

ARM Foundation
for Cell & Gene Medicine

A GUIDE TO

Understanding Cell & Gene Medicine



BROUGHT TO YOU BY HEALING GENES

A program of ARM Foundation for Cell & Gene Medicine

November 10, 2020

Patient Organization Toolkit



Dear Patient Organization leader,

Cell and gene medicines have potential to benefit millions of families who are living with a painful, disabling or terminal disease, many currently without adequate treatment options. Unfortunately, patient access to these transformative therapies will not happen as quickly as we'd like until cell and gene medicine is better understood and patients are comfortable exploring these technologies as potential treatment options.

“Cell and gene medicine will achieve its vast potential only when the public, patients, and caregivers understand and accept it as a safe and effective therapeutic option.”

Stewart Parker, Board Chairperson ARM Foundation for Cell & Gene Medicine

FOCUSED ENTIRELY ON EDUCATION

The ARM Foundation for Cell & Gene Medicine is the only nonprofit 501(c)3 organization with a mission to increase awareness and understanding of potentially curative cell and gene therapies. We draw together multiple stakeholders through education and empowerment. We serve as the educational and information catalyst to **accelerate patient access** to safe, efficacious, and potentially curative therapies. Our work begins with helping people make informed decisions about cell and gene medicine and ends when families receive the benefits of 21st Century advances in cell and gene medicine.

ENABLING INFORMED DECISIONS

Patients say their biggest concern about exploring a specific gene medicine is being able to make an informed decision. In a recent study of public perceptions about gene therapy, more than 50% of respondents said their number one concern was not receiving appropriate information. Cell and gene medicine science has accelerated in the past few years, and researchers have worked tirelessly to harness new tools and technologies for human therapeutic use.

As a patient group leader, you can be equipped to inform patients and families by using the resources of the ARM Foundation for Cell & Gene Medicine.

YOUR PARTNERS IN EDUCATION

The ARM Foundation wants to partner with you. Your unique expertise, personal insights and reach to patients can increase awareness and understanding of cell and gene medicine among multiple stakeholders in the disease or disorder communities.

On the [Healing Genes](#) website you will find a PowerPoint presentation *Understanding Cell & Gene Medicine*. This companion *Guide* is for you, to learn from so you can present to your disease communities. The *Guide* is also available on [Healinggenes.org](#).

Understanding Cell & Gene Medicine, and all our materials, are

- Based on input from a patient advisory panel and dozens of patient group leaders
- Carefully vetted by science and medical experts, patients and caregivers
- Provided for **free and unrestricted use** to support your organization's cell and gene medicine education efforts

As scientists work toward potentially curative therapies, the ARM Foundation can partner with you to help patients, caregivers and others understand cell and gene medicine.

CONTACT US

Have questions? Please contact jbraswell@thearmfoundation.org with any questions or other issue related to cell and gene medicine education.

HELPFUL VIDEOS

Introducing Healing Genes

- Length: 4:47 minutes
- This video introduced the goals and programs of the ARM Foundation in 2018

Cell & Gene Medicine: Your Questions Answered

- Length: 4:03 minutes
- A Visual FAQ with parent and Professor Dr. Matt Might, who answers 5 key questions about cell & gene therapies.
- Enhanced for the visually impaired [here](#) (length 6:38)

A Guide to Understanding Cell and Gene Medicine

BROUGHT TO YOU BY HEALING GENES

A PROGRAM OF ARM FOUNDATION FOR CELL & GENE MEDICINE

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How to Use the Patient Organization Toolkit

The Patient Organization Toolkit for Cell & Gene Medicine is centered the presentation *Understanding Cell & Gene Medicine* for you to use. The Presentation is enhanced by this **Guide** that is available as pdf and in-line on the ARM Foundation [Healing Genes](https://healinggenes.org/) site (<https://healinggenes.org/>). Healinggenes.org contains all the cell and gene medicine information found in *Understanding Cell & Gene Medicine* and provides additional ways to learn about cell and gene medicine, including videos and links to other ways to learn.

The ARM Foundation for Cell and Gene Medicine developed the Patient Organization Toolkit for patient advocacy organizations that support families and individuals whose lives are challenged by a rare, painful, debilitating, or terminal disease.

This *Guide to Understanding Cell & Gene Medicine* is the companion to the powerpoint presentation *Understanding Cell & Gene Medicine* to help patient organization leaders better understand potentially curative cell and gene therapies. This **Guide** gives background information so you can present the slide show with confidence. Your stakeholders include volunteers, employees, caretakers and family members, foundation boards, grant making organizations, community and health care partners, health care providers, medical and scientific researchers, patient advocates, and policy makers.

Our goal is to advance your understanding of Gene & Cell Medicine more fully so you can present an informative powerpoint, download resources including videos and graphics, and build your own websites by linking to resources vetted by the ARM Foundation for Cell & Gene Medicine. The Patient Organization Toolkit is designed so patient organizations can cut, paste, share and customize informational materials from the toolkit to meet the needs of specific patient advocacy groups and stakeholders using the communication channels they use best to share information.

To get the slide show, click [here](#).

Understanding Cell and Gene Medicine

As patient advocates, your message is important. Cell and gene medicine incorporates a complex lexicon that can be confusing. Within our communities, including patients, caregivers, health care providers, medical researchers and scientists, policy makers, the public and the media, there is a gap between what scientists, researchers and specialists know and what is generally known about cell and gene medicine.

The ARM Foundation slide show, *Understanding Cell & Gene Medicine*, can help different stakeholders understand the fundamentals of cell and gene medicine, including gene therapy, gene editing, cellular therapy, and regenerative medicine.

