LIFE STREAM

ANNUAL ISSUE – 2023 ***THE GENE REVOLUTION***

Human beings are at the very cusp of technologies and decisions that can change the world as we know it.

TH GENE REVOLUTION

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Cover Page: Watson & Crick with their DNA double helix model-1953 (Credit: Science Photo Library)

LIFE STREAM – ANNUAL ISSUE 2023 is a publication of the Life Science Foundation

Science moves with the spirit of an adventure characterized both by youthful arrogance and by the belief that the truth, once found, would be simple as well as pretty— **James D. Watson**

WE PRESENT

Proposing a double helical structure for DNA (De-oxy Ribo Nucleic Acid) in the middle of 20th century, followed by other landmark events, including, the unravelling the human genome in the early part of the 21st century, have unleashed a new revolution in science---the gene revolution.

It has impacted several areas of human interest---heredity, evolution, plant genetics, animal studies, biotechnology, crime detection and the like. However, the most profound impact has been in medicine, especially, immunology and in the treatment of genetic disorders, cancer as well as chronic diseases. The other field is agriculture. Scientists are also closely looking at the structure and functions of the cells and the role played by proteins in living processes.

The technique of DNA finger Printing is now extensively used in crime detection and investigation.

Gene therapy and gene editing are the new buzz words. Synthetic Biology Is transforming our everyday life.

The gene revolution has transformed the way we look at nature, in fact, the whole life process itself. We therefore, decided to have ***The Gene Revolution*** *as the theme of this Annual Issue of Life Stream.*

In this issue we have covered a range of topics relating to genes---the History of Genetics, the Human Genome Project, Gene Therapy, Gene Economy, Women in Genetics, Genetic Arts, CIMMYT, Genes & Food as well as Genes & Space Travel.

Also included are two poems, one of course, by Ms. Sudha Shrortria, our Team member who regularly contributes poems to Life Stream.

Information on the themes have been compiled from electronic and print media, reports, books, speeches and other sources so as to make them available to all, at one place.

We have great pleasure in presenting the ***Annual Issue of Life Stream, 2023****. We invite suggestions and criticisms from our readers.*

Life Science Team

It is not easy to convey, unless one has experienced it, the dramatic feeling of sudden enlightenment that floods the mind when the right idea finally clinches into place— **Francis Crick**

GENETICS: HISTORY & EVOLUTION

In this section we look at the history, evolution and development of the field of Genetics.

Genetics -History Genetics is the study of heredity in general and of genes in particular. There is evidence to show that human beings knew about heredity since the beginning of civilization. They noticed family resemblances, and also, inheritance of certain traits from parents or ancestors to their progeny. Based on that knowledge, they brought about improvements of cultivated crops and domestic animals.

The Encyclopedia Britannica cites a 6,000 years old tablet from Babylonia that shows pedigrees of horses, and indicates possible inherited characteristics. Other old carvings show cross-pollination of date palm trees. Nevertheless, the mechanism of heredity was not understood by men for centuries together.

Hippocrates (*c.* 460–*c.* 375 BCE), known as the father of medicine, put forward the a hypothesis known as *Pangenesis*-- that all organs of the body of a parent produced invisible "seeds," which were transmitted during reproduction.

Aristotle (384–322 BCE) reasoned that blood was the basis for passing on this generative power to the next generation.

In the 17th and 18th centuries scientists, with the aid of microscopes, stated to have spotted miniature replicas of human beings inside sperm heads.

French biologist **Jean-Baptiste Lamarck** proposed the inheritance of acquired characters, while explaining evolution.

Mendel and his experiments Theories on hereditary mechanism, till then, were based

Gregor john Mendel

largely on logic and speculation, not on experimentation. It was left to **Gregor John Mendel (1822 – 1884),** an Austrian monk, to demonstrate the basic mechanism of heredity through careful experimentation. He demonstrated that *invisible "factors" (now called genes) determine the traits of an organism.* The genetic make-up of the plant is known as the *genotype* and its physical appearance as *phenotype*. The *factors* or genes are transferred from parents to the offspring in pairs known as *alleles*. Of the two *alleles* for a trait, one is *dominant,* and the other is *recessive*.

Mendel's experiments on garden peas led to the framing of a set of three laws, known as **Mendel's laws** which explained the biological inheritance or heredity. These laws are the **Law of Segregation (**parental genes for a trait must segregate or separate equally and randomly into gametes at the time of reproduction)**,**

> The greatest book ever written is the one hidden in our DNA-**Spencer Wells**

Law of Independent Assortment, alleles for different traits are passed on independently of each other and **the**

Mendel & his experiments on garden peas
(Credit: studious.com)

different traits are passed on independently of each other and **the Law of Dominance** -of the two alleles of a gene, the dominant allele is always expressed, because it masks the recessive allele. These three laws form the core of classical genetics.

The painstaking work of Mendel remained in obscurity until the turn of the 20th century. The significance of Mendel's work was recognized only after three decades, with the rediscovery of his laws and their verification independently by Erich von Tschermak, Hugo de Vries and Carl Correns in 1900, ushering in the age of modern genetics.

The 20th century witnessed rapid development in the understanding of the nature of genes and how they function. Hundreds of papers showing Mendelian inheritance in a wide variety of plants and animals, including humans, were published. They validated Mendel's laws.

Genes & Chromosomes Ever since Mendel proposed that invisible factors determine the traits inherited, a feverish search was on for determining the biological and physical basis of life and inheritance.

As a gene is the fundamental unit of heredity, its identification was a landmark in the evolution of Genetics. Many biologists noted that the inheritance of genes had close parallels with that of the chromosomes during nuclear divisions, called meiosis. In 1910 American zoologist and geneticist **Thomas Hunt Morgan (1866 –1945)** and one of his students,

T. H. Morgan

identified certain genes that seemed to be linked on the same chromosome of the fruit-fly *Drosophila Melanogaster*. In 1916 another student of Morgan's, **Calvin Bridges,** through studies in fruit flies with an extra chromosome, demonstrated that the abnormal inheritance of certain genes was due to their being a part of the extra chromosome.

American geneticist **Hermann Joseph Müller (1890 –1967)** showed that mutations could be induced at high frequencies by treating cells with X-rays (mutations can also arise spontaneously).

Genetics do play a role in how you consciously or subconsciously manifest your true self---**Ben Harper quotes**

In 1931 American botanist **Harriet Creighton** and American scientist **Barbara McClintock** demonstrated the correlation between new allelic combinations and physically exchanges parts of chromosomes.

Barbara McClintock (blogspot.com)

DNA & its structure

It was Swiss chemist **Friedrich Miescher (1844 – 1895)** who identified the DNA as "nuclein" (later called "Nucleic acid", "Deoxyribonucleic acid," or "DNA) inside the nuclei of human white blood cells in late 1860. American bacteriologist **Oswald Avery (1877 – 1955),** Canadian American geneticist **Colin M. MacLeod (1909 –1972)** , and American biologist **Maclyn McCarty (1911 – 2005)** showed that *bacterial genes are made of DNA, in 1944. This was later extended to all organisms.*

In 1929, **Phoebus Levene (1869–1940)**, Russian biochemist, based on his work on yeast nucleic acids, proposed that *nucleic acids were composed of nucleotides*; and that a nucleotide in turn was composed of *one of the four nitrogen-containing bases, a sugar molecule, and a phosphate group.*

Fredrich Miescher (alchetron.com)) Oswald Avery (bbvaopenmind.com) Phoebus Levene (Fine Art America) Erwin Chargaff (Science Photo Library)

In late 1940s**, Erwin Chargaff (1905 –2002),** an Austrian biochemist, proposed that the composition of nucleotides in DNA varies among species, but the same *nucleotides do not repeat in the same order,* as proposed by Levene. The amounts of the bases varied among species, but not between individuals of the same species. *Further, the amount of A always equalled the amount of T, and the amount of C always equalled the amount of G (A = T and G = C).* These findings were known as **Chargaff's rules**. It is doubtful whether the scientists received the acclaim that was due to them.

The Double Helix

All human cells contain DNA. According to bbc.co.uk, the 3 billion pairs of bases in each cell fit into a space that is six microns across. If the DNA in one cell was extended it would be two meters long. All the DNA in a human body would extend to Pluto and back!

Ever since scientists came to know that DNA was the genetic material,

> "The greatest single achievement of nature to date was surely the invention of the molecule DNA."
> --**Lewis Thomas**

efforts were on for unraveling its structure. A major breakthrough came in 1953 when **James Watson** (born 1928) and **Francis Crick** (1916 – 2004)**,** with the aid of **Maurice Wilkins** (1916-2004), proposed a double helix model for DNA structure.

How did James D. Watson, American geneticist and biophysicist, and Francis Crick, British

James Watson and Francis Crick in 1959 © Bettmann/CORBIS

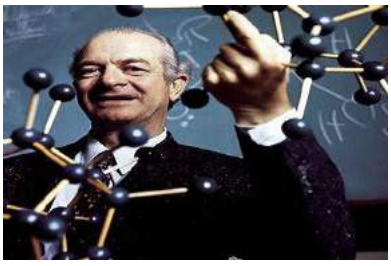
biophysicist decide to work together?

A book titled **What Is Life?** (*What is life- The Physical Aspect of the Living Cell*) written by Erwin Schrödinger, the famous quantum physicist in 1944 introduced the idea of an "aperiodic crystal that contained genetic information in its configuration of covalent chemical bonds'. The idea then generated great enthusiasm among scientists in discovering the chemical basis of genetic inheritance. Inspired by the book, James Watson, and Francis Crick, decided to work together in proposing a model for the DNA molecule.

