TreeFrog therapeutics

In the stem cell jungle

TreeFrog Therapeutics helps decipher the wood from the trees in this series dedicated to all that is **Cell Therapy**

Despite centuries of discovery since the first glimpse of a cell was captured through a microscope in the late 1600s, cell therapy is still a nascent industry. The path to where we are today, with several life-saving cell therapies available has been long with highs and lows.

However, the immense potential and the speed at which it has been advancing in the last decade alone, makes it one of the most exciting areas in medicine.

What is cell therapy?

When a cell gets damaged, gets attacked or simply grows old, they usually die and other cells are created to take their place.
But sometimes, cells do not get replaced, or damaged cells replicate instead of dying. In cell therapy, special cells are delivered to the body as a treatment.

BODY

37.2 trillion cells with specific functions[i]

- Blood
- Muscle
- Brain
- Bone

SPECIFICALLY ENGINEERED CELLS

CAN CURE

Certain types of cancer
Genetic disorders
Degenerative diseases

ADMINISTRATION

Topical, injectables, infusion, microtissues, bio scaffold, scaffold-free system[ii]

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A (very) recent history of cell therapy development

While progress towards effective cell therapies has been ongoing since the 1600s, the last 70 years saw an acceleration of progress in the understanding of diseases and conditions, alongside significant milestones in the use of cells for treatment.

Here are just a few that we believe were particularly exciting!

1950

The first Bone Marrow Transplantation took place in 1957 by Dr. Edward Donnall Thomas[iii]. This is one of the earliest forms of cell therapy and is still used to treat various forms of leukemia and blood disorders. The procedure uses hematopoietic stem cells. In 1990, Dr. Thomas received a Nobel Prize for his work in cell transplantation.

1980

This was a decade that saw a lot of progress in skin grafts and transplants such as transplanting cells to help treat burns and wounds[IV]. This decade also saw the first clinical trial of a cell-based therapy for humans with Parkinson's Disease (PD)[V].

1990

The 1998 discovery of human embryonic stem cells (hESCs) and how to grow them by James Thomson opened new possibilities for regenerative medicine[VI]. Embryonic stem cells disappear after a few days to form different germ layers and by extracting the cells before this starts to happen, they can be cultured in a lab and can self-renew continuously in the right conditions.

2000

In 2001, the first double-blind controlled trial of a cell-based therapy in PD was performed and in 2003, John Nutt organized the first randomized, double-blind clinical trial of glial cell-derived neurotrophic factor for the treatment of PD. However, several disadvantages, such as the insufficient therapeutic efficacy and ethical issues significantly limited their wide application[VII].

2006

A year that led to our existence today! 2006 is the year that Professors Yamanaka and Takahashi discovered induced pluripotent cells (iPSCs). They developed a means of transforming an adult skin cell back into a cell that behaved like an embryonic cell – i.e. a stem cell. These can then be reprogrammed into a skin, nerve, muscle or any other cell type. They won the Nobel Prize for their work[VIII].

2010

The first Chimeric Antigen Receptor T-Cell Therapies (CAR-T) were used successfully to beat cancer in 2010 in an adult patient and in 2012 in a pediatric patient. This was a major breakthrough, genetically modifying a patient's immune cells to target cancer cells when injected back into the body. The first treatments were approved in 2017[ix].

2018

TreeFrog Therapeutics was incorporated with our purpose of bringing Cell Therapy for All!

Today

Advances in the use of gene editing technologies and the use of iPSCs continue to progress and shape the landscape. In February 2026, Japan was the first country to approve the first two iPSC-derived medicines for heart disease and Parkinson's disease reinforcing the potential of regenerative medicine and hope for millions.

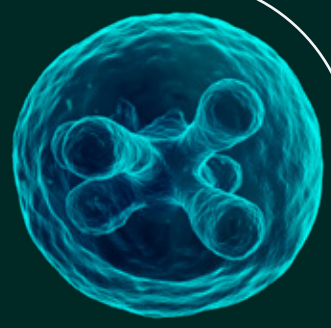
What types of cells are used in cell therapy?

There are many types of cells used depending on the disease. Some of the most common include:

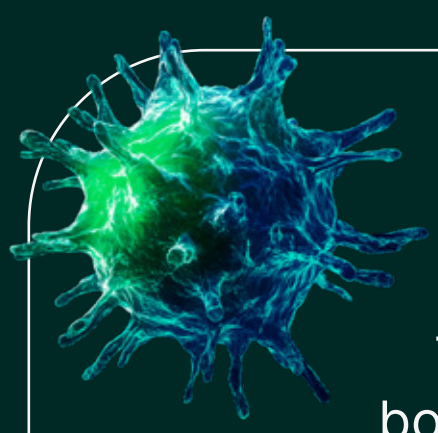
Embryonic Stem Cells (ESCs) and Induced Pluripotent Stem Cells (iPSCs)

They have the potential to differentiate into almost any cell type in the human body (the meaning of pluripotent).

Hematopoietic Stem Cells (HSCs)



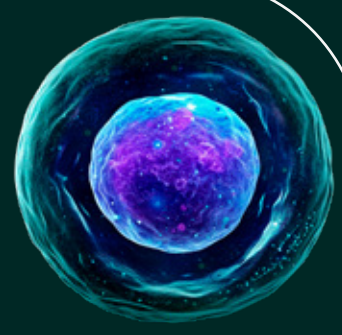
Found in bone marrow and blood, they can differentiate into various blood cell types, such as red blood cells, white blood cells, and platelets.