TALKING TO THE GENERAL PUBLIC ABOUT CELL AND GENE MEDICINE

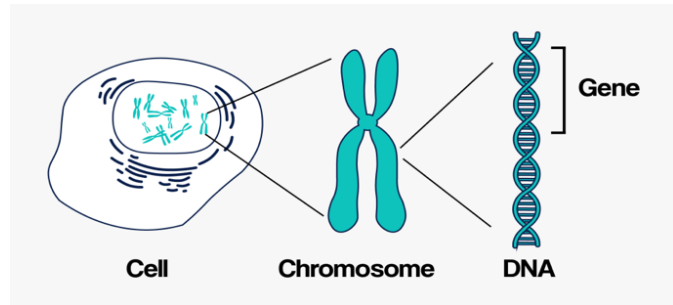
Sometimes, a disease or debilitating health condition is caused by one or more genetic changes in the body. Many diseases or conditions caused by defective genetic code have few treatment options. Conventional medicine often treats the unwanted symptoms of the disease or slows down the disease. Doctors use **cell and gene medicine** to try to resolve the underlying genetic defect that is causing an incurable disease or health condition.

Cell and gene medicine are part of **Regenerative Medicine**, which draws on insights of late 20th century cell biology, molecular biology, chemistry, computer science, bioengineering, genetics, medicine, robotics, and other fields to understand and harness the body's repair and development mechanisms. Regenerative medicine addresses many of the most challenging health issues in medicine. Treating the genes themselves, that are the root causes of gene-based diseases and disorders, is the aim of Gene Medicine. In Cell Therapy, cells themselves are used as agents of repair or restoration of function.

Understanding Genes and Genetic Disease (slides 4-10)

Genes are regions of DNA that direct the production of proteins and direct biologically important functions throughout the body. Genes are inherited from our biological parents.

- DNA is the name of a molecule.
- Each DNA molecule is made up of a sequence of building blocks called nucleotides and there are only 4, known by the letters A G C and T.
- On the rungs of the famous double helix, the DNA molecules are paired, A with T and G with C
- A gene is a specific sequence of DNA molecules that act as the instructions for making protein. The Specific sequence of the DNA is called the Genetic Sequence .
- The genetic sequence is written out as letters like TGCATTG, or GATTACA.



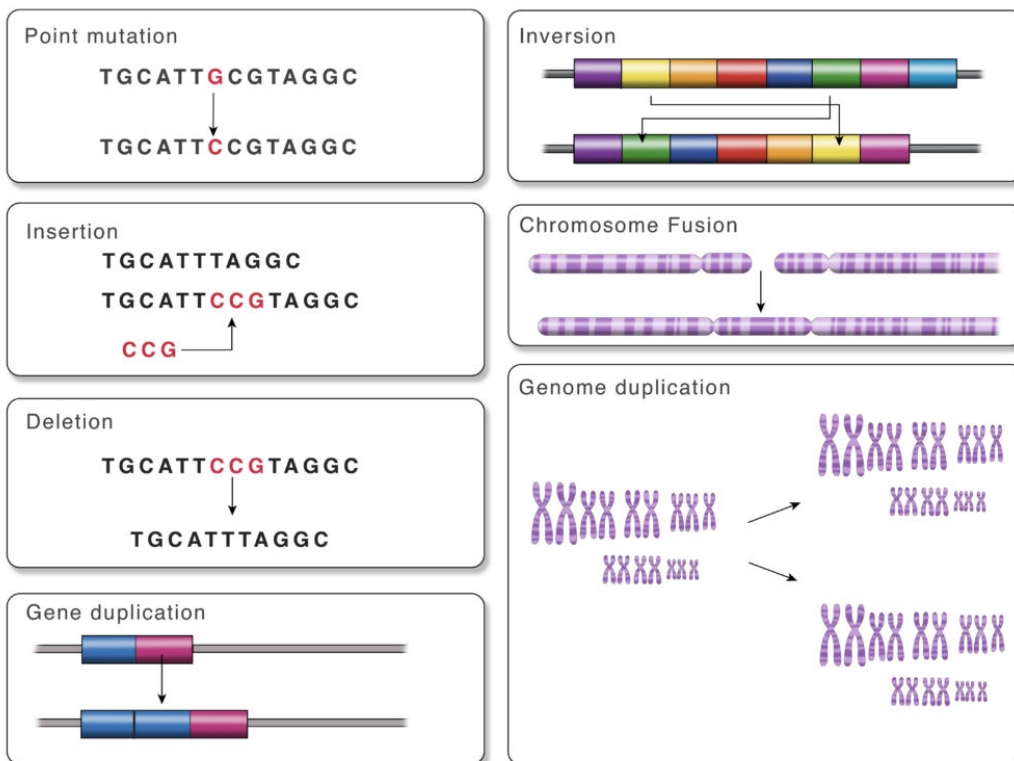
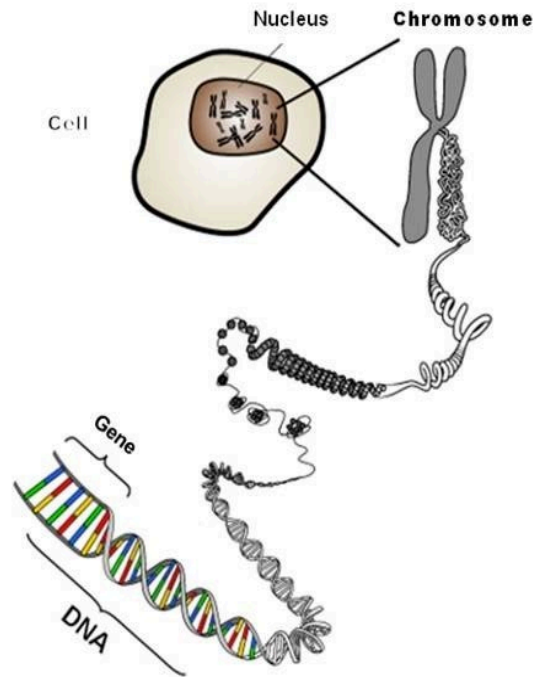
People have around 25,000 genes. We typically get two copies of each gene, one from each of our parents. These genes influence everything from the color of our hair to the power of our immune system, but genes aren't always assembled correctly. Mutations, or errors, in genes can cause disease by failing to produce sufficient levels of a functional protein. A mutation is a change in the genetic sequence. Not all mutations have bad effects.

