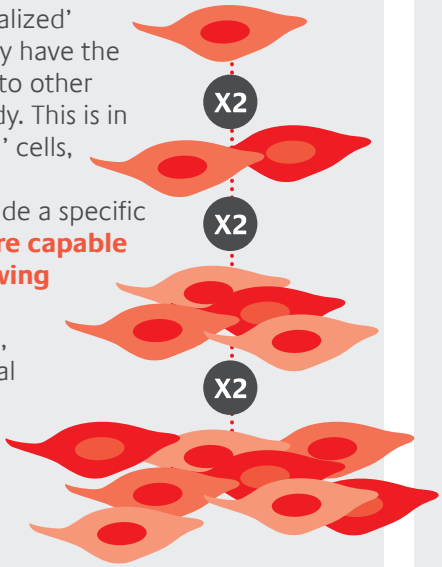
Better Health, Brighter Future

STEM CELL THERAPY

Stem cells and their use in medicine

Stem cells are 'unspecialized' cells, meaning that they have the potential to develop into other kinds of cells in the body. This is in contrast to 'specialized' cells, which have become 'differentiated' to provide a specific function. **Stem cells are capable of dividing and renewing themselves almost limitlessly.** In doing so, they retain the potential to become specialized cells, which are typically found in the tissue where the stem cell originated.[1]



These unique regenerative properties mean that **stem cells could have many applications within medicine**. Although research is ongoing in the field of stem cell therapies, there are already established uses for stem cells. For example, **stem cell transplants can be used to treat conditions which affect the blood cells, such as leukaemia, lymphoma, and myeloma**.[2] The blood cells damaged as a result of these diseases are replaced with stem cells.[2]

Types of stem cell

There are a wide variety of stem cell types and regulations on stem cell harvesting and donation vary from country to country. Typically, however, stem cells used for medical treatment are taken from the blood or bone marrow of either the patient themselves or a donor, or the placenta/umbilical cord (donated by the mothers of newborn babies).[2]

The **bone marrow** contains at least **two kinds of stem cells**: the majority are blood forming (hematopoietic) stem cells, which can form all the types of blood cells in the body. The bone marrow also has a second population of stem cells, which are **mesenchymal stem cells** (non-hematopoietic).[3] These stem cells can also be taken from other parts of the body and are an example of 'adult' stem cells, which may be extracted from adipose (fat) tissues under the skin using liposuction.[4] Human mesenchymal stem cells are thought to be multipotent and have the potential to generate mesenchymal tissues, such as bone, cartilage, fat, tendon, muscle and marrow stroma.[5]

These 'adult' cells should not be confused with embryonic stem cells. **Embryonic stem cells** are from a preimplantation-stage embryo. Most are derived from embryos developed from eggs fertilized in vitro – in an in vitro fertilization clinic – and then donated for research purposes with the informed consent of the donors. They are not derived from eggs fertilized in a woman's body.[6]

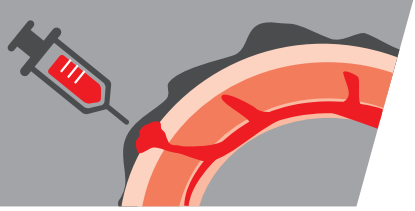
KEY STEM CELL DEVELOPMENTS

1950s
Researchers discovered that the bone marrow contained at least two kinds of stem cells[3]

1998
Researchers are able to isolate human embryonic stem cells for growth in a lab[7]

2006
Researchers reveal that embryonic-like stem cells can be created from adult cells. These are known as induced pluripotent stem cells or 'iPS'[7,8]

2014
Mesenchymal stem cells, of which Cx601 is one type, are found to have anti-inflammatory and tissue regenerative properties[9]



STEM CELL THERAPY

Few pharmacological treatments for complex perianal fistulas exist and repeated surgical procedures are usually required[10-14]

One of the areas in which the use and benefits of stem cell therapy is currently being investigated is Crohn's disease, for the treatment of complex perianal fistulas. Few pharmacological treatments for complex perianal fistulas exist and repeated surgical procedures are usually required,[10-14] which are generally associated with morbidity (e.g. incontinence)[14] and an increased risk of permanent stoma (surgically created opening on the surface of the abdomen).[15] Treatments that do exist, such as antibiotics, thiopurines (immunosuppressive treatments) and anti-tumour necrosis factor treatments are generally associated with moderate efficacy and high rates of relapse upon discontinuation.[14-22]

Investigational compound Cx601 (darvadstrocel) is a suspension of allogeneic expanded adipose-derived stem cells (eASC) (locally injected) and has been investigated in ADMIRE-CD, a randomized, double-blind, controlled, Phase III trial. The trial was designed to investigate the efficacy and safety of Cx601 for the treatment of complex perianal fistulas in adult patients with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least one conventional or biologic therapy.[23]

The study was sponsored by TiGenix. In July 2016, Takeda and TiGenix entered into an exclusive ex-U.S. license, development and commercialization agreement for Cx601.

Complexities of stem cell medicines

Stem cell therapy is a complex area of medicine. As the treatment area develops, one challenge is stem cell therapies that rely on donated cells can be limited due to a lack of available donors. In the UK, for example, **more than 400 patients each year** who could benefit from stem cell therapy are **missing out on treatment.**[24]

Additionally, as a novel therapy area, patients and healthcare professionals may need to build understanding of, and confidence in, stem cell treatment.

Developing stem cell therapies through our T-CiRA joint program[25]

Takeda Pharmaceutical Company Limited is working with Kyoto University's Center for iPS Cell Research and Application (CiRA) to investigate the development of clinical applications of iPS cell technologies.

The joint partnership, known as T-CiRA, aims to investigate the development of innovative drugs and cell treatments for diseases like heart failure, diabetes mellitus, neuro-psychiatric disorders, cancer, intractable muscle diseases and diseases that affect the nerves of the gastrointestinal tract.[25]

iPS cells are derived from skin or blood cells that have been reprogrammed back into an embryonic-like state. They enable the development of an unlimited source of any type of human cell needed for therapeutic purposes.[26]

T-CiRA promises a smoother research-development-commercialization process through direct links between Takeda and Kyoto University.

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