In the stem cell jungle

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

Cell therapy and gene therapy are related fields within the broader umbrella of regenerative medicine, but they have distinct approaches and mechanisms of action. It also depends on the disease or condition as to which approach will work best.

What is the difference between **Cell and Gene Therapy?**

Lets start with the basics.

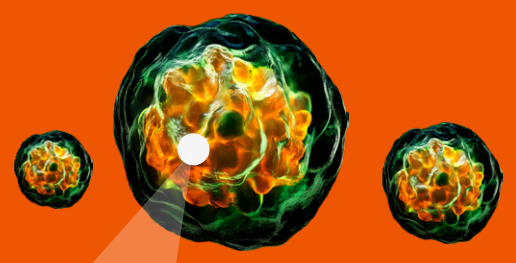
What is a gene in relation to a cell?

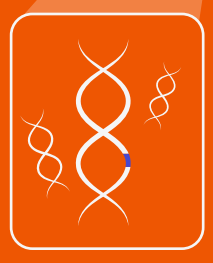
Genes and cells are mutually dependent. Genes are in each of the 37 trillion cells[I] in our body. They are made of DNA, which works as an instruction manual for the body. While genes provide instructions, cells carry them out.

We inherit one set of genes from each parent, and these genes copy themselves as cells divide. There are approximately 20,000-25,000 genes in the body. Genes can however go rogue. Sometimes, a genetic mutation may occur which can arise randomly or be inherited. Not all genetic mutations are harmful, but some cause diseases and conditions.

CELLS

37.2 trillion cells in our body





DNA

The instruction manuel for the body

GENES

20,000-25,000 genes in the body

— ATCGATCG —
— TAGCTAGC —

Genetic mutations can cause diseases

Cell Therapy

In cell therapy, cells are delivered into the body to treat or cure disease by replacing, repairing or regenerating diseased, sick cells and damaged tissues. They may involve genetically engineering or manipulations in formulation. They can be administered topically or as injectables, infusions, tissues, bio scaffold or scaffold-free systems[ii]. Cell therapy holds great promise in multifactorial diseases such as neurogenerative diseases including Parkinson's disease, blood disorders, autoimmune diseases, tissue regeneration (such as damaged liver tissue) or immunotherapy, such as the CAR-T cell therapies for cancer.

Gene Therapy

In contrast, gene therapy involves the introduction, modification, inactivation or correction of genetic material within a patient's cell to treat or prevent disease. The mechanism of action is different to cell therapy, as instead of transferring cells to the body, gene therapy is based on altering the genetic code of a patient. It could mean adding a gene to replace a defective one or repairing a mutated gene for example. Because genes are buried deep inside cells, they can't be delivered directly. Gene therapy therefore uses a carrier—called a vector—to transport genetic material into the body.

These carriers are often viruses or non-viral vectors, as viruses do a very good job of moving around the body. Once inside the cells, the therapeutic genes can integrate into the genome or operate independently, depending on the therapy's design. Gene therapy is promising for treating genetic disorders caused by mutations in a single gene, hereditary diseases such as certain types of muscular dystrophy or cystic fibrosis.

What are other differences between **Cell & Gene Therapy?**

Both cell and gene therapy hold great promise. The development of each therapy depends on the disease target and the technologies involved.

Gene Therapy

Choosing the right vector and its ability to get to the right cell to have the right impact is very complex. With gene therapy, we are altering genetic material within a patient's cells so it is critical to ensure safety, efficacy and long-term follow up data.

CRISPR-CAS9

In gene therapy, one of the major advances recently has been the development and application of the gene-editing tool, CRISPR-Cas9. Data was first published in 2012.

Jennifer Doudna & Emmanuelle Charpentier (2020)

CRISPR-Cas-9 can remove or introduce new genes as well as silence or activate genes.