Genes can operate incorrectly when:

- inherited mutations pass from parents to babies
- when 2 recessive disease causing genes are received from 2 parents
- when one dominant disease-causing gene is received from one parent in eggs or sperm
- a gene mutation occurs as the cells are replicating

Patient Organization Toolkit

- a gene mutation occurs as the chromosomes are dividing in half during the creation of eggs or sperm
- age causes mutations (changes) over time
- the genes are damaged by chemicals and radiation, or other environmental toxins. For example, Skin cancer is one disease caused by long-term changes to cells after too much exposure to sunlight's ultraviolet radiation.
- Other gene mutations can occur when a piece of genetic code is missing, defective, or duplicated in error during pregnancy. Larger mutations can affect many genes on one chromosome. Defective genes can result in a disease or medical disorder.



Introduction to Cell & Gene Medicine (slides 11-15)

Today, technologies show promise for combatting gene-based diseases and resolving other conditions that may be reduced or reversed by cell and gene medicine. Single-gene disorders are at present thought to be more amenable to gene therapy than chromosomal or complex disorders.

SINGLE-GENE DISORDERS	THERAPEUTIC APPROACH
Cystic Fibrosis	Gene therapies are in development
Sickle Cell Disease	Gene Editing approaches are in Clinical Trials
Spinal Muscular Atrophy	Zolgensma & Spinraza are approved gene therapy products
Huntington Disease	A gene therapy is in clinical trial
Fragile X Syndrome	Gene therapy approaches are in development

[ASCGT's Search Tool for Cell & Gene Therapy Clinical Trials \(by disease\)](#)

FAQ: What is the difference between traditional prescription drug therapy and gene and cell therapy?

Prescription pharmaceutical medications are typically used to manage diseases, mitigate symptoms and relieve pain. The concept behind gene and cell therapy is to target the genetic cause of the disease. The goal is to rid the person of recurring symptoms, ideally after a single treatment. Gene therapy adds working genes to specific cells.

Currently, the therapies cannot be delivered as a standard type of drug available at a pharmacy. Instead, you find approved gene therapies at designated treatment centers. Gene therapies aim to treat diseases that currently have no treatments, where treatment options do not work well, or are high risk without the possibility of a cure. Gene therapy offers promise to treat rare inherited disorders. Of the 7,000 rare diseases that exist, 95 percent have no approved current treatment.

It is worth noting that gene therapy targets somatic cells, the vast majority of cells in the body. Gene Therapy does not target our reproductive or "germline" cells, meaning the sperm or the egg cells. This means that the treatment is corrective to the patient only and is not passed to the next generation. Many diseases and health conditions may be improved by cell and gene medicine. A list of *Approved therapies* is found at the end.

Cell Therapy or Cellular Therapies (slides 16-20)

Cell Therapy is the transfer of whole cells into a patient to replace or repair damaged tissue or cells. Cell therapy transfers healthy cells into a patient's body to grow, replace, or repair damaged tissue for the treatment of a disease or trauma. The cells used in cell therapies may originate from the patient (autologous cells) or a donor (allogeneic cells). There are autologous therapies that have been approved for use. Kymriah, Provenge, and Yescarta for cancers.

The most common type of allogeneic cell therapy is blood transfusion, in which red blood cells, white blood cells, and pieces of cells called platelets are transferred from a donor to a patient.

If you collected your own blood and gave it back to yourself, that would be an **autologous** cell therapy. Sometimes before major surgery the patient is asked to 'donate' blood that would be used if she needed blood during the surgery.

A bone marrow transplant is a stem cell therapy. Blood forming stem cells from bone marrow are transfused from one person to another. The new blood forming stem cells divide and create all the cells in the blood – white blood cells, red blood cells, and many other types.

One goal of allogeneic cell therapy is so-called "off-the-shelf" cell therapy. **Allogeneic** cells are derived from a donor or donors, and prepared or manufactured in large quantities, ideally to create a treatment that could serve many patients. Allogeneic cell therapies, once demonstrated to be effective, would be manufactured and readily available to a patient.

Different types of cells can be used to create cell therapy using complex tools:

- Embryonic stem cells, pluripotent stem cells derived from embryos not needed after In Vitro Fertilization (IVF)
- Induced pluripotent stem cells (iPSC), derived from skin or blood cells that have been reprogrammed so they become stem cells. The cells can be guided to develop into specific human cells needed for therapeutic purposes.
- Hematopoietic stem cells (HSCs), stem cells responsible for refreshing our supply of healthy blood cells; they can produce billions of new blood cells each day.
- Cord blood cells. Cord blood is the blood left over in the umbilical cord and placenta after a baby is born. It can be collected and stored for future use. The primary source of stem cells in cord blood are hematopoietic stem cells

(HSCs). These cells are the building blocks of our blood and immune system. They can be used in the treatment of blood cancers such as leukemias and lymphomas, and disorders such as sickle cell disease and Wiskott-Aldrich syndrome. Additional uses for umbilical cord blood and tissue are currently under investigation.

The therapeutic use of cord blood in the United States is regulated by the FDA. Cord blood is not a cure-all. You can learn more at the US FDA website, [here](#).

- Mesenchymal stromal cells
 - Sometimes called mesenchymal ‘stem cells,’ or MSCs, these are cells that differentiate into the body’s connective tissues, blood, lymph nodes, bone, and cartilage.
- Immunotherapy cells
 - Natural Killer (NK) cells
 - Lymphocytes
 - Dendritic cells
 - CAR – T cells, Autologous cells (cells from the patient) that are specially treated and reinfused to eradicate a patient’s cancer. Two approved CAR-T therapies are available in the US Yescarta and Kymriah.
 - Lymphocytes are white blood cells that launch the body’s initial immune response. They are found in the circulation system, lymph nodes, tonsils, and spleen.
 - Dendritic cells: Cells responsible for the initiation of adaptive immune responses that allow the body’s immune system to fight against damage.
- Other types of cells
 - Epithelial stem cells: Cells that form the surfaces and linings of the body
 - Retinal Progenitor Epithelial cells are stem cells for the retina. Transplant of RPE is being tested as a cure for blinding retinal disease.
 - Neural progenitor cells are the cells that give rise to the various cells of the central nervous system, comprised of the brain and the spinal cord. They are being tested for repair of trauma to the spinal cord or peripheral nerves.
 - Pancreatic islet cells are clusters of cells inside the pancreas that produce insulin, the hormone required to move glucose (sugar) into cells for energy. Islet cells in a well-functioning pancreas contain cells that produce the hormones necessary for metabolic regulation. Transplant of islets is a

proven therapy for Diabetes Type 1, unfortunately, their effect when transplanted is not forever, and the supply of islets is limited.

