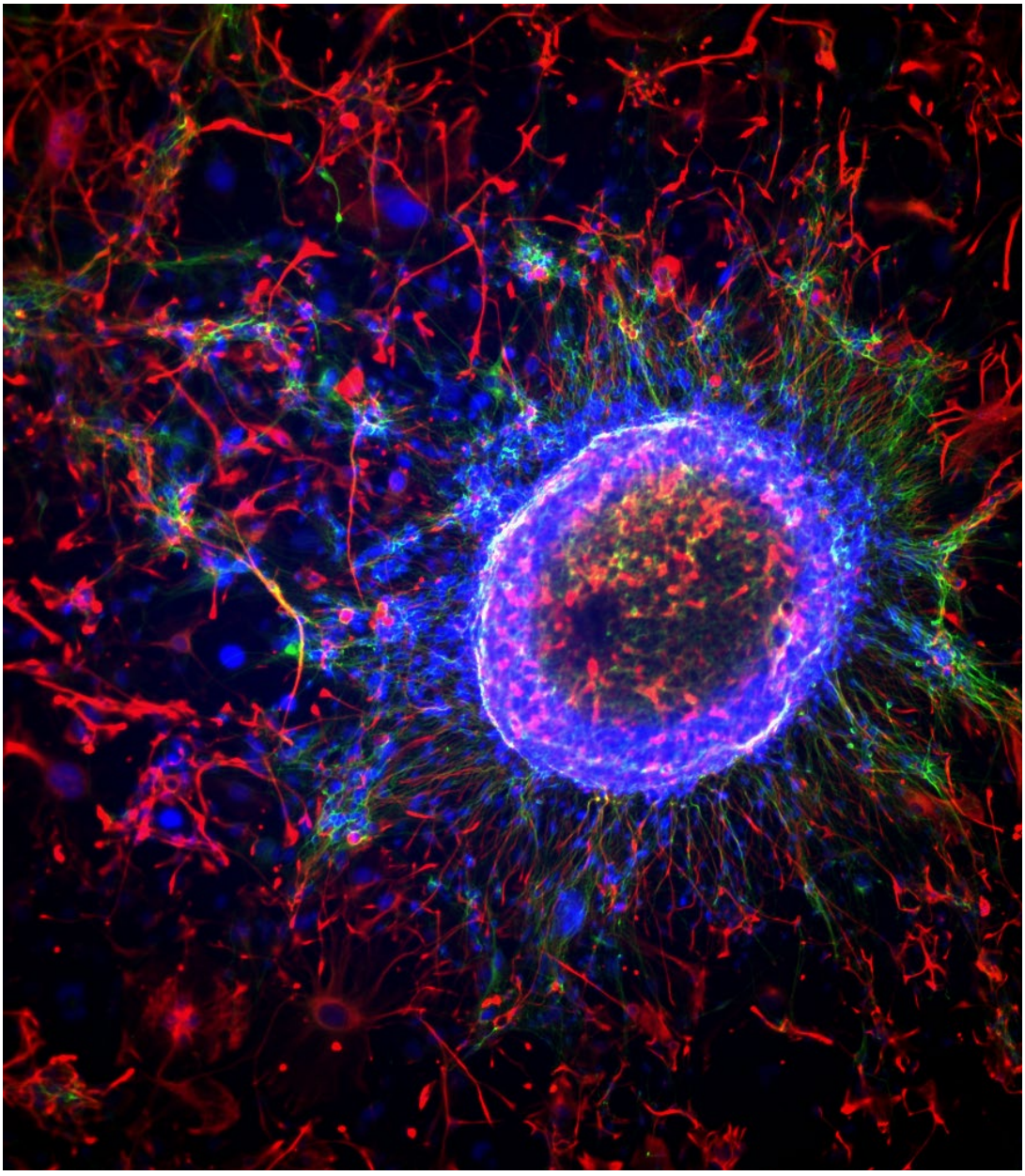
Stem cells and what makes them so special

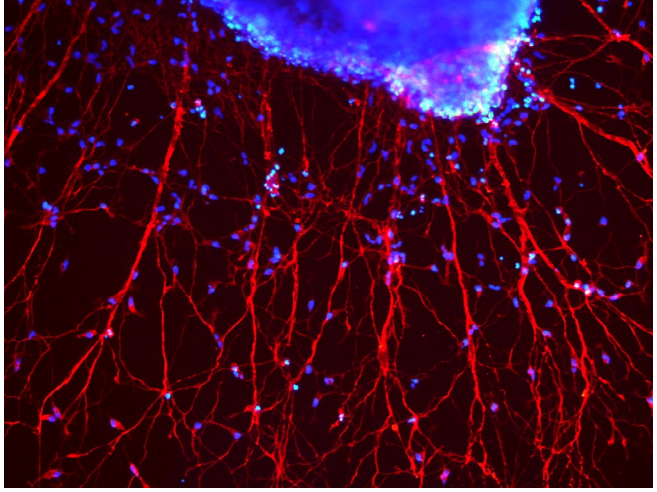
The human body is made up of over 200 different kinds of specialised cells such as muscle cells, nerve cells, fat cells and skin cells. All specialised cells originate from stem cells.

Stem cells are different from other cells in the body in two main ways:

- **Stem cells are capable of self-renewal.** Stem cells are able to divide and produce copies of themselves.
- **Stem cells can differentiate.** They can divide and produce cells that have the potential to become other more specific cell types, tissues or organs. These new cells and tissues can repair or replace damaged or diseased cells in the body. Stem cell differentiation is an essential part of normal growth, development and repair of injury and aging.

Any compromise in stem cell function can have a significant impact on health.





Types of stem cells – more than just one

Stem cells can be divided into two broad groups: tissue-specific stem cells (also known as adult stem cells or somatic stem cells) and pluripotent stem cells (including embryonic stem cells and induced pluripotent stem cells).

Tissue-specific stem cells

Tissue-specific stem cells have the potential to change into a limited number of other types of cells. Usually they grow into the type of cells existing in the tissue or organ where they are found. These stem cells are often referred to as being multipotent as they can grow into some but not all of the cells of the body.

The chief role of tissue-specific (adult) stem cells is to maintain and repair the tissue in which they are found. They are capable of some self-renewal but their differentiation (what they can turn into), is limited to the tissue or organ where they were found.

Most tissues contain adult stem cells, although in low numbers. Adult stem cells have been identified in brain, heart, eye, muscle, lung, pancreas and liver tissue, as well as in highly regenerative tissue such as bone marrow, skin and lining of the intestine.

Some adult stem cells are readily available for repair and regeneration in disease or injury, such as blood or skin stem cells. Other adult stem cells seem unable to respond. Understanding how this process works and whether it can be applied to other types of adult stem cells is driving research programs in Australia and around the world. For example, even though we have known about blood stem cells in bone marrow (also referred to as haematopoietic stem cells or HSCs) for many years, and know a great deal about how to use them in bone marrow transplantation, we still don't know how to best grow and control these cells outside the body.

Bone marrow, umbilical cord blood, and the placenta are all a good source of another type of adult stem cell called mesenchymal stem cells or mesenchymal stromal cells (MSCs). MSCs have also been identified in fat isolated by liposuction.

MSCs have a possible role in regeneration of bone, cartilage and fat and have anti-inflammatory and immunosuppressive properties. They are currently being used by researchers to:

- investigate possible regenerative therapies including orthopaedic and cardiovascular conditions
- suppress graft-versus-host disease in donor marrow transplantation
- attempt to modify various autoimmune diseases such as multiple sclerosis and systemic lupus erthematosis

Another type of tissue-specific stem cell that is being widely investigated is the human fetal stem cell. These cells are obtained from donated tissue after termination of pregnancy. Like other tissue-specific stem cells, fetal stem cells are multipotent, which means they can usually only grow into the type of cells existing in the tissue or organ where they are found.

Researchers are exploring the capacity of neural stem cells derived from fetal brain tissue to assist in the repair of spinal cord injury, stroke and neurodegenerative diseases such as Parkinson's disease and Motor Neurone Disease. In addition, fetal pancreatic cells are also being investigated for the treatment of type 1 diabetes. In Australia, the use of human fetal tissue in research is regulated through state and territory legislation, underpinned by guidelines issued by the National Health and Medical Research Council (NHMRC).

Pluripotent stem cells

A pluripotent stem cell has the ability to develop into any type of cell in the body. Both embryonic stem cells and induced pluripotent stem cells are defined as pluripotent. This unique growth characteristic makes these cells very valuable for research, but also means that they have the potential to form tumours. Safety considerations need to be addressed when these cells are used in the clinic.