Their work was essentially based on the research by many scientists before them, including **Friedrich Miescher, Phoebus Levene,** and **Erwin Chargaff**. To their credit, they made use of all available information, and, with a rare insight proposed **a simple and elegant model for DNA and its replication.** Watson has humorously described the events leading to their discovery in his famous book 'The Double Helix".

Watson & Crick knew that there were four nucleotides made of nitrogenous bases in DNA - Adenine (A), Thymine (T), Guanin (G)-and Cytosine (C). C and T bases, which have just one ring, are called **pyrimidines**, while A and G bases, which have two rings, are called **purines**. But the problem was how they were spatially arranged within the DNA molecule.

At about that time **Linus Pauling** (1901 – 1994), the well- known American Scientist and



Pauling (blogspot.com)

winner of Nobel Prize in Chemistry (1954), was working on the structures of biological molecules based on X-ray

> The results suggest a helical structure (which must be very closely packed) containing probably 2, 3 or 4 coaxial nucleic acid chains per helical unit and having the phosphate groups near the outside— **Rosalind Franklin**

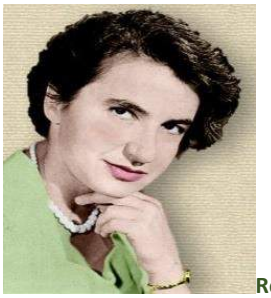
crystallography, molecular model building, and quantum chemistry. Pauling's book *The Nature of the Chemical Bond* has been considered "chemistry's most influential book of that century and its effective bible".

Gene Revolution: Summary- *The rediscovery of Mendel's laws of heredity in the opening weeks of the 20th century sparked a scientific quest to understand the nature and content of genetic information that has propelled biology for the last hundred years.*
The scientific progress made falls naturally into four main phases, corresponding roughly to the four quarters of the century.
The first established the cellular basis of heredity: the chromosomes. The second defined the molecular basis of heredity: the DNA double helix. The third unlocked the informational basis of heredity, with the discovery of the biological mechanism by which cells read the information contained in genes and with the invention of the recombinant DNA technologies of cloning and sequencing by which scientists can do the same. (Ref: Nature)

Pauling had formulated *a model for the structure of hemoglobin in which atoms were arranged in a helical pattern, and applied this idea to proteins in general.* Pauling had won the race to find the alpha helix structure of proteins. Watson and Crick were greatly influenced by Pauling's work. The duo raced against time to out- beat Pauling, whom they considered as their competitor in deriving a model for DNA.

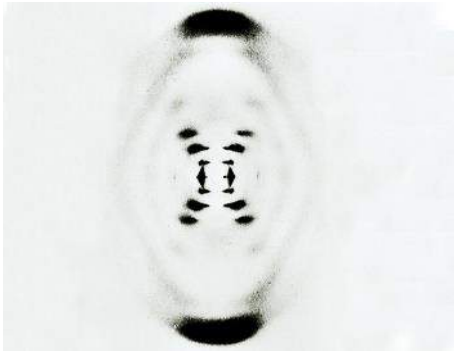
Using cardboard cut outs representing the four bases and other components, Watson and Crick 'shifted molecules around on their desktops, as though putting together a puzzle". After many trials and errors, they proposed *a three-dimensional, double-helical ('double-stranded, anti-parallel, right-handed helix') model* for the structure of DNA. The model resembled a winding stair case having sugar-phosphate backbone or banister, with the attached nucleotides forming the rungs. The nucleotides were kept in their position by hydrogen bonds, which could be broken easily by opening the two strands like a zip. X-ray crystallography work by English researchers **Rosalind Franklin** and **Maurice Wilkins** provided the crucial proof to Watson and Crick that DNA had a three-dimensional, double-helical structure.

The biggest tech revolution of the 21st century isn't digital, it's biological. -BBC Documentary


Rosalind Franklin (quotesgram.com)


Maurice Wilkins (pinterest.com)

Watson had then claimed that they studied the photographs without Rosalind's permission, and this had created lot of controversy at that time.



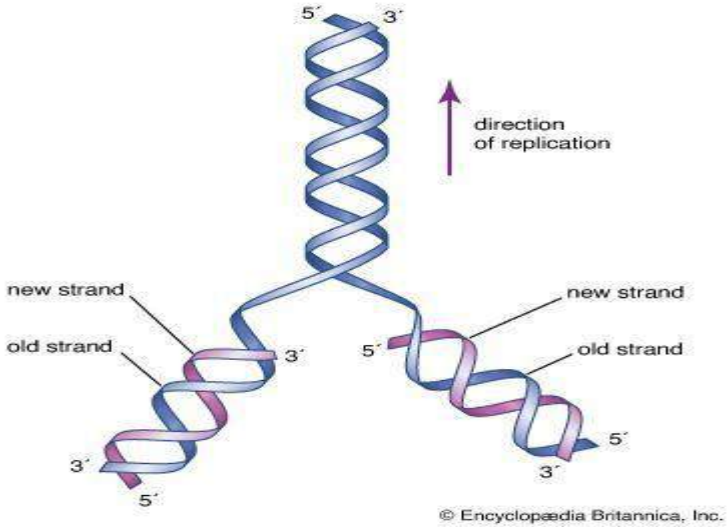
Holograph-51, the famous x-ray diffraction photograph of DNA by Rosalind Franklin

The double- helix model showed that DNA could self-replicate by separating its complementary strands and using them as templates for the synthesis of new DNA molecules.

In their article in Nature published in 1953 they famously stated 'It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material".

The DNA model proposed by Watson and Crick changed the of science and medicine forever. Crick, Watson, and Maurice Wilkins shared the Nobel Prize for their work in 1962 (Rosalind Franklin had died by that time.

> The major credit I think Jim and I deserve is for selecting the right problem and sticking to it. It's true that by blundering about we stumbled on gold, but the fact remains that we were looking for gold--**Francis Crick**



The Genetic Code Once Watson and Crick proposed a model for DNA, teams of scientists across the world started working on how genetic information is coded in the DNA, and, how genes are able to exercise control over protein synthesis in living cells. Because proteins are composed of amino acids, it was speculated that a specific nucleotide sequence of DNA could contain a code for an amino acid sequence.

- In 1955 American molecular biologist **Seymour Benzer**, through his studies of genes in *Drosophila*, prepared linear maps, which indicated that the gene itself is a linear structure.
- In 1908 **Archibald Garrod,** British physician proposed that alkaptonuria, and certain other hereditary diseases in humans, were caused by inborn errors of metabolism, *showing for the first time that linked genes had molecular action at the cell level.*
- In 1941 American geneticist **George Beadle** and American biochemist **Edward Tatum** in their studies on fungus *Neurospora crassa* showed that the *genes acted by coding for enzymes* (catalytic proteins). Further studies in other organisms also confirmed this finding.
- In 1958, American molecular biologist **Matthew Meselson** and American geneticist **Franklin W. Stahl**. experimentally demonstrated DNA replication by strand-separation for the first time.

How do genes Act? A momentous discovery was made by **Francis Crick** and South African biologist **Sydney Brenner** in 1961 that *the genetic code exists as triplets of nucleotides, called **Codons**.*

In 1966 **Marshall Nirenberg** and **Har Gobind Khorana** *decoded the complete genetic code of all 64 possible triplet coding units (codons)*, as well as the specific amino acids they code for. Subsequent studies showed that *the double helical structure of DNA, the mode of its replication, and the genetic code are the same in virtually all organisms.*

A remarkable discovery was that in 1961 French biologist **François Jacob** and French biochemist **Jacques Monod** established a model for gene regulation by showing that bacterial *genes can be turned on and off during protein synthesis*

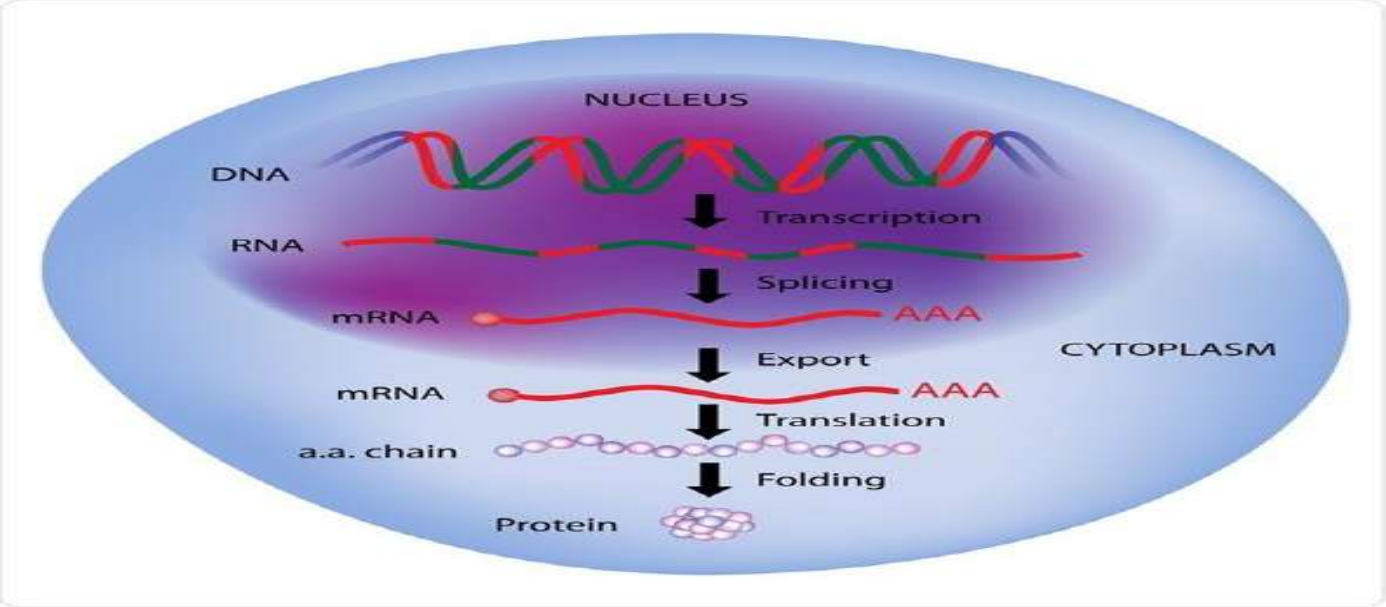


Diagram showing how proteins are synthesized by transcription of DNA to RNA to Messenger RNA (MRNA) and finally into Amino acids (AAA) and proteins (Credit: News Medical)