- Skeletal muscle stem cells. Muscle stem cells are adult stem cells in skeletal muscle tissue which can self-renew and are create new skeletal muscle cells. In healthy bodies, these stem cells are activated in response to muscle injury to regenerate damaged muscle tissue.

HOW TO LEARN MORE

- [WHAT ARE STEM CELLS, A TED-EX TALK BY CRAIG A. KOHN \(2013\)](#) - This is a video that gives a reasonable overview of stem cells, despite the many scientific discoveries since 2013. The video says, “using stem cells to replace bodily tissue is called Regenerative Medicine” (1:45). Regenerative Medicine encompasses other scientific tools in addition to stem cells.
- [Closer Look at Stem Cells \(ISSCR Website\)](#)
- [A Patient Handbook on stem cell therapies – in six languages, by ISSCR](#)
- [Stem Cell Facts \(a 6 page booklet from ISSCR\)](#)

Gene Medicines or Gene Therapy (slides 21-24)

In **gene therapy**, doctors modify a person's genes to treat or cure disease. Human gene therapy seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells to prevent disease, reduce further damage and pain, or potentially cure the patient.

Gene therapies can work by several mechanisms. Gene therapy can be done by:

- Replacing a mutated (defective) gene with a healthy copy
- Introducing a new gene to the body
- Inactivating or "silencing" a gene that doesn't function properly

If a mutated gene is causing an important protein to function poorly, gene therapy seeks to restore the function of the protein and therefore restore certain functions of the patient.

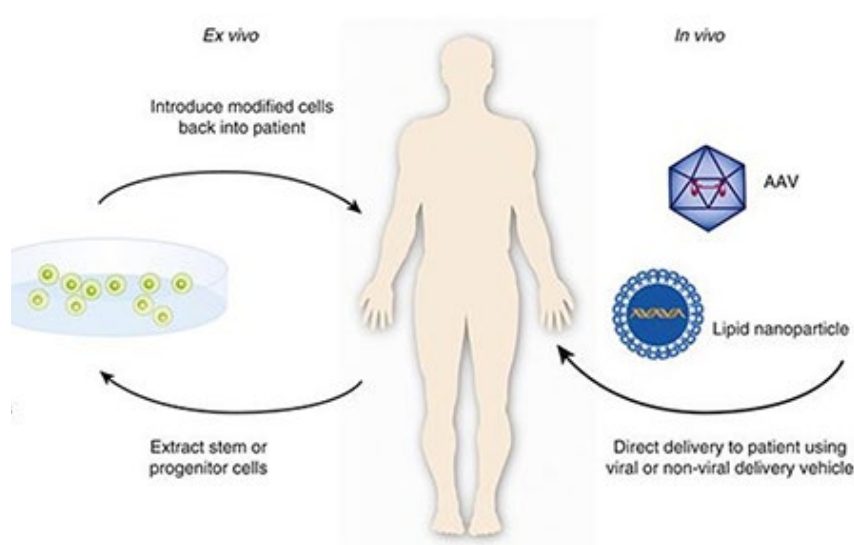
If a mutated gene causes an important cell-building protein to function poorly, gene therapy may be able to restore the function of the protein.

Replacing a disease-causing gene with a healthy copy of the gene

Inactivating a disease-causing gene that is not functioning properly

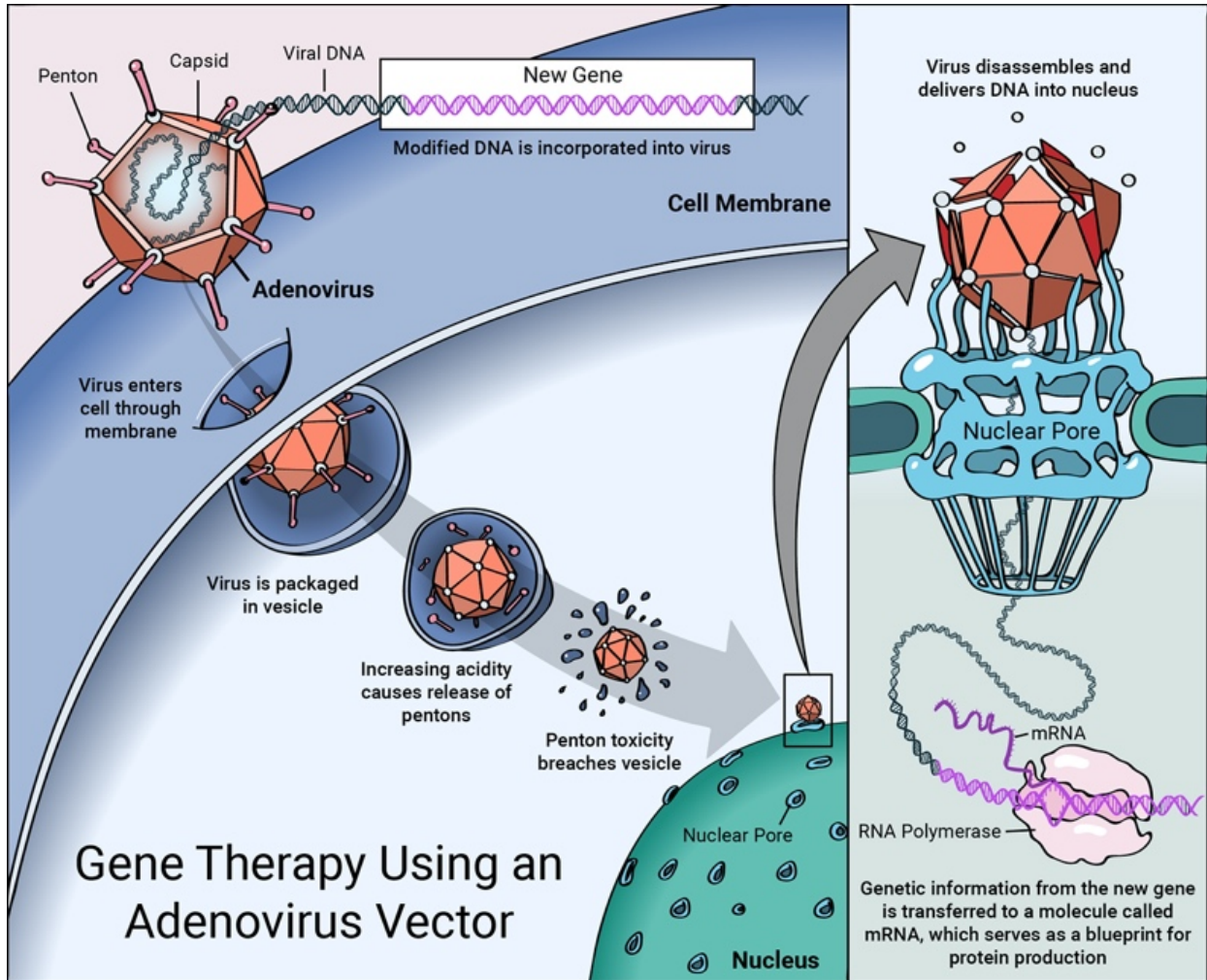
Introducing a new or modified gene into the body to help treat a disease