Embryonic stem cells

First identified in 1998, human embryonic stem cells (ESCs) are the most primitive type of stem cell. They can be maintained as self-renewing stem cells indefinitely in the laboratory (unlike most tissue-specific stem cells) and potentially can differentiate or turn into any cell type in the human body.

Human ESCs are derived from donated human embryos at a very early stage of development (approximately seven days after fertilisation). They have the ability to keep dividing (self-renewing) for a long time, possibly forever, and large numbers of human ESCs can be grown in the laboratory and frozen for future use.

Human ESCs are shared by researchers around the world as they attempt to learn more about the process of differentiation and development, and ultimately to develop new regenerative therapies. In Australia it has been legal since 2002 to use donated human embryos that are no longer required for infertility treatment to produce new ESCs, provided the researchers have obtained a licence issued by the Embryo Research Licensing Committee of the NHMRC under the Research Involving Human Embryos Act 2002.

Embryos used in research include those shown to carry a genetic mutation. For example, Genea (formerly Sydney IVF) has derived human ESCs from embryos affected by Huntington's disease, a rare and devastating neuromuscular condition. These human ESCs are available to biomedical research laboratories and provide a valuable tool to investigate the mechanisms underlying the disease and to model potential treatments for Huntington's disease.

Induced pluripotent stem cells

In 2006, scientists in Japan announced they had developed a new way to make pluripotent stem cells directly from an adult cell. These cells are referred to as induced pluripotent stem (iPS) cells, because they are coaxed, or induced, into becoming stem cells by modifying the activity in the cell's genes.

Currently, iPS cells are generated from an adult cell by reactivating a small number of genes, turning the mature specialised cells back into pluripotent stem cells (a process called reprogramming). Although the mechanism by which these genes cause adult cells to become pluripotent is not yet fully understood, the technique holds great promise for stem cell research and regenerative medicine. It presents a new opportunity to generate disease-specific stem cell lines in order to study certain disease conditions and to screen promising new drugs.

Many laboratories around the world are now working with iPS cells. Scientists are using different types of donor cells to make iPS cells, and trying to improve the efficiency of the reprogramming process. For example, the first attempts to make iPS cells relied on the use of special viruses to introduce key genes into the adult cells. This raises concerns about cancer-related genes being incorporated into the stem cell and the potential consequences of this in forming tumours. New techniques have since been developed that reduce the reliance on the use of viruses.

Scientists are also focusing on ways to change one type of adult cell directly into another, a process termed direct reprogramming. This process has already been reported for the generation of heart muscle, nerve, blood and pancreatic cells.

It remains to be seen which reprogramming methodologies are most robust, safe and potentially clinically useful. Nevertheless, these examples highlight the rapidly changing and somewhat unpredictable nature of iPS cell reprogramming.

While the discovery of iPS cells is a significant breakthrough, as was recently acknowledged when the discoverer, Shinya Yamanaka, was awarded the 2012 Nobel Prize for Medicine or Physiology, they are only just entering clinical trials. The first of these trials (being run in Japan) is in macular degeneration, and the world awaits the results of this trial, both for its effectiveness in treating blindness, and for safety and side effect data. Although there are several other groups moving towards clinical trials, more research is required into issues such as the genetic stability of iPS cells, safety and the methods for generating the desired differentiated cells.

However, the use of disease-specific iPS cells is likely to be extremely valuable in better understanding the underlying mechanism of specific diseases, potentially leading to new treatments.

Stem cell treatments that are proven as effective therapies

Although there is a great deal of attention surrounding the potential of stem cells, in reality the range of diseases for which there are current proven treatments using stem cells is quite small.

Within Australia the only proven treatments available involving stem cells are corneal and skin grafting, and blood stem cell transplants for the treatment of some blood, inherited immune and metabolic disorders, cancer and autoimmune diseases. There are many other potential treatments, but these are still in the research phase or in clinical trials, and are yet to be proven safe and effective.

HSC transplants for disorders of the blood, immune system and some cancers

Blood stem cell or haematopoietic stem cell (HSC) transplants have been used successfully around the world for many years in the treatment of patients with a variety of life threatening disorders resulting from inherited or acquired disorders of the haematopoietic stem cell. Examples of inherited disorders are severe immune system defects, thalassaemia and a variety of metabolic disorders which affect many organ systems. The commonest acquired disorders for which HSC transplants are regularly used are leukaemia, multiple myeloma, lymphoma and aplastic anaemia. HSCs are either collected from the peripheral blood after mobilisation from the bone marrow using growth factors, or now less commonly directly from the bone marrow. Transplantation of these HSCs can restore blood and immune system function in patients after their own bone marrow stem cells have been suppressed or destroyed as a consequence of underlying bone marrow disease, chemotherapy, radiotherapy or a combination of these mechanisms.

Whether the stem cells are obtained from the patient themselves (autologous) or from a donor (allogeneic), will depend on the condition being treated. Following high-dose chemotherapy and radiotherapy, HSCs can 'restore' the function of the bone marrow. Allogeneic transplantation will result in a new donor immune system being established, restoring immune function and potentially mediating an immune effect on the underlying disease.

Figure 1 illustrates the many disorders for which HSC treatment has been used, with varying success. This is not an exhaustive list but its diversity illustrates the variety of disorders that may benefit from this procedure.

The use of HSC transplants for some autoimmune disorders remains controversial. In many of these diseases HSC transplant is still considered to be an experimental form of therapy reserved for aggressive cases of the disease that do not respond to any other available treatments. Responses to HSC transplantation can be highly variable and more research is required to understand which patients are most likely to benefit.

Umbilical cord blood is a rich source of HSCs with similar characteristics to those of bone marrow HSCs. With parental consent, blood can be collected from the umbilical cord of a newborn baby shortly after birth and stored in public cord blood banks for general use, or private banks for the child's own possible later use.

It is over 20 years since the first successful umbilical cord blood stem cell transplant. These cells are currently used mostly in children to treat the same range of disorders as listed in Figure 1.

Umbilical cord blood as a source of HSC has a number of potential advantages for both adults and children as an alternative to bone marrow. This includes rapid availability, a lower incidence of graft-versus-host disease, and a higher degree of tolerance of donor mismatch (ie human leukocyte antigen or HLA mismatch).

The main disadvantage of umbilical cord blood is the small number of stem cells in a cord blood collection, which limits recipients to children and small adults. For adults this limitation is being addressed through using two cord blood units for a single transplant, as well as intense research into ways of increasing the number of HSCs in umbilical cord blood.

Corneal and skin grafts

These forms of surgical transplantation have been around for decades. They work because of the stem cells that reside within the tissues of the cornea and skin. There is active research, including in Australia, into ways of increasing the success rate of both these forms of treatment.

Figure 1: Some conditions that are routinely treated with HSC transplants

Autologous HSC transplantation		Allogeneic HSC transplantation	
Malignant disorders	**Non-malignant disorders**	**Malignant disorders**	**Non-malignant disorders**
Neuroblastoma	Autoimmune disorders	AML	Aplastic anaemia
Non-Hodgkin lymphoma	Amyloidosis	Non-Hodgkin lymphoma	Fanconi anaemia
Hodgkin lymphoma		Hodgkin lymphoma	Severe combined immunodeficiency
Acute myeloid leukaemia (AML)		Acute lymphoblastic leukaemia (ALL)	Thalassemia major
Medulloblastoma		Chronic myeloid leukaemia (CML)	Diamond-Blackfan anaemia
Germ-cell tumors		Myelodysplastic syndromes	Sickle cell anaemia
Multiple myeloma		Multiple myeloma	Wiskott-Aldrich syndrome
		Chronic lymphocytic leukaemia (CLL)	Osteopetrosis
		Myeloproliferative neoplasms	Inborn errors of metabolism
			Autoimmune disorders

Adapted from Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med*. Apr 27 2006;354(17):1813-26.

How stem cells are being used in research laboratories

While stem cells hold lots of promise for future clinical treatments, it is in research laboratories that stem cells are already making their mark.

Research scientists around the world are using a variety of stem cells to better understand the big questions - how do stem cells 'decide' what to become and how can we influence and control these processes? We need answers to these important questions if the promise of stem cells in regenerative medicine is to be fully realised.