Recombination The field of recombinant DNA technology came to dominate molecular genetics in the 70's. Step by step progress achieved is noted below: -

- Discovery of a specialized class of enzymes that cut DNA at specific nucleotide target sequences in 1970 by American microbiologists **Daniel Nathans** and **Hamilton Othanel Smith** which could cleave DNA into fragments. They shared the 1978 Nobel Prize for Physiology or Medicine, for enabling scientists to manipulate genes by removing and inserting DNA sequences.
- Synthesis of the first artificial recombinant DNA molecule by American biochemist **Paul Berg** by isolating DNA molecules from different sources, cutting them, and joining them together in a test tube.
- Development of recombinant plasmids by American biochemists **Herbert W. Boyer** and **Stanley N. Cohen** which replicated naturally when inserted into bacterial cells.
- Cloning of individual genes by splicing them into self-replicating DNA molecules, (Plasmids or viruses), and inserting these into living bacterial cells.
- Invention of two different methods for determining the nucleotide sequence of DNA-- by American molecular biologists **Allan Maxam** and **Walter Gilbert** and English biochemist **Fred Sanger** for which they shared the 1980 Nobel Prize for Chemistry .
- Development of a technique known as site-directed mutagenesis. by Canadian biochemist **Michael Smith** through redesigning genes by devising a method for inducing specifically tailored mutations at defined sites within a gene.
- American biochemist **Kary B. Mullis** invented the *Polymerase Chain Reaction* (PCR), a simple technique that allows a specific stretch of DNA to be copied billions of times in a few hours for which Mullis received the 1993 Nobel Prize for Chemistry.

> Almost all aspects of life are engineered at the molecular level, and without understanding molecules we can only have a very sketchy understanding of life itself— **Francis Crick**

- Improvements in recombinant DNA technology and the development of automated sequencing machines paved the way for the sequencing of complete DNA in the last decade of the 20th century.

The Human Genome Project (HGP) In 2001 the complete sequence of human DNA, approximately three billion nucleotide pairs, was made public (pl. see the section on Human Genome Project). By the time of its completion in 2003, HGP researchers had successfully determined, stored, and rendered publicly available the sequences of almost all the genetic content of the human genome .

The International HapMap Project, which was designed to identify genetic variations contributing to human disease through the development of a haplotype (haploid genotype map of the human genome), began. By completion of Phase II of the project in 2007, scientists had data on some 3.1 million variations in the human genome.

The 1000 Genomes Project, an international collaboration in which researchers aimed to sequence the genomes of a large number of people from different ethnic groups worldwide with the intent of creating a catalog of genetic variations, began. The project was completed in 2015.

Areas of study Modern Genetics has expanded and diverged into different areas.

1. **Classical genetics** -We already have seen its development.
2. **Cytogenetics -** microscopic study of chromosomes, with reference to the structure and activities of the cells.
3. **Microbial Genetics**-the genetical studies on microbes
4. **Molecular genetics -** the study of the molecular structure of DNA, its cellular activities (including its replication), and its influence in determining the overall make-up of an organism.
5. **Genomics -** the study of the structure, function, and evolutionary comparison of whole genomes.
6. **Population genetics**- the study of genes in populations of animals, plants, and microbes
7. **Behavioural Genetics**--Studies to explore the genetic factors involved in complex human traits such as behaviour.
8. **Human Genetics/ Medical genetics** specializes in the understanding and treating genetic diseases and genetically influenced ill health.

Methods While the field of genetics branched out into different areas, the techniques used in the studied got perfected over a period of time.

"Our own genomes carry the story of evolution, written in DNA, the language of molecular genetics, and the narrative is unmistakable." - **Kenneth R. Miller**

1. **Cytogenetic** techniques focus on the microscopic examination of genetic components of the cell, including chromosomes, genes, and gene products
2. **Biochemical techniques.** Biochemistry is carried out at the cellular or subcellular level, generally on cell extracts, to study DNA, RNA, and protein.
3. **Physiological techniques** - used for exploring functional properties or organisms, are also used in genetic investigations
4. **Molecular Techniques** --involved with the direct study of DNA.
5. **Immunological techniques** - antigens are studied in immunogenetics.
6. **Mathematical techniques** Because much of genetics is based on quantitative data, mathematical techniques are used extensively in genetics.
7. **Bioinformatics** uses computer-centered statistical techniques to handle and analyze the vast amounts of information accumulating from genome sequencing projects.

Applied genetics **Medicine:** Genetic techniques are used in medicine to diagnose and treat genetic disorders**; Agriculture and Animal Husbandry--** apply genetic techniques to improve plants and animals; **Industry-** Various industries like the brewing industry, the pharmaceutical industry employ geneticists. Biotechnology, based on recombinant DNA technology, is now extensively used in industry.

Nobel prizes In 2007, the Nobel Prize for Physiology or Medicine was awarded to Mario Capecchi, Martin Evans and Oliver Smithies "for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells". In 2020, the Nobel Prize in Chemistry was awarded to Emmanuelle Charpentier and Jennifer Doudna for "the development of a method for genome editing".

Future The revolution in Genetics started with Mendel's experiments on Garden peas is continuing its march ahead. The kind of changes that are sweeping the world of modern genetics are discussed in the succeeding sections in this issue.

----------Ref: en.wikipedia.org; www.britannica.com;www.nature.com; pubmed.ncbi.nlm.nih.gov;www.encyclopedia.com; www. researchgate.net; biologydictionary.net; www.nature.com Discovery of DNA Structure and Function: Watson and Crick by: Leslie A. Pray, Ph.D.

DNA neither cares nor knows. DNA just is. And we dance to its music."— Richard Dawkins

SCIENCE: DRAWING THE MAP OF LIFE

Logo of the Human Genome project

The Human Genome Project *(HGP) is considered as one of the greatest scientific feats in human history 'by generating the first sequence of the human genome and providing fundamental information about the human blueprint'. According to Francis Collins, American Geneticist who headed it, the HGP, 'transformed biological research, medicine and our whole approach to open data access'. Now when the HGP is reaching 23 years of its completion, we take a look back at the project, what it has achieved, and whether it fulfills the expectations scientists had at the time of its launching.*

At the time when the Austrian monk Gregor John Mendel was conducting his experiments in garden peas, no one could imagine that his studies on inheritance would one day lead to the unravelling of the human genome. Thanks to the HGP, today most people know about the scientific basis of human inheritance. But none can imagine the kind of dedicated efforts made by a group of institutions under the guidance of eminent scientists, supported by a large number of technicians to unravel the human genome. The drama that unfolded during the process and the excitement generated at every turn of the project are still etched in our collective memory. It was a defining moment when US President Bill Clinton and UK Prime Minister Tony Blair jointly announced to the world the completion of the project, at the turn of the century. Let us now briefly recapitulate the details of the project.

HGP- Chief Features

- International scientific research project
- World's largest collaborative biological project.
- Publicly funded
- Adopted in 1984 by the US government
- Initiated in 1990
- Declared complete in 2003

HGP- Goals

- Identifying, mapping and sequencing all of the genes of the human genome.
- Creating genome sequence databases to store the data.
- Optimization of the data analysis.
- Taking care of the legal, ethical and social issues that the project may pose.

We are here to celebrate the completion of the first survey of the entire human genome. Without a doubt, this is the most important, most wondrous map ever produced by human kind **(Bill Clinton & Tony Blair)**

How it was done

- Hierarchical shotgun sequencing approach
- The genome was broken into ~150-kb segments
- Cloned into bacterial artificial chromosomes
- Sequencing selected bacterial artificial chromosomes
- Matching with a physical map comprising~94% of the entire human genome)
- Finally reassembled to generate the draft sequence.
- Celera Genomics used both HGP and their own private data in their whole-genome shotgun sequencing approach
- Celera fragmented the genome into ~500-bp segments and subjected them to pair-wise end sequencing, to reconstruct the original sequence.

Where was it done?

The 'International Human Genome Sequencing Consortium', as the Human Genome Project team was known, involved scientists from 20 institutions in six countries: France, Germany, Japan, China, the UK and the USA.

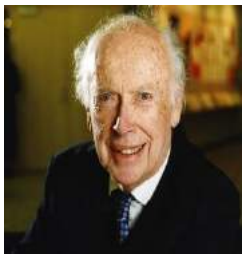
Project Cost The project itself would end up costing a huge $3 billion over 13 years.