Researchers select the right approach based on the best current understanding of the CAUSE of the disease. This is an important point.



Gene therapy may be performed *in vivo*, in which a gene is transferred to cells inside the patient's body, or *ex vivo*, in which a gene is delivered to cells in a laboratory setting and the treated cells are then transferred back into the body.

Vectors and Viruses (slide 25-27)



NIH U.S. National Library of Medicine

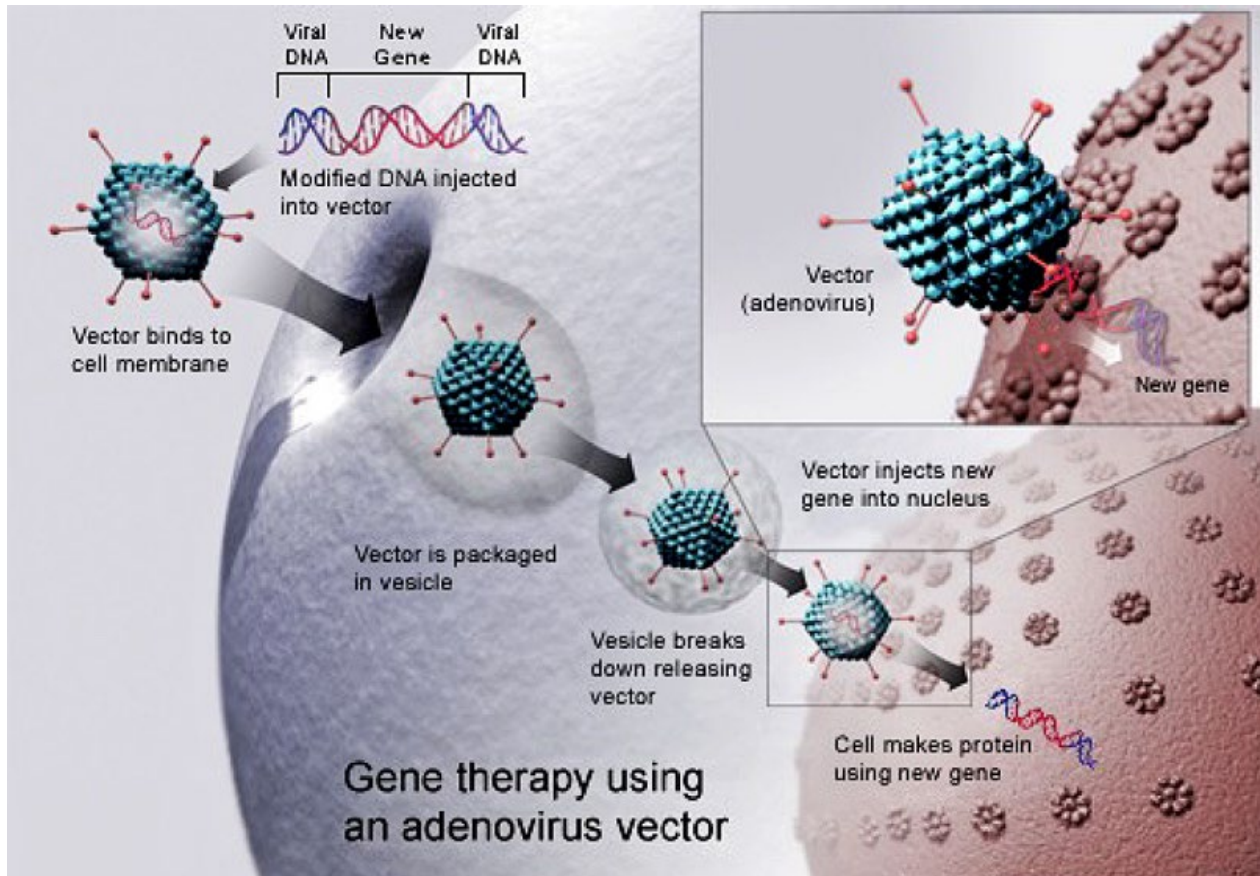
Currently, gene therapy developers develop medicines to introduce new or corrected genes into patient cells using vectors. **Vectors** are delivery vehicles, or carriers, that encapsulate therapeutic genes for delivery to cells. Currently used vectors include disabled viruses and nonviral vectors, such as lipid particles.