Scientists are already able to influence and direct the growth of stem cells in the laboratory. For example, researchers at Monash University and the Murdoch Childrens Research Institute have been able to grow blood cells, insulin producing cells and heart muscle cells from human ESCs. By growing these cells in the laboratory, scientists can better understand how normal tissues develop and what can go wrong in disease. An example of a practical application is the potential use of heart muscle cells made from stem cells in screening for new drugs to treat heart disease. The same possibilities apply to other cell types and diseases.

The majority of the public discussion and debate concerning stem cell research has focused on the development of cellular therapies for incurable, often fatal diseases (known as regenerative medicine). However, researchers are equally as excited by the possibilities that stem cell research offers for studying human disease in the laboratory. Scientists have developed methods to grow stem cells affected by particular diseases, in very large numbers in the laboratory. These cells are then able to be used to study how a disease occurs at the cellular level. A better understanding of the diseased cell then allows researchers to design hundreds or even thousands of candidate drugs to treat a disease, and then select the most effective drugs to trial in human patients.

In this way, stem cells can be used to create a 'disease in a test tube' and rapidly expand the pathway to discovery of new treatments.

One such condition is the devastating neurodegenerative disorder Motor Neurone Disease (MND).

Scientists at Harvard University have made iPS cells from people with MND and have coaxed them into forming the motor neurons that are destroyed by the disease process. This means the researchers have overcome one of the greatest hurdles to studying MND and can now study the nerves that are affected by this disease. In addition to MND, researchers have now derived pluripotent stem cells for many other diseases, including Parkinson's disease, Friedreich's ataxia, Down's syndrome and Huntington's disease.

The study of tissue-specific stem cells also provides the opportunity to understand the origin and regulation of cells in disease. Researchers at the Walter and Eliza Hall Institute for Medical Research are studying normal and malignant breast stem cells with the goal of identifying markers of, and potential treatments for, breast cancer.

Other groups are trying to unlock the secrets held by tissue-specific stem cells in the brain and heart. It is known that stem cells are present in these organs and that they retain a limited ability to grow in response to disease or damage; but can they be coaxed to do more? Can new treatment approaches be developed that stimulate tissue-specific stem cells at the site where they exist and encourage them to self-repair? Only more research will enable us to answer these questions.

How experimental stem cell research becomes accepted and proven medical therapy

To test a proposed therapy, scientists and doctors perform clinical trials.

While there are widely accepted and clinically proven stem cell treatments, they are limited to corneal and skin grafts, and blood stem cell or HSC transplantation for diseases of the blood and immune system. All other stem cell treatments are not considered to be accepted medical practice and still require clinical research to fully evaluate their safety and proposed benefit. Under exceptional circumstances, doctors may decide to treat a patient with a 'one-off', unproven treatment outside the clinical trials framework. This is known as 'medical innovation'.

Clinical trials

Clinical trials of proposed stem cell treatments are undertaken to determine their safety and effectiveness.

In Australia, clinical trials are reviewed by a Human Research Ethics Committee (HREC) in accordance with the guidance provided in the National Statement on Ethical Conduct in Human Research, 2007. The HREC is composed of individuals with expertise in ethics, research, law, pastoral care and health, as well as members of the general public.

The results of approved clinical trials are usually published in scientific journals. In this process, respected peers in the field of research critically evaluate whether the research was ethical and based on sound scientific and statistical principles and whether the results stand up to rigorous scrutiny.

Peer review of clinical trials looks carefully at whether the trial was carried out ethically, whether the results are collected and interpreted correctly, and ensures that the claims made by the authors are reasonable and factual.

Publishing results of clinical trials is crucial, so that the broader medical, scientific and patient communities can benefit from this knowledge.

Recognised clinical trials are listed in various Registries including the Australian New Zealand Clinical Trial Registry, US National Institutes of Health Clinical Trials Registry and the World Health Organization International Clinical Trials Registry Platform.

Clinical trials are conducted in four phases. The first three phases must be successful before the product or treatment is approved and made available for use in clinical practice. For more information visit:

www.australianclinicaltrials.gov.au/home

Phase I: is the first testing of a new drug, treatment or clinical device on a small group of people (about 6-80) to evaluate **safety**, the best way of administering the drug and how the body handles the drug, including the maximum tolerated dose. Phase I research studies classically include drugs or treatments that have been tested in animals but never in humans. In many Phase I studies new drugs are tested on healthy volunteers. However, in some Phase I studies - particularly those involving anti-cancer drugs or stem cell interventions - patients who have advanced disease that has failed to respond to standard therapies maybe enrolled. The patient should be aware that they may not directly benefit from the therapy but by participating, important information on safety can be gathered, benefiting others in the future.

Phase II: generally involves a larger group of people to further evaluate safety and **explore the efficacy** of the intervention. Often these studies are double blinded where the trial participants and assessing doctors are unaware to which group (placebo or treatment) they have been assigned. This removes potential subjective biases when interpreting the results. Phase II studies also often investigate different doses to determine the dose to be used in the Phase III trial. Patients in Phase II studies usually have recurrent (in the case of cancer) or advanced disease which is not responsive to standard therapies.

Phase III: continues to **investigate the efficacy** of the intervention in larger groups of people (up to several thousand) usually by comparing against accepted standard treatments for the same condition, while monitoring for undesired effects. Once a Phase III study is successfully completed, regulatory approval can be sought for the drug or therapy to be made available for use in clinical practice. Often more than one Phase III trial is required for regulatory approval.Once a Phase III study is successfully completed, regulatory approval can be sought for the drug or therapy to be made available for use in clinical practice. Often more than one Phase III trial is required for regulatory approval.

Phase IV: once the intervention has obtained regulatory approval and is available for use, further studies are performed to **monitor** effectiveness and collect more information regarding undesired effects. Late Phase III/Phase IV studies often compare an investigational drug or therapy with one already available.

The design of clinical trials that evaluate stem cell therapy is similar to that for any new drug, procedure or medical device. However, determining whether the proposed stem cell therapy is beneficial can be complex. This is especially so in neurological conditions such as spinal cord injury, cerebral palsy, Parkinson's disease and stroke, where some degree of recovery may occur spontaneously as a result of limited endogenous nerve cell regrowth, often in the context of intensive physical and occupational therapy.

The importance of the clinical trial process cannot be overstated. The process ensures the proper collection of evidence and prevents dangerous and ineffective therapies moving beyond early stages (Phase I/II).

This limits the number of people put at risk of harm from a dangerous or ineffective treatment, as well as ensuring patients are not denied more effective therapies. Recent reports of faulty breast implants and artificial hip joints causing harm to patients in Australia demonstrate how critical the clinical trial process is in evaluating new products.

In the case of a conceptually new and different therapy like regenerative medicine using stem cells, the risk of unexpected harm is considerable and very real. Such risks strongly justify the need for the classical clinical trial process, even though it may appear to slow the development of new treatments.

Medical innovation

In special circumstances, doctors may offer a patient a 'one-off', unproven treatment outside the clinical trials framework. Such treatments, referred to as 'medical innovations', are only offered by specialist doctors with extensive experience in the patient's specific disease, deep knowledge of the scientific justification for the treatment and the experience and skills to apply the relevant techniques. Such treatments are usually only offered in an academic teaching or university hospital setting and payment is not usually expected. There is an extensive list of regulatory and ethical requirements that must be met before a medical innovation can be offered to a patient. One-off innovations are also usually expected to proceed to formal clinical trial. These requirements are detailed in Figure 2. The Australian Regulatory authority (the Therapeutic Goods Administration) also has the capacity to allow Special Access to patients for an unapproved treatment provided the treatment meets specific criteria, and provided that the practitioner is a registered practitioner with an expertise in the relevant field of medicine, and provided the practitioner is willing to take the medico legal risk of providing this treatment for a patient.

Any stem cell treatments that are not accepted medical standard practice (HSC transplants and skin and corneal grafts), are not part of a clinical trial, and are not a medical innovation provided in accordance with strict requirements, are unproven treatments that when offered to you should be viewed with extreme caution. Figure 2 highlights some of the key differences that distinguish unproven stem cell treatments.