Mesenchymal Stem Cells (MSCs)

Typically derived from bone marrow or adipose tissue, they have the potential to differentiate into bone, cartilage, and fat cells.

Immune System Cells (T cells and NK cells)



Natural Killer (NK) cells are what they say! Immune cells play a crucial role in recognizing and destroying abnormal cells, including cancer cells.

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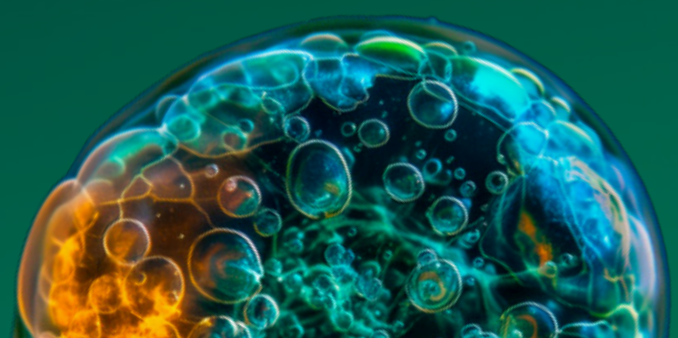
What is the difference between **autologous and allogeneic** therapies?

AUTOLOGOUS	ALLOGENEIC
The patient's own cells are used for the development of the treatment	A donor cell is used for the development of the treatment
The treatment is personalized to the donor patient	The same treatment is used to cure many patients.
No need for immunosuppression	Need for immunosuppression
Patient-derived cells may carry pathogenic mutations, potentially increasing safety risks	Donor cell lines are screened to confirm the absence of pathogenic mutations.
Time-consuming and costly development	Optimized development and cost as treatments can be 'off-the-shelf' and used for many patients

What diseases **can be treated with cell therapy ?**

The promise of cell therapy to treat and even cure certain health conditions is immense. Traditional pharmacological approaches cannot always address complex diseases. Cell therapy can treat diseases and conditions at a more fundamental level, targeting the root cause at a cellular or tissue level. In diseases and conditions where degeneration happens, such as Parkinson's disease or liver disease, allogeneic cell therapy has the potential to promote tissue repair and cell regeneration. Presently, there are still relatively few approved therapies available and most of these are autologous, but there are now allogeneic treatments for certain types of cancer and blood disorders such as leukemia, lymphomas, for skin grafts & wound healing. There are over 1000 companies working to target diseases of the major organs including the central nervous system, pancreas, heart and liver.



What therapies are TreeFrog therapeutics **focused on?**

We are an R&D biotech advancing a pipeline of cell therapies based on a proprietary technology platform, C-Stem™ that can amplify and differentiate cells in one closed GMP-compliant system.
Our lead program is in Parkinson's disease.

TRANSFORMATIONAL TECHNOLOGY

Unprecedented amplification factor with high quality & viability

Single-batch of 15bn cells in one run, in one week

Unique 3D microtissue that provides protection to cells and facilitates their transplantation

GMP compliant & commercial scale-up ready

PARKINSON'S DISEASE FOCUS

Generation of 3D neural microtissues containing mature dopaminergic neurons to restore those that have been lost to disease

Excellent pre-clinical results with fast & full recovery at 4 months, sustained at 8 months[x]

Regulatory studies ongoing and on track to be ready for first-in-human trial in 2027

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[I] Bianconi E, Piovesan A, Facchin F, et al. An estimation of the number of cells in the human body. PLOS Biol. 2013;11(8):e1001639.]

[II] Front Med (Lausanne). 2021; 8: 756029. Cell Therapy: Types, Regulation, and Clinical Benefits. Abed El-Hakim El-Kadiry, Moutih Rafei and Riam Shammaa. Accessed 2.02.2024 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8645794/

[III] Thomas ED, Lochte HL Jr, Cannon JH, Sahler OD, Ferrebee JW. Supralethal whole body irradiation and isologous marrow transplantation in man. J Clin Invest. 1957;36(11):1701-1716.]

[IV] https://www.ncbi.nlm.nih.gov/books/NBK223690/

[V] Milestones of Parkinson's Disease Research: 200 Years of History and Beyond - PMC (nih.gov)

[VI] Thomson JA, Itskovitz-Eldor J, Shapiro SS, et al. Embryonic stem cell lines derived from human blastocysts. Science. 1998;282(5391):1145-1147.

[VII] Milestones of Parkinson's Disease Research: 200 Years of History and Beyond - PMC (nih.gov)

[VIII] Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors
Kazutoshi Takahashi 1, Shinya Yamanaka.
https://pubmed.ncbi.nlm.nih.gov/16904174/

[IX] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10225594/

[X] Prudon, N, Cordero-Espinoza L, Abarkan M et al.
Bioreactor-produced iPSCs-derived dopaminergic neuron-containing neural microtissues innervate and normalize rotational bias in a dose-dependent manner in a Parkinson rat model. Neurotherapeutics Journal 21 (2024)

Cell Therapy for All

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