Deactivated or disabled viruses cannot make patients sick, even though they rely on the biology of viruses to operate. Viral vectors are made from parts of virus and act as the vehicle to transfer new genetic material into the cell where it is incorporated into the chromosomes in the nucleus.

Deactivated viruses that have been used for human gene therapy vectors include:

- **Lentiviral vectors:** A Lenti- vector can integrate its genome into both dividing and non-dividing cells in the body, leading to new gene expression that is designed to be stable and durable. Lentivectors can carry genetic information into the nucleus of cells, potentially allowing for stable and durable expression of the genetic information that it integrated into the cells.
- **Adeno-associated virus (AAV):** These viruses are small single-stranded DNA viruses grouped with parvoviruses. One parvovirus causes a rash in children known as “fifth disease.” Nevertheless, AAVs are a different class of parvoviruses and they are dependent on a helper virus co-infection to replicate. Viruses that have difficulty replicating make them better candidates to use to create vectors.
- **Adenoviruses:** Adenoviruses is a group of common viruses that can infect the lining of your eyes, airways and lungs, intestines, urinary tract, and nervous system. They are common causes of fever, coughs, sore throats, diarrhea, and pink eye.
- **Retroviruses:** Retroviruses have genes that are encoded in RNA instead of DNA. They are widely used and well-known in laboratory biology. Because they enable persistent gene expression they might be a good approach for several monogenic diseases. Immunogenicity and insertional mutagenesis are obstacles to a wider clinical use of these vectors.
- **Herpes simplex virus** can be used to create vectors that can carry a large amount of genetic material, for example, for delivery to neural cells.

Gene Modified Cell Therapy (slide 28)



In gene-modified cell therapy, specific cells are genetically modified outside the body and returned to the patient's body in order to help the patient fight a disease. After removing specific cells from the body, the cells are transferred to a laboratory where a new gene can be introduced or a faulty gene can be corrected in the cells. Therapies created this way can also be called *ex vivo* gene therapies. The modified cells are then returned to the patient. *Chimeric antigen receptor T-cell (CAR T-cell) therapy* for cancers works this way.

Gene-modified cell therapy includes:

- **Chimeric antigen receptor (CAR T-cell) therapies:** This is a way of modifying the patient's immune cells (T cells) to recognize structures (antigens) on the surface of cancer cells. Once the T-cell receptor binds to a tumor antigen, the T cell is stimulated to attack the cancer cell.

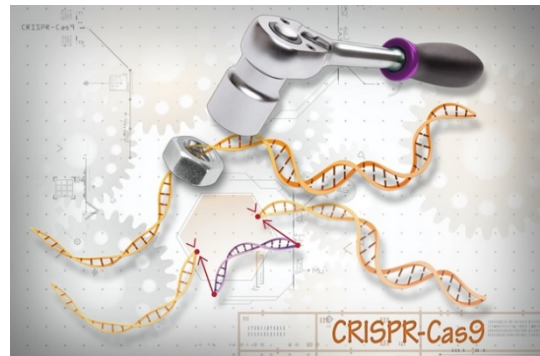
- **T-cell receptor (TCR) therapies:** T Cell Receptors (TCRs) can recognize tumor-specific proteins on the inside of cells.
- **Tumor infiltrating lymphocytes (TILs):** TILs infiltrate solid tumors. The therapy removes T cells from a patient and treats them so the T-cells are primed to recognize tumors. The TILs are reintroduced into the patient, generally after the patient has a low white blood cell count due to treatment with chemotherapy. TILs have been demonstrated to be effective in some forms of cancer.
- **Natural killer (NK) cell therapies:** NK cells in the body can naturally recognize mutated or infected cells and eliminate them. NK cells can escape some immune attacks that might prevent them from being effective against diseased cells. They release signaling proteins that recruit and activate the body's immune system. NK cells derived from stem cells are being tested at present.
- **Marrow derived lymphocytes (MILs):** MILs are bone marrow-derived cells that house a reservoir of T-cells. The T-cells can be prepared to fight disease.
- **Dendritic cell vaccine:** Dendritic cell vaccines, made from dendritic cells, promote antitumor immune responses. Dendritic cells are rare cells found in the circulation system and in tissues. These specialized immune cells play a critical role in promoting an immune response, including an ability to regulate and control T-cell responses.

HOW TO LEARN MORE:

[Gene Therapy: Your Questions Answered](#) - This video is presented by NORD's RareEDU™ to address a vital topic to today's rare disease community.

Gene Editing (slide 29-31)

Gene Editing (also called **genome editing**) makes targeted changes to existing DNA in genes located on the chromosomes. With gene editing, researchers can enable or disable targeted genes, correct harmful mutations, and change the activity of specific genes. Gene editing is a set of techniques that enable researchers and clinicians to rewrite the instruction encoded in the DNA of genes. These molecular-biology techniques can enable or disable targeted genes, correct harmful mutations, modify expression of genes or change activity of a specific cell, with the goal of restoring normal function. CRISPR is an example of a gene editing technique that has entered clinical trials.



This illustration is meant to give the message that CRISPR-Cas9 is a gene editing tool for certain purposes, just like a socket wrench performs a specific function.

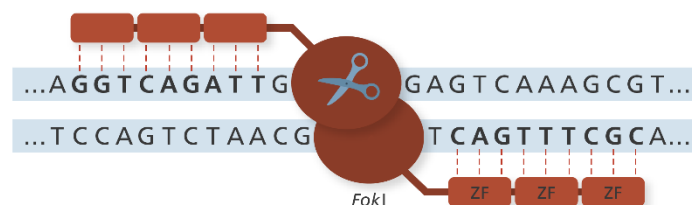
The goal of gene editing is to remove, disrupt or correct faulty elements of DNA within the gene rather than replace the gene as gene therapy would. Gene editing uses systems that are highly precise to make this change inside the cell. The cells can be from the patient or donor.