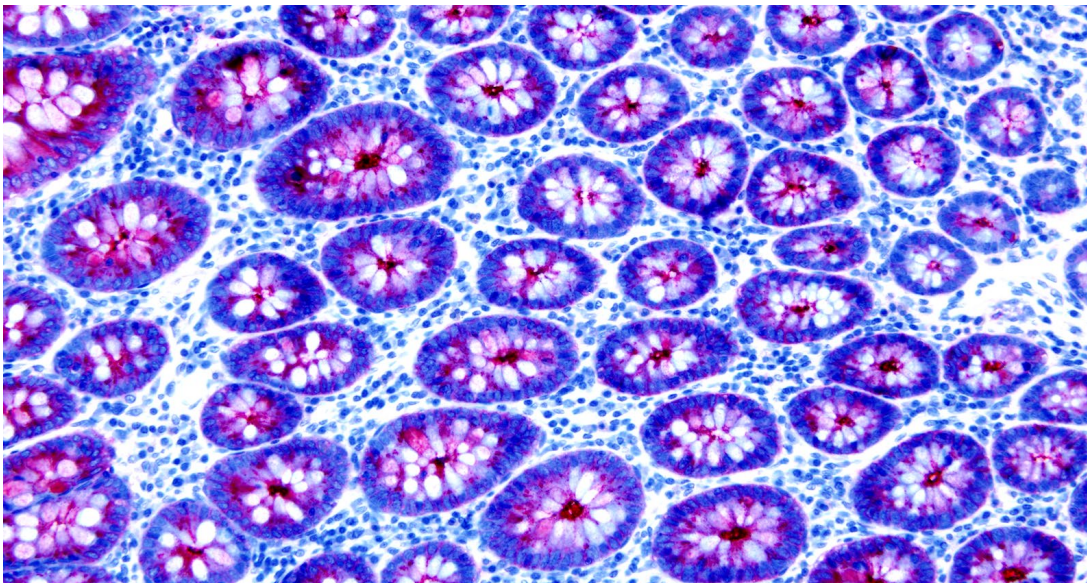
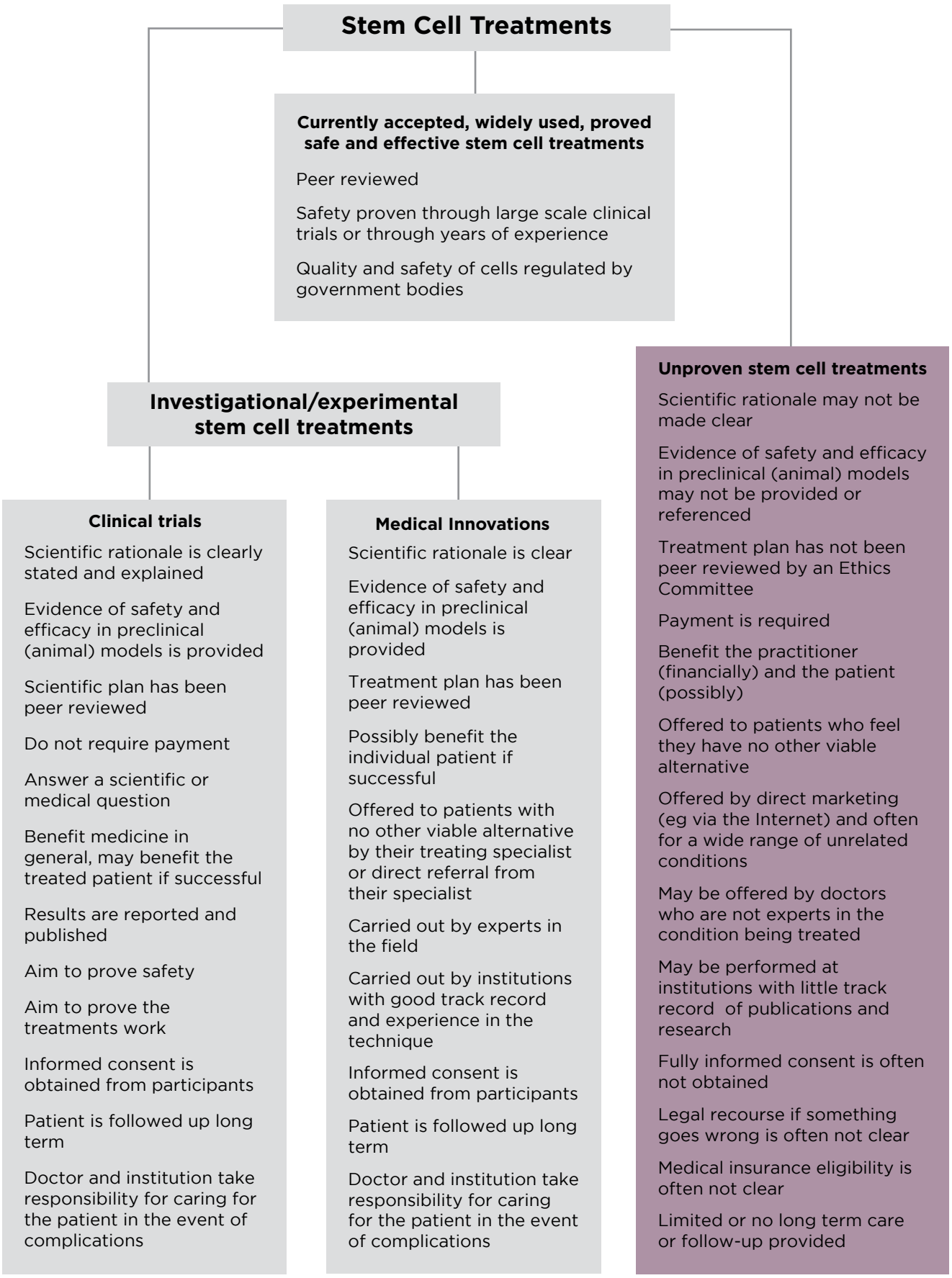
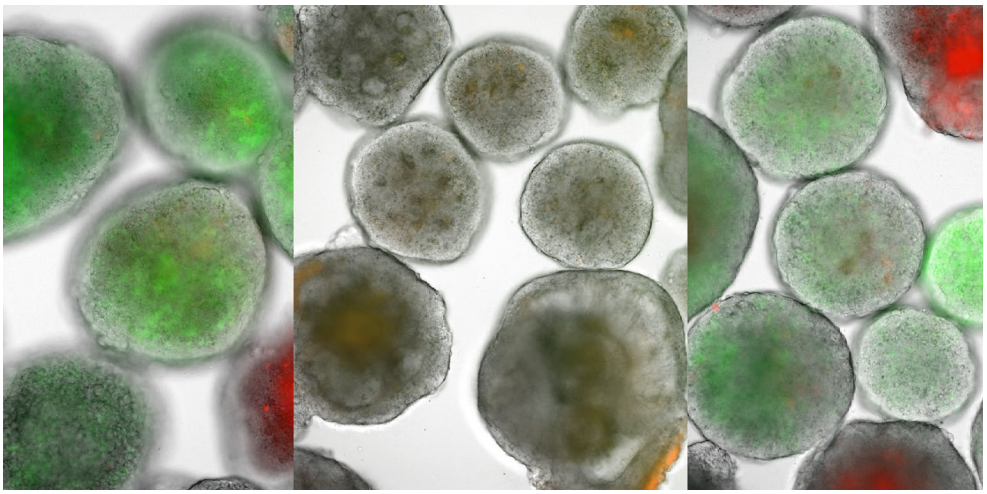


Figure 2: Key features that distinguish unproven stem cell treatments from other accepted stem cell treatments or investigations



Features of unproven stem cell treatments

Unproven stem cell treatments are those where doctors offer to treat patients without first properly evaluating the proposed treatment, effectively circumventing the clinical trial process.



Unlike the careful pace of legitimate preclinical and clinical stem cell research (as explained above), the doctors offering unproven stem cell treatments are effectively selling hope with little or no medical or scientific evidence to back up their claims around both safety and actual benefit. These unproven, highly experimental treatments also are not cheap, with prices ranging from $9,000 to $60,000 per treatment, and patients are often encouraged to consider multiple treatments.

Having heard about stem cells and the promises that these cells may hold for regenerative medicine, for many Australians it is difficult to recognise that the treatment being offered is unproven. Many of these services are promoted on very impressive websites, with persuasive patient and/or carer testimonials supporting the benefit of the treatment. However there are some simple points to consider which will help you to identify providers of unproven stem cell treatments. These are detailed in Figures 2 and 3.

For many years there has been concern about patients traveling overseas for unproven stem cell treatments that are not available here. Such travel is often referred to as ‘stem cell tourism’. However in recent years, there have been a growing number of Australian doctors and medical clinics offering unproven stem cell treatments here in Australia.

The fact that such treatments are being offered in Australia can make it more difficult to determine if the stem cell treatments are legitimate. Especially when the treatments use your own cells.