Funding came from the United States government through the National Institutes of Health (NIH), as well as numerous other groups from around the world.

Leadership

The US side of the Human Genome Project was initially led by James Watson, and later by Francis Collins. John Sulston, who was the director at the Wellcome Trust Sanger Institute (at that time called the Sanger Centre), was principal leader of the UK side of the project.

HGP-----The Leaders



James D. Watson, American Bio-physicist

Francis Collins-American Geneticist

John Sulston-UK biologist

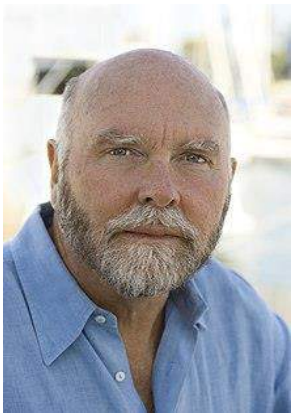
I never dreamed that in my lifetime my own genome would be sequenced- **James Watson**

Public Vs Private

- The Celera Corporation, or Celera Genomics, was formally launched in 1998.
- In 1998, it announced that the new company, would 'race' the publicly funded HGP to complete the sequencing of the human genome.
- It also intended to sell subscriptions to its database, release data quarterly, and obtain patents on genes and related technologies.
- Celera's presence became a threat to the HGP.
- Soon the HGP and Celera Genomics brokered a deal. The rivalry between Celera and the NIH ended when they joined forces, thus speeding completion of the rough draft sequence of the human genome.
- In April 2003, coinciding with the 50th anniversary of the publication that described the double-helical structure of DNA, the HGP was declared complete.

Features of the Human Genome

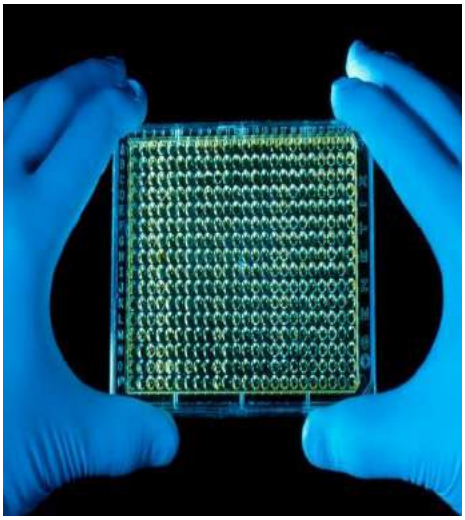
- Our entire genome is made up of 3164.7 million (appx 3.1 billion) base pairs.
- On average, a gene is made up of 3000 nucleotides.
- The function of more than 50 percent of the genes is yet to be discovered.
- Proteins are coded by less than 2 percent of the genome.
- Most of the genome is made up of repetitive sequences which have no coding purposes specifically
- More than 95% of the human genome is a fragment of DNA whose function is unknown, and the gene with the actual function is very small, about 1.1% of the genome.
- The number of human genes is about 20,000 to 25,000, much less than the 100,000 expected.
- The rate of mutation in cell division (meiosis) that occurs in the process of producing germ cells is twice as high as that of women.



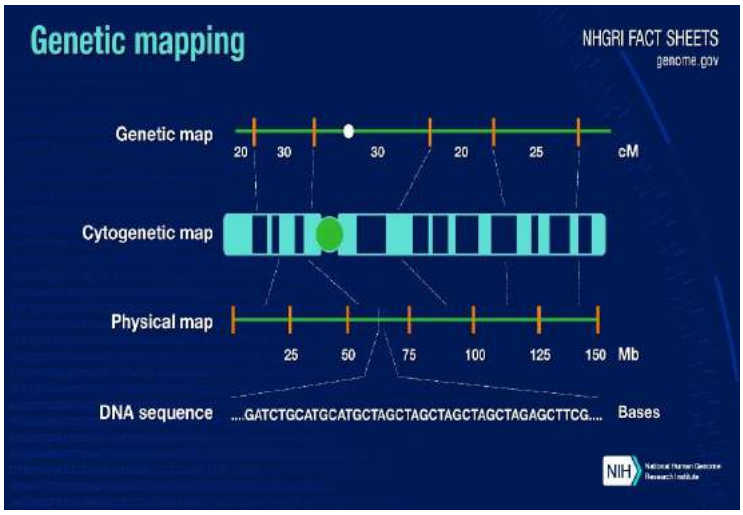
John Craig Venter (born 1946), an American biotechnologist and businessman is known for leading one of the first draft sequences of the human genome. Venter founded Celera Genomics, the Institute for Genomic Research (TIGR) and the J. Craig Venter Institute (JCVI).He has been a prime mover in some of the most exciting developments in the relatively new science of Genomics. He is seen with Francis Collins in the second picture.

Wikipedia points out that the genome published by the HGP does not represent the sequence of every individual's genome. "It is the combined mosaic of a small number of anonymous donors, of African, European and east Asian ancestry. The HGP genome is a scaffold for future work in identifying differences among individuals".

"Human beings are ultimately nothing but carriers-passageways- for genes- **Haruki Murakami**



A tray containing part of a human genome. The wells each hold a different fragment of cloned DNA. Credit: James King-Holmes /Science Photo Library



(Credit: Genome.gov-National Human Genome Research Institute)

"----It is the first vertebrate genome to be extensively sequenced. It is the largest genome to be extensively sequenced so far, 'being 25 times as large as any previously sequenced genome and eight times as large as the sum of all such genomes'

After the HGP, several other programs followed which had more sophisticated data sharing, comparison and analysis. Programs, including the Haplotype Mapping (HapMap) Project, the 1000 Genomes Project, and, the Cancer Genome Atlas (TCGA) were taken up after multiple mammalian genome projects.

Benefits

- The sequencing of the human genome holds benefits for many fields, from molecular medicine to human evolution.
- It helps researchers understand diseases including: genotyping of specific viruses to direct appropriate treatment; identification of mutations linked to different forms of cancer; the design of medication and more accurate prediction of their effects
- Advancement in forensic applied sciences
- Biofuels and other energy applications
- Agriculture, animal husbandry, bioprocessing risk assessment
- Bioarcheology, anthropology and evolution
- Commercial development of genomics research related to DNA-based products, a multibillion-dollar industry.

The genome is a book that wrote itself, continually adding, deleting and amending over four billion years~ **Matt Ridley**

Concerns

- Several ethical, legal, and social concerns were raised in regard to how increased knowledge of the human genome could be used to discriminate against people.
- The main concerns were the fear that both employers and health insurance companies would refuse to hire individuals or refuse to provide insurance to people because of a health concern indicated by someone's genes
- In 1996, the United States passed the Health Insurance Portability and Accountability Act (HIPAA), which protects against the unauthorized and non-consensual release of individually identifiable health information to any entity not actively engaged in the provision of healthcare services
- The Ethical, Legal, and Social Implications (ELSI) program was set up in 1990.
- Five percent of the annual budget was allocated to the program i. e. approximately $1.57 million in the year 1990, but increased to approximately $18 million in the year 2014. (Ref: en.wikipedia.org)

The draft genome sequence published in *Nature* offered immediately free to access, which was in accordance with the Bermuda Principles, an agreement on data sharing signed by members of the international consortium that made the Human Genome Project possible.

Whole Genome Sequencing (WGS)

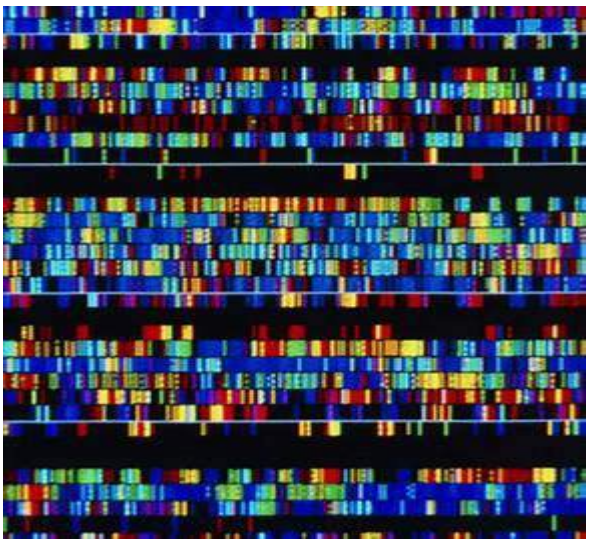
- WGS is now accessible to millions of people around the world.
- Major companies involved- Illumina, Pacific Biosciences, Full Genomes Corp., 454 Life Sciences, Veritas Genetics, Dante Labs
- Solexa HiSeq X Ten System of Illumina- the first sequencing platform to achieve WGS for less than $1,000.
- Costs have further dropped- likely to do so in future.
- In UK too genetic testing at similar prices to the US or slightly lower.
- The National Health Service (NHS) plans to make WGS available as part of their routine procedures.
- The 100,000 Genomes Project, aims to sequence the genome of 100,000 individuals suffering from genetic disorders, cancer, and infectious diseases.
- WGS in India costs approximately Rs.25,000 Rs ($338 USD) to 50,000 Rs ($676 USD).
- A huge genomics project IndiGen to find common genetic traits and incidence of rare genetic diseases in the country.
- Single-gene testing costs much more than WGS- the costs range from around $100 to several thousand dollars.
- BRCA testing, for example, traditionally costs $3000 to $4000 for a single gene.