DNA may be inserted, replaced, removed, or modified at particular locations in a genetic sequence for therapeutic benefit in order to treat cancer, rare inherited disorders, HIV, or other diseases. Several approaches rely on the use of molecular scissors, often an engineered enzyme, to make precise cuts at a specific location in the genome. The gap that results is then repaired, using healthy genetic material, to create a corrected gene.

Genome editing enzymes that are currently used in genome editing include:

- Nucleases such as Cas9 and Cas 12a that derive from Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas)
- Meganucleases
- Zinc finger nucleases (ZFNs)
- Transcription activator-like effector-based nucleases (TALEN)

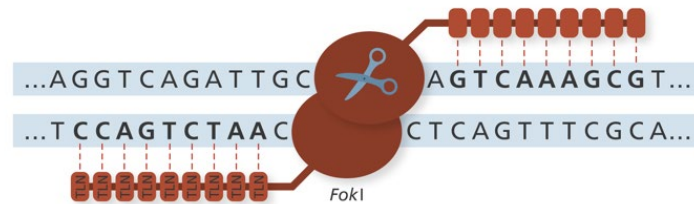
Zinc-finger nucleases (ZFNs)



Alternatively, genome editing can also be performed by homologous recombination of adeno-associated virus (AAV)-derived sequences into the patient's DNA.

Homologous recombination is a type of genetic recombination that occurs during meiosis (the formation of egg and sperm cells). Paired chromosomes from the male and female parent align so that similar DNA sequences from the paired chromosomes cross over each other. Crossing over results in a shuffling of genetic material and is one reason for the genetic variation and yet similarities in appearance we see in our biological children.

Transcription activator-like effector nucleases (TALENs)



HOW TO LEARN MORE

[What is Gene Editing?](#) – Video by The Royal Society (2016)

RNA medicines (slide 32)

Zinc finger and CRISPR-Cas9 gene editing are also used to silence genes. Gene silencing might be used if a gene mutation is causing overproduction of a protein.

Another method to ‘turn off’ a gene is RNA interference (RNAi). Specific genes are prevented from producing protein by prevent messenger RNA (mRNA) from creating the disease-causing proteins.

- To make RNAi into medicine, developers need to deliver delicate molecules of RNA safely to their target organs. They need to shield the RNA from degradation in the bloodstream, prevent it from being filtered out by the kidneys, and let it exit blood vessels and spread through tissues.
- Antisense oligonucleotides (ASOs), are short, synthetic DNA fragments that bind RNA through base pairing and modulate its function to silence the effect of the gene.

Tissue Engineering (slide 33)

Tissue engineering is a process of restoring, maintaining, improving, or replacing damaged tissues and organs that seeks to create or recreate functional human tissues or organs. A combination of cells and bioengineered materials are used to restore, maintain, improve, or replace damaged tissue.

Tissue engineering often begins with a scaffold, using various materials like naturally occurring proteins or biocompatible synthetic polymers to provide the structural support for cell attachment and subsequent tissue growth.

Certain tissue engineering therapies may use an existing scaffold by removing cells from a donor organ, a process called decellularization, until only the pre-existing protein-based scaffold or extracellular matrix (ECM) remains. Cells—and in some cases, additional growth factors to encourage the cells to take root—are added, allowing a tissue or organ to develop and grow ex-vivo.

Researchers have successfully engineered skin, bladders, small arteries, skin grafts, cartilage and a full trachea.

Regenerative Medicine (slide 34)

Regenerative medicine includes cell therapies, gene therapies, and tissue-engineered products intended to augment, repair, replace or regenerate organs, tissues, cells, genes, and metabolic processes in the body to restore or establish normal function.

HOW TO LEARN MORE

[60 Seconds of Science: What is Tissue Engineering? \(2016\)](#) – NIBIB Video

- This video uses a different definition of Regenerative Medicine than Healing Genes uses, saying “Tissue Engineering, also called Regenerative Medicine, refers to the attempt to create functional human tissue from cells in a laboratory.”

[Tissue Engineering: How to Build a Heart \(2013\)](#) - Nature Video

Approved Cell & Gene Therapies (Slide 35)

Several cell and gene medicines have been approved in the United States and in Europe.

NAME OF CONDITION	THERAPY	NAME	BRAND NAME	MANUFACTURER	LOCATION OF APPROVED USE
Heart Abnormality	Tissue Engineered Medical Product Bio-scaffold material	Intracardiac Patch	CardioCel	Admedus	USA, Europe, Canada, Singapore
Cancer - leukemia	CAR -T cell therapy (CD19-directed genetically modified autologous T-cell immunotherapy)	tisagenlecleucel	Kymriah	Novartis Pharmaceuticals Corporation	USA, Europe, Canada, Japan
Cancer - B Cell Malignancies	CAR -T cell therapy (CD19-directed genetically modified autologous T-cell immunotherapy)	axicabtagene ciloleucel	Yescarta	Kite Pharma, Incorporated	USA, Europe, Canada
Retinal dystrophy	Gene therapy (Adeno-associated virus vector-based gene therapy)	voretigene neparvovecrzyl	Luxturna	Spark Therapeutics, Inc.	USA, Europe
Cartilage defects in the knee	Tissue engineered medical product - Autologous cellularized scaffold product	Autologous Cultured Chondrocytes on a Porcine Collagen Membrane	MACI	Vericel Corporation	USA
Severe burns	Tissue Engineered medical product - autologous keratinocytes	Cultured Epidermal Autografts	Epicel	Vericel	USA