Despite the exacting standards usually imposed by the Therapeutic Goods Administration (the TGA – which is the Australian regulator of all medical devices, drugs and biologicals), there is currently a controversial loophole in our Australian regulations. This means that unproven stem cell treatment is excluded from the regulatory framework provided the treatment is being offered by a registered Australian doctor, is using the patient’s own cells and is a one-patient treatment. It is not a requirement that such treatments have to be first proven safe and effective in clinical trials. This issue is currently under review by the TGA, who are considering whether there is a need to introduce additional regulation to protect Australians and visitors who are at risk of medical or financial harm by seeking unproven autologous stem cell treatments.

The treatments using the patient’s own cells are often marketed as having ‘no risks’ and are ‘natural’ because the cells come from you (ie are autologous). It is important for you to know that even treatments using your own cells can be dangerous. There have been reports of cells from fat growing into bone, as well as deaths reported overseas. There have also been reports of tumours arising at sites where patients stem cells have previously been injected.

When deciding on what is best for you, not compromising the state of health that you currently have, is an important consideration.

Figure 3: Key features of unproven stem cell treatments

Distinguishing characteristics	Why this is a problem
The experimental treatment being offered is not part of a registered clinical trial	Clinical trials are the appropriate way to evaluate an experimental stem cell treatment. There are no guarantees that a new treatment being tested in a clinical trial will be shown to be safe and effective. Evidence should be collected through clinical trials before the treatment is offered widely to patients.
The treatments are being advertised on the Internet, TV, Facebook or in newspaper articles or ads rather than via referral from your treating doctor	Direct to consumer advertising generally uses very persuasive language, rather than accurate information, and implies benefit and 'success' where there is little evidence to justify the claims. You would usually expect your treating specialist to refer you for any new treatment. If they don't know about it, chances are that it is unproven.
The doctor or clinic is offering to treat many different diseases or conditions with the same stem cells and procedure	Unless the diseases are related, different conditions in different organ systems, such as cerebral palsy, diabetes and heart disease, would usually have very different treatments. In addition you would usually expect to be treated by a doctor who is a specialist in your condition. Just because a new treatment may offer improvements in one condition, it does not mean that it will work for lots of different conditions. Stem cells are not a 'silver bullet'.
The use of patient testimonials to support claims of benefit with no independent verification or published data	While they can be very convincing, individual reports of apparent success have to be viewed with caution. Claims made are often difficult to substantiate and verify. The benefit may be real, or may be due to the placebo effect, or due to a desire to report a positive outcome because of the amount of time and money invested in obtaining the treatment. Without proper medical and clinical research scrutiny of these claims they remain unproven and are not valid 'evidence' of success.
Where there is no scientific rationale offered or the 'evidence' is implied from the work of others	Many treatments being offered use completely unproven techniques which have not been tested for their safety or efficacy in clinical trials in humans. 'Patents pending' is not an acceptable excuse to conceal scientific methods from the scrutiny of respected colleagues. A doctor or clinic offering experimental treatment is usually expected to operate in a registered clinical trial and to collect data and publish their results in peer-reviewed medical journals so that others can learn from their experience.
When there is a lack of after care and follow-up once the procedure is completed	After any medical procedure, patients are at risk of complications. Responsibility should be taken by the doctor for the management of complications. A simple phone call after the treatment is not sufficient. For those seeking treatment abroad, if complications occur, they may be left with large bills and even expensive medical evacuations to get them home. Such costs are unlikely to be covered by their travel insurance.
When you are asked to pay for a treatment that is not yet an accepted medical practice	It is not usual to have to pay for an experimental treatment in a registered clinical trial and those unproven treatments currently being offered are very expensive and not reimbursed by Medicare or private health insurers.
Where there is no Medicare or private insurance rebate for the treatment	Accepted medical procedures are usually recognised by Medicare or other insurance rebates. This not only provides financial assistance, it also ensures that the cost is a reasonable reflection of the actual cost in providing the treatment and not inflated.
The stem cells are prepared on-site at the doctor's surgery	Any manipulation of cells, even if they come from you, carries risk of infection and other complications. They should be prepared in an accredited laboratory, where there are exacting quality control standards independently verified, or using a device that has been approved by regulators such as the TGA.

Why you should be careful pursuing unproven stem cell treatment, and what questions to ask

There are a number of questions that we would recommend you ask anyone who is offering stem cell treatments. It is a good idea to have a written list of questions and write down the answers, or preferably obtain the answers in writing from the provider of the treatment. You can take the answers away and spend some time thinking about them, and discussing them with your treating doctors (eg your GP or specialist).

Importantly, ask for the evidence that backs up the claims you may have read about or been told about. Whilst patient testimonials can be very compelling, they are not enough. These treatments are unproven because the risks to you, and the effectiveness of the treatment, are unknown. There should be peer-reviewed scientific publications that document the development and progress of any experimental stem cell treatment.

There is much that we still don't know about the behaviour of stem cells. It is important that you understand where the cells come from and the inherent risks associated with their use. For example, pluripotent stem cells and cells taken from a patient's nose have been shown to form tumours. Even stem cells taken from a patient's own fat have formed unexpected growths such as bone fragments.

How and where the cells are prepared, stored and handled is also an important consideration. The cells should be prepared in an accredited laboratory with the appropriate quality control standards to avoid infections and other complications. Current practices for patients receiving blood transfusions in Australia make sure that the donated blood cells are screened for known blood-borne diseases and stored properly before the transfusion. The same standards should apply to any stem cell treatment offered here or overseas.

How the cells are delivered to the patient is also an important consideration. Treatments may use subcutaneous (under the skin), intravenous (into the vein) and intramuscular injections. Other providers may suggest injecting the cells directly into a joint, the spinal cord, the fluid surrounding the spinal cord or even into the brain. All carry risks, which should be fully considered. We recommend that you discuss the risks posed by any treatments you may be considering with your usual treating doctor.

Some treatments use cells that are not even human. One high profile, overseas company has offered injections of rabbit fetal stem cells for conditions ranging from Down's syndrome to ageing and impotence.

Be exacting in your research. Above all, make sure that the proposed treatment will not further compromise the health that you do have. Your treating Australian doctors are in the best position to review your research into stem cell treatments and provide you with independent advice on the potential risks posed by the treatment, and whether the proposed treatment is likely to be beneficial for you.

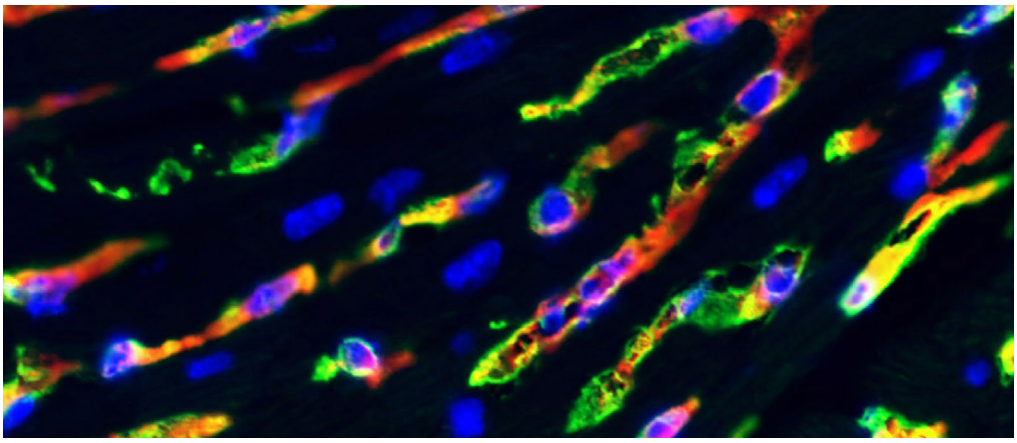


Figure 4: The checklist – Questions to ask the doctor or clinic offering the treatment

The treatment

- ☐ Is this an accepted medical procedure, if so by whom is it approved?
- ☐ Is the treatment considered 'experimental'? If so, is it being offered as part of a clinical trial?
- ☐ If part of a clinical trial, is the trial registered on ANZCTR, NIH Clinical Trials or other recognised registries?
- ☐ What is the evidence that this treatment will work for my condition?
- ☐ Can you provide me with peer-reviewed publications that can support the likely benefit?
- ☐ Have you published your data? If so, where?
- ☐ Are there any risks associated with the treatment? What are the side-effects?
- ☐ Could the cells harm me? Could they form tumours or cause problems with my immune system?
- ☐ What is the cost and exactly what does this include?
- ☐ How many visits are required? Is there a new fee for each visit?
- ☐ Has this treatment been reviewed by an ethics committee, and if so which one?
- ☐ If being offered in Australia, is this treatment eligible for a Medicare or private health insurance rebate?