Two decades on

Now that the HGP has completed two decades of decoding of the human genome, it will be appropriate to make an assessment whether it has lived up to all its promises.

'Nature', the esteemed scientific journal, noted that the project was initially conceived with fairly sober predictions of benefits of a complete cancer genome, advances in genetics and the development of improved technologies. However, closer to the program launch in 1990, there was lot of hype that was shared with the media and the wider community on the claims of revolutionizing biology, biotechnology, drug

Life is a DNA software system-- **Craig Venter**



The 1000 Genomes project maps 95% of all gene variations (credit: BBC news) development, personalization of therapies, unravelling the architecture of common complex diseases, the possibility to breed 'super babies' based on this new knowledge, and, perhaps even predict criminality. Although critics cite a failure to meet 'the most outlandish visions' as evidence that the HGP has not lived up to all promises, the criticism is considered unfair, according to scientists who worked in the project. However, it remains a fact that the fruits of gene-therapy and other advancements in medical genetics are yet to reach ordinary people.

The ethical, legal and social implications of genome research — including questions of privacy, informed consent and equitable representation of researchers and participants — remain unresolved. In genomic research to achieve the best results, genetic information needs to be read with physical characteristics, medical histories and other identifiable traits that can be linked to variants in the genome. But this increases privacy risks for research participants. Since the participants have a right to choose how their data will be used, scientists need to ensure that participants have given the appropriate consent and that their interests are protected.

Open Data-sharing According to nature.com, twenty years later, compromises and delays are becoming the norm in three domains of genome research: data collection from participants; deposition in approved, publicly accessible databases; and access for research and health care.

US President Clinton and UK Prime Minister Tony Blair jointly declared on 14 March 2000 that the human genome sequence "should be made freely available to scientists everywhere". However, according to researchers, the promise of a fully open data-sharing environment has not yet been realized, and free and open access to genome data remains unevenly implemented. As example, researchers pointed out the problems caused by lack of accessibility to coronavirus genomes in the middle of a pandemic.

DNA is like a computer program but far, far more advanced than any software ever created– **Bill Gates**

The Diversity Deficit

The potential **social consequences** of mapping the human genome are also pointed out by critics of the HGP. Although global databases and repositories ought to represent vast genetic diversity among the human beings, so far genome databases mostly represent DNA from people of European descent, who live in high-income countries. African people and Indigenous populations do not find adequate representation. These communities perceive that they have little chance of benefiting them; some even fear that when diseases are linked with a particular population, it can result in stigma and discrimination.

Significance Despite all criticisms, the HGP is considered as one of the greatest scientific feats in history. 'Nature' has beautifully summed up the positive impact of the project thus. "The real fruits of the HGP lie in the contrast between the primitive state of digital biology in the late 1980s and the current ease with which all scholars can access, harness and analyze biological data, making the entire sequence freely available in the public domain, for both research and development, in order to maximize its benefits to society. Today, the HGP remains notable for an estimated US$800 billion of revenue----Offering a first view into the entire human genome, the HGP acted as a gateway to an era of high-throughput digital biology, ushering in rapid technological and computational developments and team-oriented research, the fruits of which continue to be felt across the clinical and life sciences. The Human Genome Project provided an excellent opportunity to encourage international cooperation in biological science, setting standards in techniques and technologies across the globe to influence future medical research".

Future Scientists around the world, both in academia and industry, need to work further towards the fulfilling of the vision of the HGP. The project needs to ensure that genome data are available 'rapidly, freely and without restriction' to researchers in different parts of the world. Moreover, equity, diversity and human rights issues need to be given priority.

There is no doubt that this century will witness rapid advancements in genomic research, and medical genetics, that will have a huge impact in the treatment of cancer and other chronic diseases, as well as congenital disorders.

Ref: www.genome.gov; www.nature.com;researchgate.net;newscientist.com;www.nature.com Initial sequencing and analysis of the human genome; sequencing.com

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Heritability pertains to the entirety of the genome, not to a single gene ~ **Steven Pinker**

MEDICINE: GENE THERAPY-UNLOCKING THE POWER OF THE GENOME

The remarkable advances in genetics, including the human genome project, have opened new vistas in medicine for prevention and treatment of human diseases. Here, in simple terms, we explain what gene therapy is, what are the techniques used, how it is done and what are the pros and cons of its use, and, what future holds for it.

Background We have already seen that a gene is the fundamental physical and functional unit of heredity. Each gene comprises of an orderly sequence of nucleotides occupying a particular position on a specific chromosome. Each gene encodes a specific function.

As the cost of sequencing decreased and the efficiency of sequencing technology increased, huge data became accessible. This enabled scientists to gain valuable insights into the causes of diseases and to look for new ways of treating diseases by gene manipulation. During the Covid-19 pandemic gene sequencing enabled the rapid identification of the virus and played a vital role in developing vaccines at an astonishing speed.

The genomic revolution progressed through three phases, with gene sequencing forming the first phase, gene-editing the second, and, the creation of new genomes and the manipulation of genes to create a variety new product, being the third.

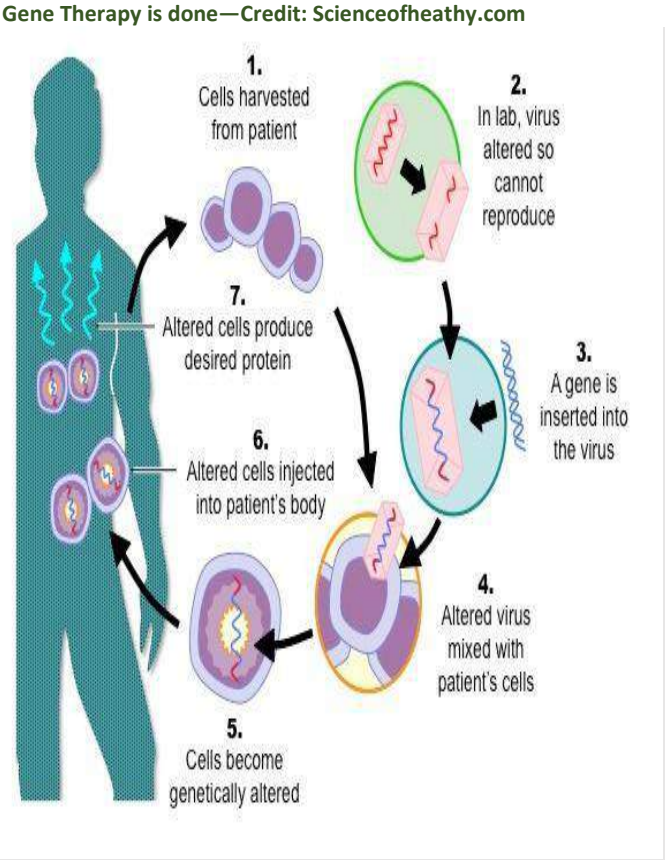
Gene therapy It is possible that genes from one organism can often function in another organism. However, transferring genes between organisms is not an easy task. Finding a reliable way to get genetic material into cells involves targeting the correct cells and reducing the risk of side effects. Gene Therapy involves both.

What is gene therapy?
According to NIH, Gene therapy is a technique that uses gene(s) to treat, cure or prevent a disease or medical disorder

How does Gene Therapy work

- **Turn on** a gene to help fight a disease.
- **Turn off** a gene that causes a disease
- **Remove** a piece of DNA that is impairing gene function and causing disease.
- **Replacing mutated genes.**
- **Making diseased cells more evident to the immune system.** Gene therapy could be used to train the immune system to recognize the cells that are a threat.

How Gene Therapy is done—Credit: Scienceofheathy.com



In the past, when we've tried gene therapy, we haven't had tools that have allowed targeted gene correction- **Jennifer Doudna**

Results of Gene Therapy

- Replaces missing or defective genes; For example, a gene called p53 normally prevents tumour growth. Replacing the defective p53 gene, might trigger the cancer cells to die.
- Delivers genes that speed the destruction of cancer cells;
- Supplies genes that cause cancer cells to revert back to normal cells;
- Delivers bacterial or viral genes as a form of vaccination;
- Provides genes that promote or impede the growth of new tissue; and
- Delivers genes that stimulate the healing of damaged tissue. **Ref: www.medicinenet.com**

What is Genome Editing?

Genome Editing is a technique that helps to ***edit the genetic code to change the existing DNA*** in the cell, instead of introducing new genetic material into cells.

It can be done in two ways-**base pair editing or genome editing**

- Editing plant genomes has progressed rapidly, as they present fewer ethical concerns.
- This technology helps improve crop yields, reduces pesticide and fertilizer use, increases shelf life, and enhances nutrition.
- The first human trial for a genome editing medicine to treat high cholesterol is currently underway in the US by Verve Therapeutics. The first phase of clinical trials has been successfully completed and Phase 2 trials are planned.

CRISPR technology

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)

- This type of gene editing involves cutting the desired region of the genome and introducing desired changes.
- It is easy to use, but can have unintended consequences due to the cutting and reattachment process.
- Unlike CRISPR, base-pair editing targets specific letters for modification, minimizing potential side effects.