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Cancer - Prostate cancer	Autologous cellular immunotherapy	Autologous Cellular Immunotherapy	Provenge	Dendreon Corp	USA
Cancer - melanoma	Gene therapy directed at the tumor itself	Talimogene laherparepvec	Imlygic	Amgen	USA, Europe, Australia
Spinal Muscular Atrophy	Adeno-associated virus vector based gene therapy	Onasemnogene abeparvovec-xioi	Zolgensma	AveXis, Inc. (Novartis Gene Therapy)	Europe
Oral soft tissue	Tissue engineered medical product - Allogeneic cellular sheet with other factors	Allogeneic cultured keratinocytes and fibroblasts in bovine collagen	Gintuit	Organogenesis Inc.	USA
Sickle Cell Disease	Gene modified autologous CD34+ cells that contains HSC transduced with lentiviral vector (LVV) encoding the β A-T87Q - globin gene	Betibeglogene autotemcel	Zynteglo	Bluebird bio	Europe
Spinal Muscular Atrophy	survival motor neuron-2 (SMN2)-directed antisense oligonucleotide	Nusinersen	Spinraza	Biogen	USA, Europe
Facial Wrinkles	Autologous cellular product	Laviv	Azficel-T	Fibrocell Technologies, Inc.	USA
Diabetic Foot ulcers	tissue engineered medical product - Bilayer dermal regeneration matrix	bilayer matrix for dermal regeneration	Omnigraft	Integra	USA

The use of cord blood has been approved by the FDA for therapeutic treatment of blood system disorders when allogeneic cord blood transplant is indicated. Cord blood transplant is a cellular therapy.

Making Informed Decisions (slide 36-37)

Patient-oriented organizations

- [Global Genes](#)
- [ELF](#), the Every Life Foundation
- [Genetic Alliance](#)
- [NORD](#), the National Organization for Rare Disorders
- [The Alliance for Cancer Gene Therapy](#)

Academic and research societies

- [ASGCT](#), American Society of Gene & Cell Therapy
- [ISCT](#), International Society for Cell & Gene Therapy

Information for people considering clinical trials

- [CISCRP](#), Center for Information and Study on Clinical Research Participation

Industry and policy

- [Alliance for Regenerative Medicine](#)

Cell and Gene Medicine Glossary of Common Terms

More glossary items can be found [here](#).

Cell therapy: Cell therapy is the transfer of whole cells into a patient to replace or repair damaged tissue or cells. A bone marrow transplant is the most frequently used cell therapy.

Clinical practice: Treatments and procedures performed by doctors.

Clinical translation: The process of taking a treatment that has been proven in the laboratory to testing in human volunteers.

Clinical trial: A test of a new medical treatment or procedure in human volunteers.

Gene therapy: Gene therapy is a technique that modifies a person's genes to treat or cure disease. Human gene therapy seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use. Gene therapies can work by several mechanisms:

- Replacing a disease-causing gene with a healthy copy of the gene
- Inactivating a disease-causing gene that is not functioning properly
- Introducing a new or modified gene into the body to help treat a disease

Gene therapy products are being studied to treat diseases including cancer, genetic diseases, and infectious diseases.

Gene-modified cell therapy: A therapeutic approach in which a person's cells are genetically modified in order to help the patient fight a disease. Therapies created this way can also be called Ex Vivo gene therapies.

The patient's cells are modified outside the body, genetically recoded, and enhanced. These cells then are returned to the patient to help the patient fight a disease, for example, in CAR T-Cell therapy for cancers.

Gene or Genome editing: Gene editing makes targeted changes to existing DNA in genes located on the chromosomes. With gene editing, researchers can enable or disable targeted genes, correct harmful mutations, and change the activity of specific genes. Gene editing is a set of techniques that enable researchers and clinicians to rewrite the instruction encoded in the DNA of genes. These molecular-biology techniques can enable or disable targeted genes, correct harmful mutations, modify expression of genes or

change activity of a specific cell, with the goal of restoring normal function. CRISPR is an example of a gene editing technique that has entered clinical trials.

CRISPR – CRISPR is a gene-editing technique that allows scientists to alter DNA sequences easily and precisely in order to modify gene function. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats that are a type of DNA sequence in a gene. This type of DNA sequence is understood by scientists who can use molecular tools to modify how the gene functions.

Regenerative medicine: A field of medicine that aims to improve, replace, or repair cells, tissues, genes or organs. Doctors use cell therapies, gene therapies, and tissue-engineered products to replace or regrow human cells, genes, tissues or organs. This field holds the promise of repairing damaged tissues and organs and restoring function lost due to age, disease, damage, or birth defect.

Somatic cells – Somatic cells are any cells in the body except sperm and egg cells. Changes made to the genes in a somatic cell will not be inherited by a patient's future children. Most genetic diseases manifest in somatic cells. The DNA in these cells is non-heritable, which means that somatic cell gene editing affects only the patient and will not be genetically transmitted to future children.

Stem cells: Stem cells distinguish themselves from other cell types by two unique characteristics. One, they are unspecialized cells capable of renewing themselves through cell division. When a stem cell divides, each new cell has the potential to remain a stem cell or become another more specialized cell type like a red blood cell or a muscle cell. Two, a stem cell can be induced to become tissue or organ specific stem cells with specific functions. This makes them useful in medical treatments.

The most commonly used stem cell treatment is hematopoietic (blood) stem cell transplantation, for example, bone marrow transplantation, to treat certain blood and immune system disorders or to rebuild the blood system after treatments for some kinds of cancer.

Given their unique regenerative abilities, stem cells offer new potential for treating disease but not all stem cell treatments have been proven to be effective and should be considered experimental.

DISTINCTIONS AMONG CERTAIN CLOSELY RELATED TERMS

Genomic medicine, gene medicine, and precision medicine are terms that are important, complementary, and distinctive. It is important to understand how they differ.

Genomic medicine is an interdisciplinary medical specialty involving the use of genomic information that has rapidly grown since the completion of the Human Genome Project in 2003.

Gene medicine is the medical discipline that uses various techniques to replace, regulate, block, or edit one or more genes that are the underlying cause of a particular disease. It enables physicians to make therapeutic, personalized medical decisions that can dramatically improve a person's health outcome and in many instances provide a functional cure. Gene medicine takes genomics medicine to the clinical level.

Precision medicine is informed by a genetic understanding of the disease and the individual patient, instead of seeking a "one size fits all" approach by disease type. Precision medicine not only involves studying the genome, but also considers factors like where a person lives, what they do, and their family health history. Prevention or treatment approaches are targeted to help specific individuals stay healthy or get better instead of relying on approaches that are the same for everyone.