The procedure

- ☐ What type of cells are you using – mine or someone else's?
- ☐ If using donor cells, where do they come from – fetal tissue, embryos, umbilical cord blood? Are they human or from other species and if so which?
- ☐ Are the donor cells screened for viruses (HIV, Hepatitis B, Hepatitis C, HTLV-1 and HTLV-2)?
- ☐ Are the cells prepared in a licensed laboratory or using an approved device? And if so, by whom?
- ☐ Do you use animal products to grow the cells and how do you guarantee there is no contamination? [1]
- ☐ How are the cells delivered? Are they injected? If so, what are the possible complications of the injection? [2]
- ☐ Do I need to take medication after the treatment?

Medical care and other considerations

- ☐ Who is the doctor performing the treatment?
- ☐ Is he/she a specialist in treating my condition? [3]
- ☐ Will I receive any other treatments or therapies when I am at the clinic? If so, does this attract an additional cost?
- ☐ What ongoing care will I receive? Does this attract additional charges?
- ☐ How will my health be evaluated after the treatment?
- ☐ What happens if something goes wrong? Whom do I contact?
- ☐ Who will cover the costs of any medical complications?
- ☐ If travelling overseas, will my travel insurance cover my treatment? Will my travel insurance help me get home if I have a reaction or get sicker? [4]
- ☐ If travelling overseas, are there likely to be additional costs or are these included in the fee (eg travel, accommodation, meals, insurance, medications, hospital bed costs, consumables used during the treatment, cell processing costs)?

1. *Many techniques used to prepare cells rely on products made from cows. This carries a potential risk of serious disease such as a variant of Creutzfeldt Jacob disease (Mad Cow Disease).*
2. *The injection itself can carry risk. Deaths have occurred as a complication of the stem cell treatments being injected into the fluid around the spinal cord and into the brain.*
3. *Some clinics market their doctors as 'stem cell specialists'. This is not a recognised qualification.*
4. *These questions may be more appropriate to ask your insurer. However, they remain important considerations.*

Current stem cell clinical trials and how to find out more about them

There are many clinical trials involving stem cells underway around the world. Keeping up to date is a challenge, but there are several online registries you can search to provide information:

Australian New Zealand Clinical Trial Registry

United States National Institutes of Health Clinical Trials Registry

European Union Clinical Trials Registry

World Health Organization International Clinical Trials Registry Platform

It is important to remember that while a treatment is still being evaluated as part of a clinical trial, it remains experimental and is yet to be shown to be a safe and effective therapy. Furthermore there are some 'clinical trials' registered on these sites that do not meet the criteria of proper clinical trials. Unfortunately, providers of unproven therapies are able to register their 'trials' on these sites seeking to appear legitimate. Asking your treating doctors for independent advice is critically important.

To assist you in your research, we have provided below a brief overview of some of the stem cell clinical trials for specific conditions.

Stem cells for heart repair

Over the past ten years, numerous clinical trials have been conducted to explore the effect of autologous and allogeneic HSCs and MSCs on congestive cardiac failure (heart failure), refractory angina (cardiac chest pain) and acute myocardial infarction (heart attack). To date, the trials have demonstrated that these treatments are generally safe. However, only limited benefit has been observed. No stem cell treatments are approved yet for cardiac disease.

The next step is to determine which type of stem cell treatment is most beneficial for different heart conditions. There is some evidence that suggests that HSCs from bone marrow may release certain factors (paracrine effects) that act on cells already in the heart to cause repair and relieve angina. Other conditions, such as restoring the heart muscle cells after a heart attack will probably require treatment with cells that can actually regenerate new heart tissue.

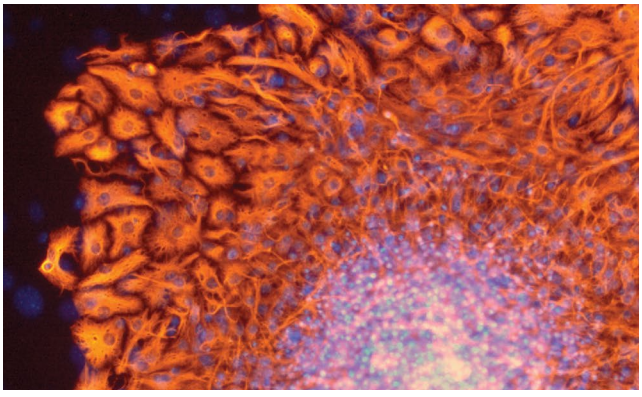
Cerebral palsy

Speculation exists about the use of umbilical cord blood for a variety of acute and chronic conditions.

One example is the ongoing Phase II clinical trial at Duke University, which is testing whether the infusion of autologous cord blood will improve the neurodevelopmental function of children between 12 months and 6 years of age with cerebral palsy.

The study, which will treat 120 children, has attracted significant media attention based on anecdotal reports. In addition, a recent Korean study has recently provided support for the possible use of cord blood for treating cerebral palsy with some improvement noted following treatment with donated cord blood.

In Australia, the Cerebral Palsy Alliance in collaboration with several clinical and research groups is planning trials of autologous cord blood re-infusion in neonates with cerebral trauma and in children with cerebral palsy.



Stem cells for spinal cord injury

After many years of basic and pre-clinical research and preparation, clinical trials are in progress for acute and chronic spinal cord injury treatments using stem cell derived products.

In 2010, the Californian biotechnology company Geron commenced a clinical trial to explore the use of early nerve cells derived from differentiated human ESCs (called oligodendrocyte progenitor cell product or GRNOPC1). The trial aimed to treat up to 10 patients with acute spinal cord injury where it was hoped the GRNOPC1 cells would reverse the loss of myelin – the crucial insulating material around nerve fibres - in the injured spinal cord. The primary objective of this Phase I study was to assess the safety and tolerability of GRNOPC1 when administered by injection into the lesion site in the thoracic spinal cord between 7 and 14 days after injury with the endpoints of the trial being safety and monitoring sensory and motor lower limb function.

As this was the first trial involving human ESC derived cells, the USA Food and Drug Administration (FDA) were understandably cautious. In the interest of patient safety, Geron's final submission to the FDA famously included no less than 28,000 pages of detailed pre-clinical experiments in animals, processes and long term follow-up procedures. While Geron has presented data on the first two patients enrolled in the trial, the final outcomes will not be known for some time. Geron has also made the decision to cease this clinical trial after only five patients were treated. Rather than continue to pursue their cell therapy platform, Geron recently announced that it has divested its stem cell assets and trials to another company, BioTime, Inc. and BioTime's recently formed subsidiary, Asterias Biotherapeutics. It is not certain whether this study will continue but there have been no adverse outcomes reported to date.

In Switzerland, StemCells Inc has recruited 12 patients for a Phase I/II clinical trial for chronic spinal cord injury using neural stem cells derived from fetal tissue. Four of eight assessable patients with at least six months follow-up have had improved sensation below the spinal lesion. In December 2014 the company enrolled the first patient in a Phase II trial in cervical spinal cord injury.

Numerous other studies using bone marrow stromal cells exist, and while these have been shown to be relatively safe, the effect was limited. There remain many challenges to address in the development of such therapies.

Blindness

Corneal disease is a common cause of blindness. The cornea is the transparent front part of the eye that covers the iris and pupil. Limbal stem cells, which are present in the eye at the border of the cornea and the sclera (white of the eye), can produce differentiated cells to replace the damaged or missing cornea. The technique involves taking autologous adult limbal stem cells from the healthy part of the eye, culturing the cells and then transferring them to the diseased cornea that has had damaged areas removed.

The largest published trial, undertaken in Italy, tested the technique in 112 patients and reported that the sustained restoration of a transparent, renewing corneal epithelium was attained in more than three quarters of the treated eyes.

In Australia, a group at the University of NSW trialled a similar treatment using contact lenses to culture and deliver the cells. They have recently reported that the surface of the cornea was restored in 10 out of 16 patients using this new approach. Importantly, symptoms such as pain and photophobia resolved in many patients.