Genome editing (Credit: dreamstime)

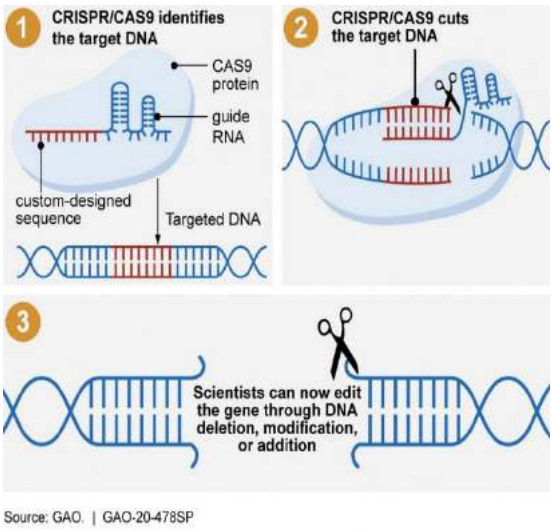
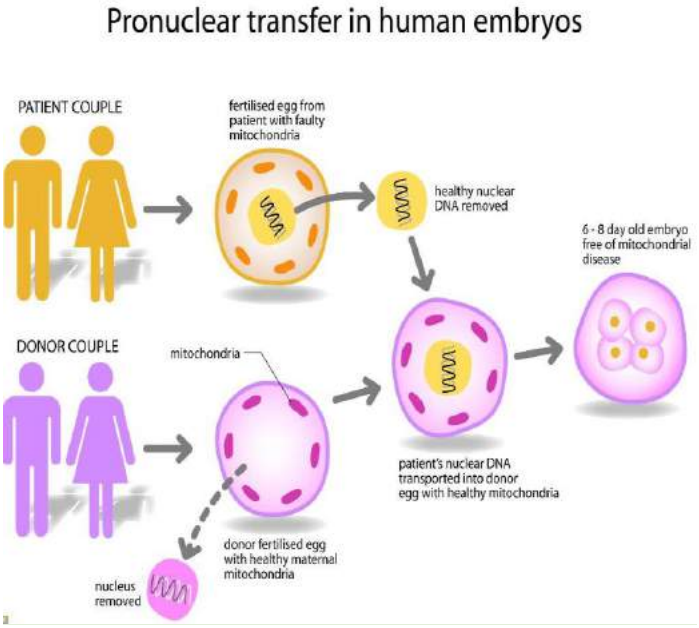


Illustration of Genome editing using CRISPR tool kit (Credit: lavenderandlabcoat.com)

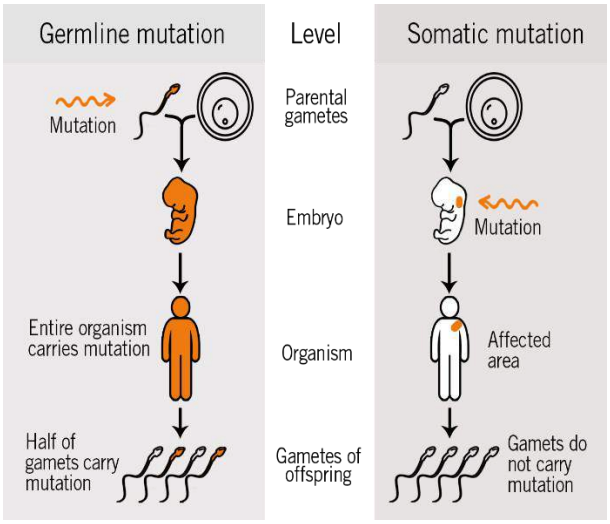
> The ability to cut DNA where you want has revolutionized the life sciences-anonymous

What is Germline Therapy?

- Modifications caused by gene therapy in somatic cells (non-reproductive cells) are not passed onto the next generation.
- In Germ line Therapy the gene is inserted into the reproductive cells or into the genome of an early pre-embryo before cell differentiation
- ***Modifications are passed on to the next generation.***
- It has been achieved experimentally *only in animals* so far;
- Currently, it is considered too risky to be done on human beings.



Germline Therapy (Credit:(trpicalcyclocross.com)



Germline & somatic mutations (Credit:the-DNA-universe.com)

New Methods

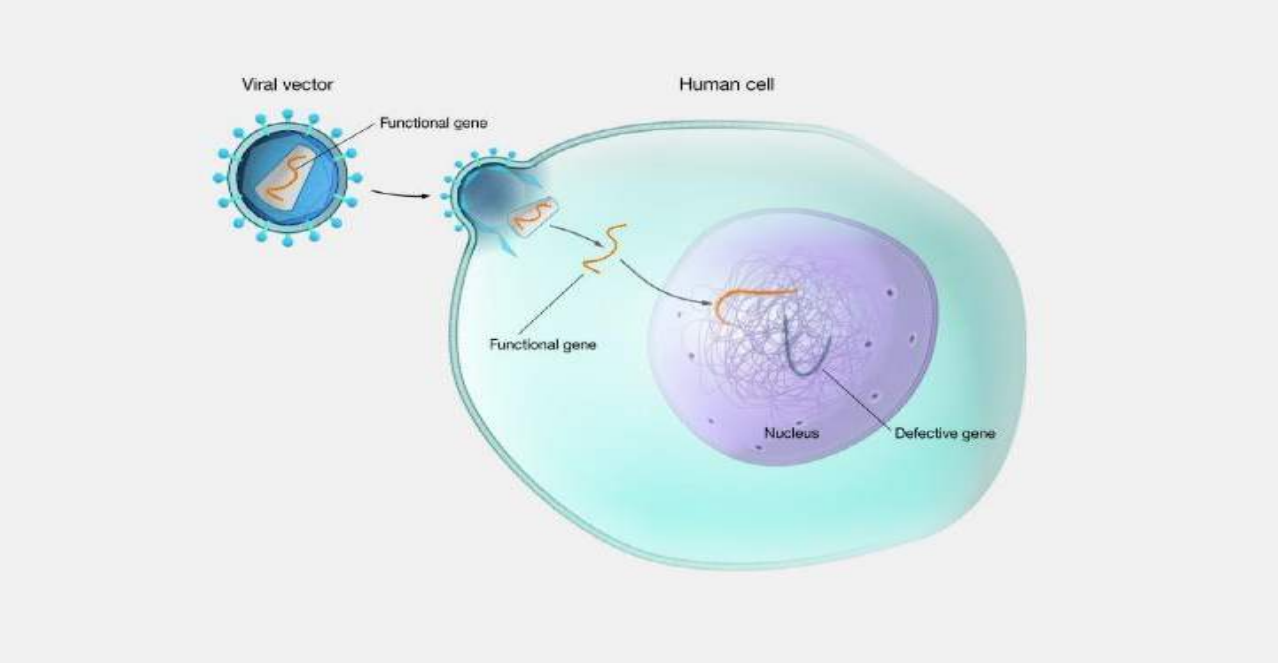
1.**Combining gene therapy with stem cell therapy**. Skin cells from a patient with alpha-1 anti-trypsin deficiency (an inherited disorder associated with certain types of lungs and liver disease)-reprogrammed the cells into stem cells, corrected the causative gene mutation, and then stimulated the cells to mature into liver cells. The reprogrammed, genetically corrected cells functioned normally.

2. Safe and efficient delivery system by using nano technology that involves packaging genes into nano particles that are targeted to cancer cells, thereby killing cancer cells specifically and leaving healthy cells unharmed.

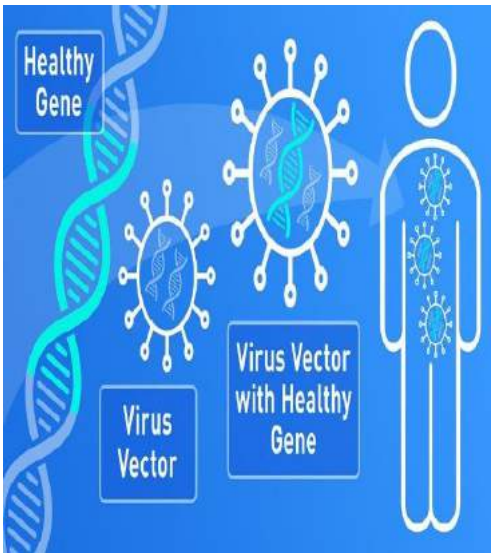
How is Gene Therapy administered?

- Currently, the only way for one to receive gene therapy is to participate in a clinical trial.
- In clinical trials blood is drawn or bone marrow is removed from the patient's hipbone with a large syringe
- Then, in a lab, cells from the blood or bone marrow are exposed to a virus or any other vector that contains the desired genetic material.
- Once the vector has entered the cells in the lab, those cells are injected back into the body into a vein or into tissue, where the patient's cells take up the vector, along with the altered genes.