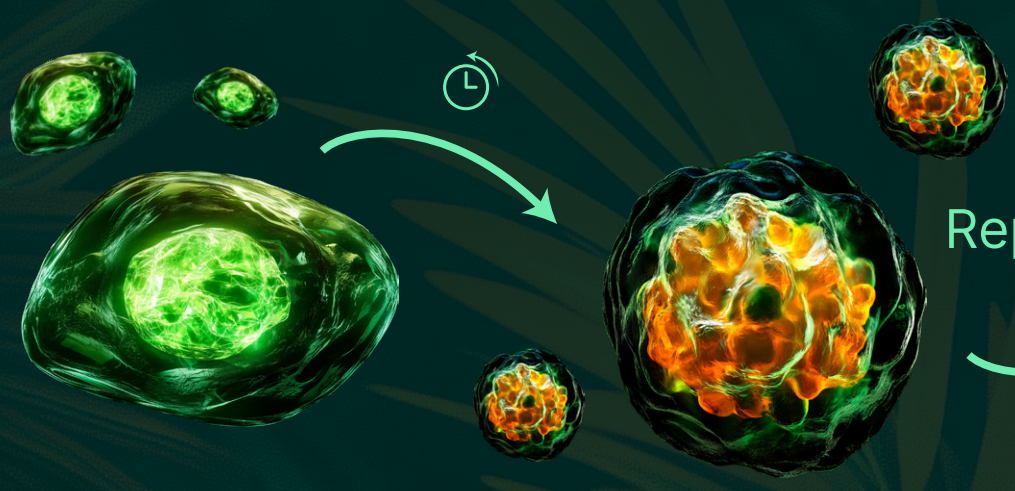
The first gene therapy product using CRISPR-Cas-9 was approved in December 2023 for sickle cell disease[III].

Cell Therapy

Selecting the right source cell and ensuring its genomic integrity and viability is crucial as millions or perhaps even billions of cells are needed for a therapy. Being able to amplify, differentiate and produce at commercial scale are three of the biggest challenges facing companies today.

iPSC

A bone marrow transplant is an example of one of the earliest cell therapies in 1957. But in 2006 Professors Yamanaka & Takahashi discovered induced pluripotent cells (iPSC)[IV]



Brain
Bone
Muscle

Adult skin cells

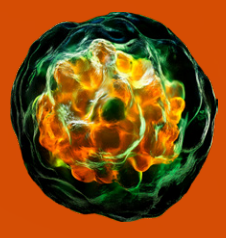
Embryonic-like cell

iPSC

iPSC discovery has opened up a whole new area of R&D for potential cell therapies.

What is TreeFrog therapeutics doing in Cell & Gene Therapy?

TreeFrog Therapeutics currently focuses on cell therapy. We are unique in our approach bringing together biophysicists, cell biologists and bioproduction engineers to address the challenges of the industry - producing and differentiating cells of quality at unprecedented scale, cost-effectively.



+ cstem by TreeFrog therapeutics =

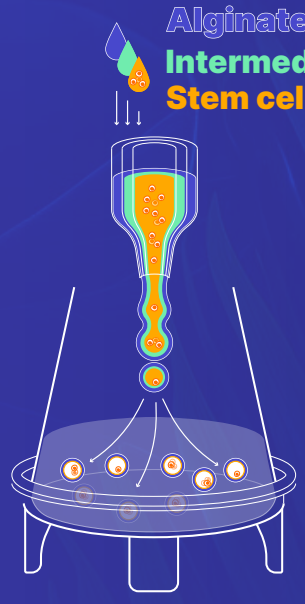
iPSC **GMP compliant** **Therapies**

e.g. Parkinson

cstem by TreeFrog therapeutics

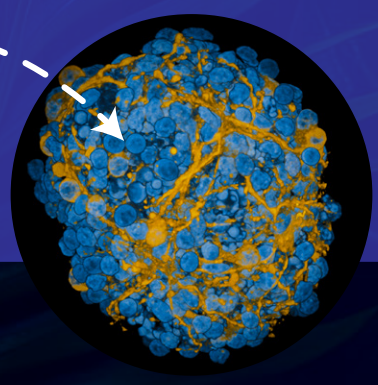
Blends microfluidics and stem cell biology.

- 1000s capsules per second
- Seeding of up to 10L bioreactors
- Billions of cells per batch



Engineered to mimic the in vivo stem cell niche, the capsules protect the cells and allow them to grow exponentially in 3D

- No impeller-induced shear stress
- Equal access to nutrients



Our lead program is in Parkinson's disease:

- Several proof of concept studies completed;
- Results show rapid onset full recovery at sixteen weeks, sustained at 8 months post-transplant;
- First-in-human trial to be ready by 2027.

Ready-to-transplant 3D microtissue

TreeFrog therapeutics

[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] https://bitesizebio.com/47927/history-crispr/

[IV] Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors

Cell Therapy for All

To learn more visit

treefrog.fr