In a new clinical application of human ESCs, US based company Advanced Cell Technology has commenced Phase I/ II trials. Using human ESC derived retinal pigment epithelial cells, one trial will target dry age-related macular degeneration (AMD) and the other will treat younger patients with Stargardt's macular dystrophy. The macula is an oval-shaped 1.5mm spot near the center of the retina at the back of the eye. It is responsible for our central vision. The trials are evaluating whether the treatment is safe and the effect of different doses of the cells.

Initial reports suggest that there has been some improvement in vision but it remains too early for a conclusive finding. Similarly, a consortium in the UK known as the London Project to Cure Blindness is working with human ESC derived retinal pigment epithelial cells and expects to begin a clinical trial within the next 12 months to treat 12 patients with acute AMD. Stem Cells Inc has reported a decrease in progression of dry age related macular degeneration after direct injection of their foetal derived human neural stem cells.

Stroke

Although animal models of stroke have demonstrated that stem cells can improve function, this is yet to be seen in human patients. In a recent review of stem cell treatments for stroke the authors noted that although no adverse transplant related events were reported, there is 'insufficient evidence to support stem cell transplantation in treating ischemic stroke'.

One company that is pursuing stem cell treatment for ischemic stroke is UK based ReNeuron. Using fetal neural stem cells that have been genetically engineered and expanded in culture, the company has commenced a clinical trial of intracerebral injection in patients with significant disability 6 to 24 months after stroke. In this Phase I study, they plan to follow 12 patients for a minimum of 2 years. Interim results on the first 11 patients were reported in 2014 and reductions in neurological impairment and spasticity were observed in most patients treated at that time compared with their stable pre-treatment baseline performance and these improvements were sustained in longer term follow-up. No adverse cellular or immunological affects were reported - adverse events were attributed to the surgical procedure for implantation of the cells into the brain or to pre-exsiting injury. They have begun a Phase II placebo controlled trial with results from the first cohort expected in late 2015.

Multiple sclerosis

Multiple sclerosis (MS) is now recognised as an immunological disease. It has been suggested that high dose chemotherapy and/or radiotherapy to 'delete' the immune system, followed by HSC transplantation, may 'reset' the immune system of patients with MS and halt the progress of the disease.

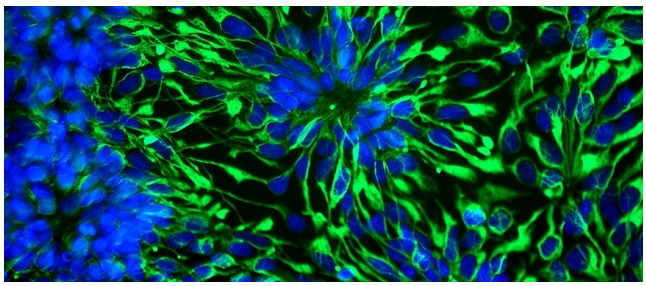
Globally, several ongoing or completed clinical trials are investigating autologous HSC transplantation in highly active forms of MS with a poor prognosis. By destroying the patient's immune system through chemotherapy and reintroducing HSCs taken from the patient's own bone marrow or peripheral blood, the immune system can be theoretically reconstituted without the immunologic memory that caused the MS. In doing so, it is hoped that the reappearance of autoimmunity is made unlikely.

The largest study is being carried out by Northwestern University in Chicago with an ongoing Phase III trial of 110 patients based on their Phase I/II clinical trial. In the initial published trial, 21 patients with a minimum five year history of relapsing-remitting MS that had not responded to at least six months of treatment with interferon (standard treatment) were treated with HSC therapy. The patients had MS for an average of five years, and when reviewed around three years following transplantation, 17 patients (81%) improved by at least one point on a disability scale (Kurtzke scale of 1-10) with the disease stabilising in all patients. While it is important to note that the Phase I/II clinical trial was not randomised and had no control group, the data was sufficiently encouraging to progress to the randomised Phase III trial in progress.

Similar clinical trials are ongoing or have been completed in other US states, Canada, the UK and Greece. To date results have been variable and more data is required to understand which patients are most likely to respond to this high-risk therapy.

In Australia, the treatment is generally only considered for a small sub-population of patients with aggressive forms of MS that have not responded to other available forms of treatment. Other aspects of the patient's health and disease course are also taken into consideration. A clinical trial testing the procedure is being undertaken at St Vincent's Hospital in Sydney and is open to enrolment; and several transplants have been performed on Australian patients as medical innovations (rather than clinical trials). The St Vincent's group has joined the above mentioned Chicago trial and Australian patients may be eligible. MS Research Australia has funded an Australian Register of HSC therapy for MS so that the progress of those Australians who have had these experimental treatments can be followed.

There are several trials registered on the NIH Clinical Trials site using MSC in attempts to modify the immune response in aggressive MS. Some are completed, some are still recruiting, however, none have reported their results.



Diabetes

Pancreatic islet cell transplantation has been available for some years to treat patients with type 1 diabetes. However, while most recipients of cadaveric islet cell grafts (ie from donors) can achieve partial or complete independence from insulin injections, the effect may not be life-long. There are also potential difficulties such as:

- side effects of immunosuppressants (to prevent rejection of donated cells)
- access to sufficient donor tissue given the need for multiple donors
- problems in isolating islet cells.

The ability to make pancreatic cells from human ESCs provides a possible alternative source of insulin producing human cells. The USA company Viacyte commenced clinical trials in 2014.

Given the autoimmune nature of type 1 diabetes, another potential approach is to use the immunosuppressive properties of MSCs.

Osteoarthritis

There is a growing body of research regarding MSCs for the treatment of osteoarthritis. It is thought that the MSCs may have immune modulating and anti-inflammatory properties and that they may contribute to the regeneration of cartilage in the damaged joint. Around the world many groups have commenced clinical trials using autologous MSCs to treat osteoarthritis of the knee, which is the joint most commonly affected.

Within Australia, veterinary company Regeneus has attracted media attention for its treatment of arthritic dogs using autologous adipose derived cells. Based on its animal results, Regeneus sponsored a clinical trial using the same technology in humans with arthritic knees. The initial trial has enrolled 40 patients at the Royal North Shore Hospital in Sydney. The study is reported on the Regeneus website and shows equal pain relief in treated and placebo patients. The treated patients had a reduction in one marker of cartilage breakdown. More and larger studies are required.

Australian biotechnology company Mesoblast has a strong interest in osteoarthritis using its allogeneic MSC product RepliCart™ but does not have any active clinical trials.

Medipost, a Korean biotech company, has also developed a MSC-derived stem cell preparation called CARTISTEM® for delivery into joints affected by cartilage loss due to osteoarthritis or repeated traumatic injuries. This product, which has been approved by the Korean FDA, has been through numerous clinical trials but the results are yet to be published.

In addition, there have been some positive results for cartilage grafting in the knees of people with arthritis, but further studies are required to prove such a treatment is truly effective and safe.

Other conditions

We suggest you should search the NIH and ANZCTR websites for information about such trials. You should look for trials being carried out by universities in countries such as the UK, USA and Europe, where regulation generally meets internationally accepted standards.

Studies without university affiliation, and those where fees are requested for participation are likely to be less well-founded, and are more likely to fit into the category of unproven stem cell treatments.

More information

We hope that by reading this NSCFA and SCA Handbook and suggested resources, doing your own online research, and discussing it with your treating Australian doctors, you will have a informed opinion about potential treatment with stem cells.

Before making any decision about stem cell treatments, we believe the more information you are armed with the better. Here is a list of websites and other resources you may find helpful.