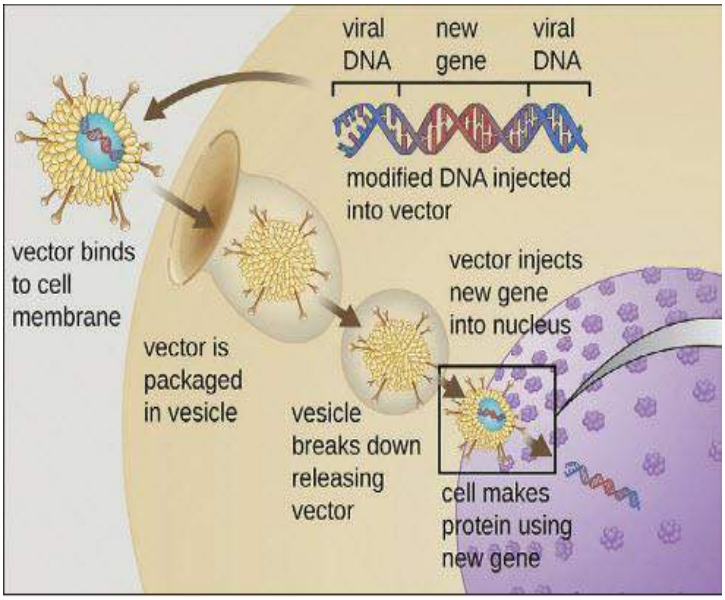
The advance of genetic engineering makes it quite conceivable that we will begin to design our own evolutionary progress."— **Isaac Asimov**



1. Gene Therapy illustration (Photo Credit-NIH)



2.Gene Therapy illustration (Photo Credit-NIH



3. Gene transfer using a virus (Credit: ophthalmologymanagement.com)

I am simply pointing out that at the rate at which we are going the whole genetic engineering technology will end up in the hands of the political system to be used for the complete control and subjugation of man.
U.G. Krishnamurti

Diseases treated using Gene therapies

Only a small number of diseases are treated so far- including an eye disorder called **Leber congenital amaurosis** and a muscle disorder called **spinal muscular atrophy.** According to **mayoclinic.org,** clinical trials have shown some success in treating **Severe combined immune deficiency, Haemophilia, Blindness caused by retinitis pigmentosa and Leukaemia**.

www.britannica.com also notes that human gene therapy has been attempted on somatic (body) cells for diseases such as **cystic fibrosis, adenosine deaminase deficiency, familial hypercholesterolemia and cancer**.

Safety Concerns

- Early studies showed very serious health risks, such as toxicity, inflammation, and cancer.
- Gene therapy techniques being relatively new, some risks may still be unpredictable.
- Clinical trials have revealed risks in use of somatic gene therapy may affect germ cells.
- A gene has to be delivered using a carrier, called a vector. The most common gene therapy vectors are viruses. Researchers remove the original disease-causing genes from the viruses, replacing them with the genes needed to stop disease. This can cause unwanted immune system reaction. Other problems include targeting the wrong cells, infection caused by the virus, the possibility of causing a tumour.

Safety measures

- **Improved techniques** - less likely to cause dangerous immune reactions or cancer.
- **Comprehensive federal laws, regulations, and guidelines** help protect people who participate in research studies and clinical trials.
- **The U.S. Food and Drug Administration (FDA)** regulates all gene therapy products in the United States and overseas research in this area.
- Clinical trials must first obtain permission from the FDA.
- **The National Institutes of Health (NIH)** provides guidelines for clinical trials with gene therapy to investigators and institutions to follow.
- An **Institutional Review Board (IRB)** and an **Institutional Biosafety Committee (IBC)** must approve each gene therapy clinical trial before hand.
- In 2021 the WHO released a Governance Frame-work for human genome editing. It provides a guideline to countries seeking to pursue gene therapies while minimizing any nefarious use of the technologies
- **(Ref: en.wikipedia.org)**

Ethical concerns have been expressed about some aspects of gene therapy- genetic manipulation and selection, research on embryonic tissue, and experimentation on human subjects

One view is that humans should not "play God" and interfere in the natural order.

Others argue that it is consistent with the purposes of God as creator.

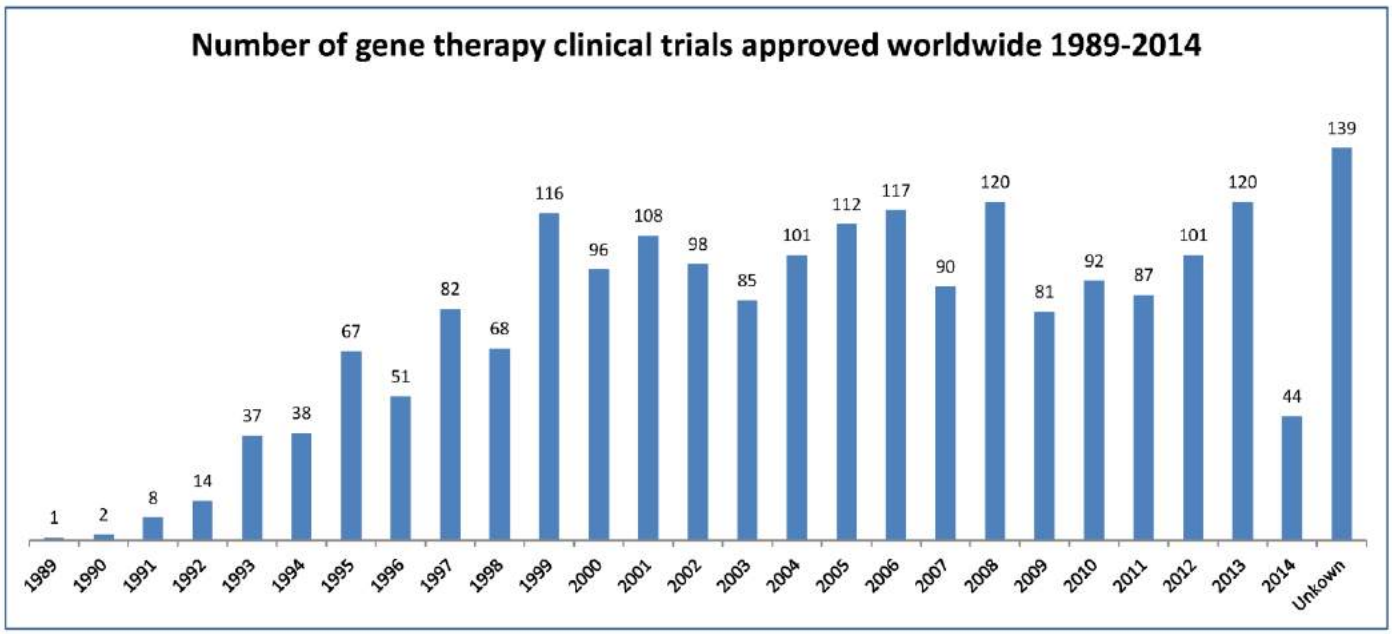
Yet others express concerns about the safety of germline gene therapy, wherein any harm caused by such treatment could be passed on to successive generations.

While scientists engage in the inevitable ethical debate regarding the role of CRISPR/Cas9 in society, remember that embryo modification is only one chapter of the story, not the entire book- **Catherine Buchaniec**

Commercial Gene Therapy

- The first attempt at modifying human DNA was in 1980, by Martin Cline
- The first successful nuclear gene transfer in humans, approved by the NIH, in May 1989.
- The first therapeutic use of direct insertion of human DNA into the nuclear genome- by French Anderson in September 1990.
- Between 1989 and December 2018, over 2,900 clinical trials, with more than half of them in phase I.
- China- the first country in the world to approve a commercial gene therapy product.
- China's regulatory body, CDFA, approved *Gendicine* in 2003 that delivers a p53 gene into tumor cells.
- Since that time, further gene therapy drugs were Approved (Pl. see illustration below)

(Credit: researchgate.com)



(Credit: americangene.com)

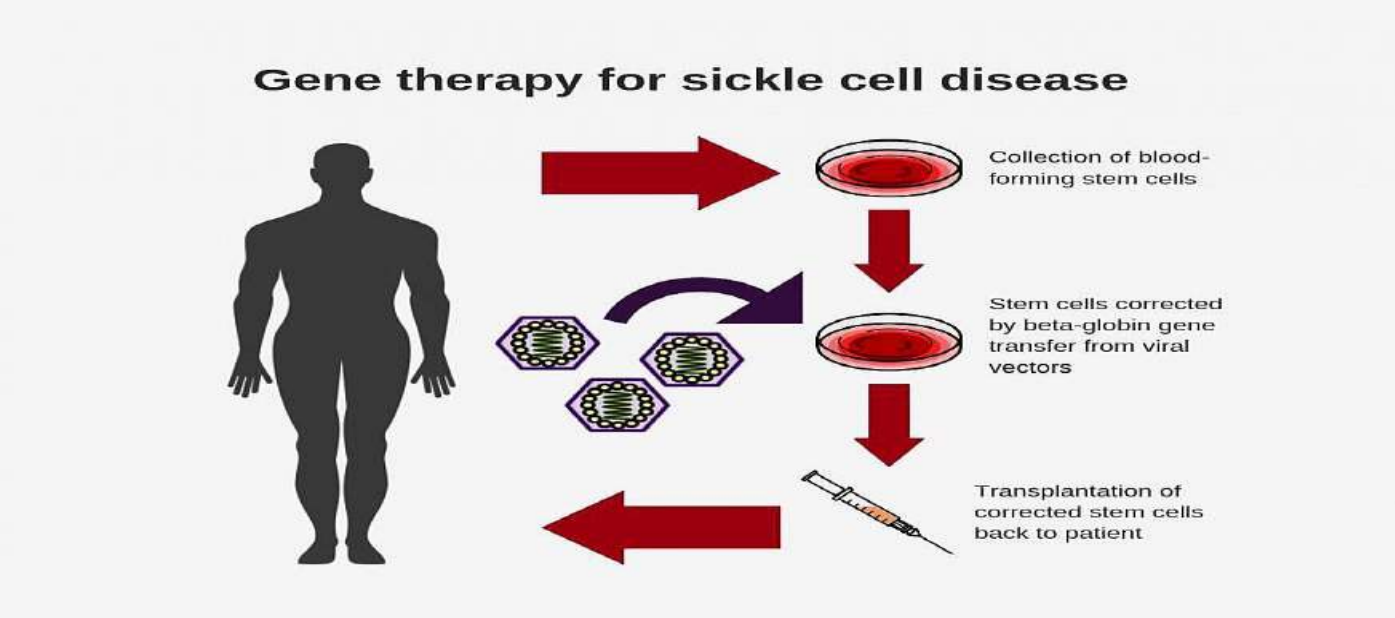
Advantages of Gene Therapy

- It is **patient- friendly**. For e.g., many patients with hemophilia and diabetes normally need repeated injections in order to manage their disease. The delivery of genes may result in longer-term expression of the necessary proteins.
- **Accuracy**- Gene therapy has the potential to eliminate cancer cells without damaging normal, healthy tissue.
- **Providing alternative treatment** when a disease does not respond to other older treatments. E. g. Cancer
- **Leads to new possibilities** ---improving safety, efficacy and feasibility
- **Targeting** an increasing number of diseases
- **Emergence of new companies** due to the development of new tools.