International Society for Stem Cell Research (ISSCR) - Closer Look at Stem Cells & Patient Handbook

Closer Look at Stem Cells is a website that aims to assist patients and the general public understand how stem cell science becomes medicine, including useful information to help patients and their families evaluate claims made by those offering unproven stem cell interventions. There is also a link to the ISSCR Patient Handbook which is available in many languages.

www.closerlookatstemcells.org

National Health and Medical Research Council

The NHMRC has released documents on stem cell therapy for patients 'Frequently Asked Questions - A Resource for Patients' and doctors "Stem Cell Treatments – a quick guide for medical practitioners". These documents provide invaluable additional information.

www.nhmrc.gov.au/guidelines-publications/rm001

NHMRC provides some information on issues relating to embryonic stem cell research and cloning.

www.nhmrc.gov.au/about/nhmrc-committees/embryo-research-licensing-committee/human-embryos-and-cloning

Australian Clinical Trials

Provides information on Australian clinical trials, why they are important and how to participate in one.

www.australianclinicaltrials.gov.au

California Institute for Regenerative Medicine (CIRM)

Information on the progress of CIRM's stem cell research toward developing treatments for chronic, debilitating diseases.

www.cirm.ca.gov/patients

Canadian Stem Cell Foundation

The Canadian Stem Cell Foundation has a comprehensive section on their website summarising current research on how stem cells could be used to achieve new treatments.

www.stemcellfoundation.ca/en/toward-treatments/

Canadian Stem Cell Patient Handbook

This Handbook provides information about stem cells and stem cell therapies for patients and the public.

www.amc.edu/Academic/bioethics/stem_cell_patient_booklet.cfm

Cerebral Palsy Alliance

This group is seeking to establish Australia's first clinical trial to evaluate the effectiveness of stem cell treatment for people with cerebral palsy.

www.cerebralpalsy.org.au

MS Australia

MS Australia provides help and advice for people with multiple sclerosis, maintains a register of patients having immunosuppressive bone marrow transplants for MS, and its website is a useful source of information.

www.msaustralia.org.au/stem-cells

Additional information can be found about autologous haematopoietic stem cell transplants for MS here:

www.msra.org.au/autologous-haematopoietic-stem-cell-transplant-ahsct-ms-0

MS Society UK

The MS Society UK has joined with other patient groups to publish 'I've got nothing to lose by trying it' a booklet which explains how to tell the beneficial from the bogus in the face of miracle cure stories, new wonder drugs and breakthrough therapies that are increasingly promoted in the media and elsewhere.

www.senseaboutscience.org/resources.php/11/ive-got-nothing-to-lose-by-trying-it

MND Australia

Visit MND Australia for the latest research on MND as well as their concerns regarding unproven stem cell treatments. Various state-based MND associations also provide help and advice for people with MND and are another source of information.

www.mndaust.asn.au

National Institutes of Health Clinical Trials Registry

This website has an easily searchable online registry of clinicial trials. Search for stem cell trials by typing 'stem cells AND [your condition of interest]' into the search function.

www.clinicaltrials.gov

Spinal Cord Injury Network, Australia New Zealand

The Spinal Cord Injury Network website includes information on clinical trials and a position statement on Stem Cell Interventions for Spinal Cord Injury as well as video footage of a workshop on stem cells and spinal cord injury.

www.spinalnetwork.org.au

Sports Injury Bulletin

For more information on cartilage transplants visit this website.

www.sportsinjurybulletin.com/archive/cartilage-transplants.html

Glossary and Acronyms

Adult (tissue-specific) stem cell: Adult (tissue-specific) stem cell: An unspecialised stem cell found in a tissue or organ that can renew itself, and differentiate to develop mainly into the cell types of the tissue from which it originated.

Allogeneic transplantation: Cell, tissue or organ transplants from one individual to a genetically different person (ie from a donor).

Age-Related Macular Degeneration (AMD): A common eye condition among people age 50 and older, and is a leading cause of vision loss. It gradually destroys the macula, the part of the eye that provides sharp, central vision needed for seeing objects clearly.

Australian Research Council (ARC): A statutory agency under the Industry, Innovation, Climate Change, Science, Research and Tertiary Education portfolio within the Australian Government. Its mission is to deliver policy and programs that advance Australian research and innovation globally and benefit the community.

Autologous transplantation: Cell, tissue or organ transplants from one individual back into the same individual (ie. it involves own cells). Such transplants are often performed with blood products or bone marrow, do not induce an immune response and are not rejected. However, these transplantations still involve potential risks to the patient.

Blastocyst: An early stage embryo about seven days following fertilisation and containing about 150 cells. A blastocyst consists of two types of cells: the inner cell mass cells, which give rise to all the organs and tissues of a future embryo and foetus; and the trophoblast which forms a portion of the placenta. Embryonic stem cells are derived from the inner cell mass of donated IVF embryos.

Cell culture: The growth of cells in a laboratory where nutrients, growth factors and all other requirements for cell survival are provided.

Cell division: The process by which one cell divides into two cells, thereby increasing the cell population.

Cell based therapies: A treatment that administers cells required to repair or rebuild depleted cell populations or tissues. These may include cells derived from stem cells.

Differentiation: The process whereby an unspecialised (undifferentiated) stem cell develops into specialised cells such as those in the liver, brain or heart.

Efficacy: The capacity to produce an effect.

Embryo: A stage of development immediately following fertilisation of an egg by a sperm. Stages of embryonic development can be divided into pre-implantation (early development before pregnancy is established) and post-implantation (once the embryo has implanted into the lining of the uterus).

Embryonic stem cells (ESCs): Stem cells derived from human embryos (at the blastocyst stage). ESCs are self-renewing (can replicate themselves) and have the potential to differentiate into all cell types in the body.

Food and Drug Administration (FDA): An agency of the United States Department of Health and Human Services, which is responsible for protecting and promoting public health through the regulation and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices and veterinary products.

Fetal stem cells (fetal tissue): These are stem cells derived from donated fetal tissue and share many of the characteristics of the adult stem cells.

HTLV-1 - Human T-Lymphotropic Virus Type I: A transmissible human RNA retrovirus that causes T-cell leukaemia and T-cell lymphoma in adults and may also be involved in certain demyelinating diseases, including tropical spastic paraparesis.

Haematopoietic stem cell (HSC): The parent stem cell or 'precursor' of mature blood cells which are found in adult bone marrow, umbilical cord blood, peripheral blood and foetal liver.

Human Research Ethics Committee (HREC): Assists Australian institutions in meeting their obligation for the effective governance of research involving humans and is the Australian equivalent of an Institutional Review Board in the USA.

Induced pluripotent stem cells (iPS cells): Stem cells which resemble pluripotent embryonic stem cells. They are derived from mature, fully differentiated cells of the body that have been reprogrammed through genetic manipulation and other techniques to restore developmental potential.

In vitro fertilisation (IVF): An assisted reproduction technique where fertilisation is achieved outside the body. Sperm and eggs are brought together in the laboratory (ie in vitro) to achieve fertilisation before being transferred to the uterus (or womb) to attempt to achieve a pregnancy.

International Society for Stem Cell Research (ISSCR): An independent, nonprofit organisation formed in 2002 to foster the exchange of information on stem cell research. With more than 3,500 members worldwide, the ISSCR has become the voice of the stem cell research community.

Mesenchymal stem or stromal cells (MSCs): A type of adult stem cell found in several tissues of the body including bone marrow, umbilical cord blood, placenta and adipose tissue which can give rise to a number of tissue types such as bone, cartilage, fat tissue, and connective tissue, as well as display immunosuppressive properties.

Motor neurone disease (MND): Also known as Amyotrophic Lateral Sclerosis (ALS) in many parts of the world, and as Lou Gehrig's disease in the USA. MND is a progressive neurological disease.

Multipotent: The potential of an individual stem cell to develop into a restricted number of (but not all) types of cells. Many adult stem cells are multipotent.

Multiple sclerosis (MS): A disease which affects the central nervous system and can, to varying degrees, interfere with the transmission of nerve impulses throughout the brain, spinal cord and optic nerves. Since identification, MS has been the subject of intense, world-wide research but still its cause and cure remain elusive.

National Health and Medical Research Council (NHMRC): Australia's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research.

National Stem Cell Foundation of Australia (NSCFA): A not-for-profit company limited by guarantee and an Australian Tax Office endorsed charity, established in 2011 as the follow-on organisation from the Australian Stem Cell Centre.

Peer review: The process of subjecting an author's scholarly work, research, or ideas to the scrutiny of others who are experts in the same field.

Pluripotent: The ability of a stem cell to develop into any type of cell in the body. ESCs and iPS cells are examples of pluripotent stem cells.

Progenitor cell: A transitional form of stem cell that can differentiate, but can no longer renew itself. Progenitor cells are restricted to the generation of a few types of specialised cells.

Regenerative medicine: A treatment in which stem cells are induced to differentiate into a specific cell type required to repair damaged tissues or to replenish a depleted cell population. They are then used to treat disease.

Stem cell: An unspecialised or undifferentiated cell with the ability to self-renew, and to differentiate to produce specialised cell types in the body.

Stem cell line: Stem cells that have been established and propagated in culture and which maintain consistent characteristics and developmental potential.

Stem Cells Australia (SCA): ARC funded special research initiative in stem cell science which commenced in 2011.

Therapeutic Goods Administration (TGA): Australia's regulatory authority for therapeutic goods. It carries out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard with the aim of ensuring that the Australian community has access, within a reasonable time, to therapeutic advances. The TGA is the equivalent of the USA FDA.