Gene Therapy- Limitations

- The potential of gene therapy is great but, compared to its promise, the results to date are still quite limited.
- Access is limited to patients in the US or European Union. Low and Middle-income countries (LMIC), carrying 90% of the disease burden have very little access.
- Of 1000 open gene therapy clinical trials reported in august 2022, only four trials were reported from Africa.
- Ethical questions still remain

Crisper is great. The future of gene therapy looks bright." - **Liz Parrish,** CEO of BioViva Sciences



Stem cell therapy (Credit: NIH)

Overcoming Challenges The current processes in gene therapy are **expensive and inaccessible** to average patients across the globe. However, there is a growing movement to close the global gap in receiving gene therapy treatments. The Bill & Melinda Foundation is collaborating with Novartis, NIH and others to develop single-shot therapy cures for HIV and sickle cell disease. The Global Gene Therapy Initiative (GGTI) an alliance of clinicians, scientists, advocates and community members aim to launch clinical trials in LMICs over the next years.

Researchers are exploring various approaches to make allogenic **CAR T-cell therapies** that use T cells from a few donors and modifying them to be suitable for anyone with specific cancer and gene mutation, more feasible and affordable. By mass manufacturing, the cost of these therapies could be significantly reduced. However, overcoming the adverse immune response is a major challenge.

Developing CAR T-cell therapies that effectively address **solid cancers** (e.g., mesothelioma, sarcomas, lymphomas, sarcomas as well as cancers of the breast, prostate, kidney, ovaries, pancreas, thyroid, and colon) is another issue. The current CAR T-cell therapies (Chimeric Antigen Receptor T-cells) primarily target liquid cancers such as Leukaemia, Lymphoma and Myeloma.

Viruses have been used as vectors in Gene therapy, but in many cases produce adverse immune reactions in patients. Apart from viruses, other vectors are being tried, including, Stem cells and Liposomes, in clinical trials**.**

Most gene therapy for diseases such as cystic fibrosis and hemophilia has been designed only to ease, not to cure, the disease. However, gene therapy provides a potential method to correct a disease at its most basic level.

> I suspect any worries about genetic engineering may be unnecessary. Genetic mutations have always happened naturally, anyway- **James Lovelock**

The unique nature of personalized treatment makes gene therapy **difficult to regulate**. Nevertheless, efforts are on to keep regulatory frame-work in pace with new research and also harmonize it.

Future New technologies being developed in gene therapy such as the "bionic chip", could revolutionize gene therapy. They could make gene therapy more accessible and affordable, and, thereby, improve the quality of life of millions of people across the globe.

Numerous companies are actively working on various diseases, including rare diseases that carry a significant burden in India that are caused by single gene mutations, often involving just a single letter in the genetic code. The use of base pair editing technology, as mentioned earlier, holds great potential for addressing these diseases.

Over the next 10-20 years, we can expect significant advancements in gene editing that will contribute to the treatment of many diseases. “With a possibility to eliminate and prevent AIDS, malignancies, hereditary disorders and cure for cardiac disorders, gene therapy is nothing short of a medical phenomenon”, points out researchgate.net.

The third phase of the genomic revolution will involve synthetic biology, which encompasses the creation of new genomes and the manipulation of genes to manufacture a wide range of products, including medicine (Pl. see the Economic Section in this issue of Life Stream).

There is no doubt that Gene therapy will be a crucial part of 21st century medicine and its benefits will be increasingly felt in the near future.

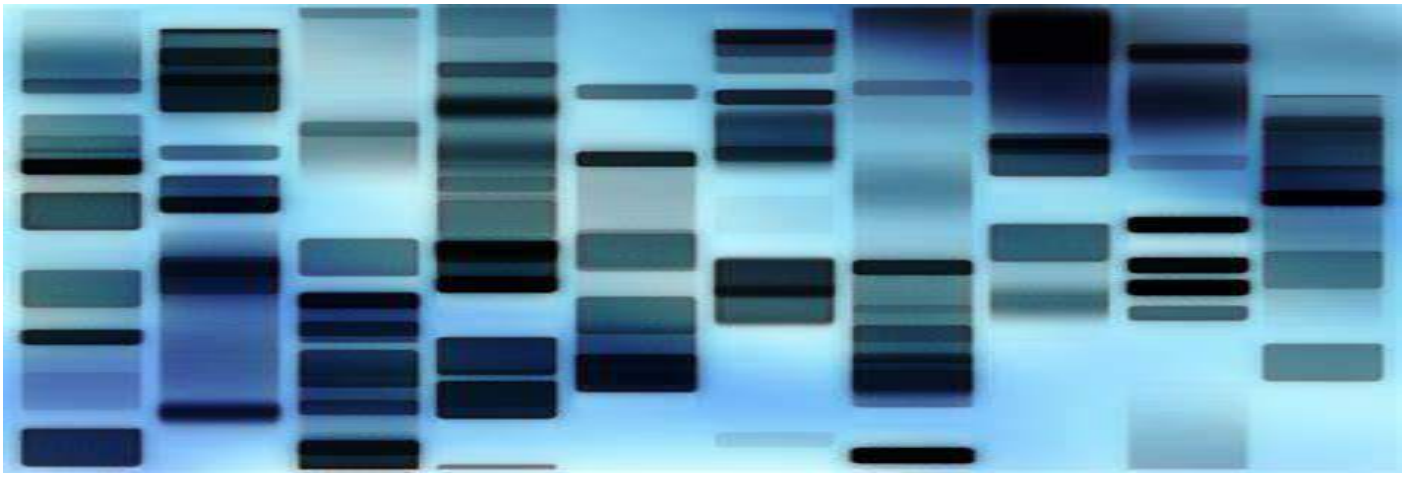
Ref: medicineplus.gov; www.britannica.com; researchgate.net; mayoclinic.org; www.weforum.com; www.genome.gov; www.fda.gov

In a world first, a teenager with sickle cell disease reportedly achieved complete remission after an experimental gene therapy at Necker Children’s Hospital in Paris, according to researchers (Fox News)

Cell and gene therapies seek to correct the root cause of an illness at the molecular level. These game-changing medicines are reshaping how we address previously untreatable illnesses – transforming people’s lives- **Biopharma**

TECHNOLOGY: DNA FINGERPRINTING

In the world of crime investigation, the discovery of DNA has been a game-changer. DNA, the unique code inside us, helps not only in defining our identity but also in solving crimes. Here we explore the fascinating account of how this tiny molecule revolutionized the field of criminal investigation.



DNA Fingerprint (credit: veteranstoday.com)

Deoxyribonucleic Acid, or DNA, is the intricate code that not only defines who we are, but also serves as an invaluable tool in solving crimes and establishing identities. One of the several applications of genetics is in the investigation of crimes, with the aid of DNA finger printing.

Today DNA finger printing has transformed the landscape of criminal investigation.

Our DNA contains the instructions required to develop, live, and reproduce, making it the fundamental building block of life. Each of us carries a unique DNA code, inherited from our parents, making our genetic makeup as distinct as a fingerprint. This inherent individuality forms the basis of its application in forensic science.

Forensic experts compare specific regions of an individual's genetic makeup, creating what is commonly referred to as a DNA profile or genetic fingerprint. This profile is unique to each person, except for identical twins, making it a unique tool for identification. Even the smallest biological samples - a strand of hair, a drop of blood, or a fragment of skin - contain enough DNA to create an accurate profile.

The History of Development of DNA Fingerprinting

The history of DNA fingerprinting, traces back to 1983. The first patent covering the direct use of DNA variation for forensics (US5593832A) was filed by Jeffrey Glassberg in 1983, based upon work he had done while at Rockefeller University in the United States in 1981.The term DNA fingerprinting,

> "That was a real eureka moment because we were suddenly onto something completely new, which was DNA-based identification."-**Sir Jeffrey Alec**

was coined by Sir Alec Jeffreys in 1984. Jeffreys, while researching genetic variations in inherited diseases, stumbled upon minisatellites, **DNA** regions that are stretches of repetitive **DNA** which do not code for any specific protein. These non-coding sequences form a major chunk of the **DNA** profile of humans. Jeffreys recognized that each individual has a unique pattern of minisatellites.

Sir Alec Jeffreys in his lab (credit: Getty images)

Realizing the potential of these minisatellites in identifying individuals, Jeffreys developed the first DNA fingerprinting technique.

The breakthrough came in 1985 when DNA fingerprinting was first employed in a criminal case. A young girl named Dawn Ashworth had been raped and murdered in Leicestershire, England. The DNA evidence collected from the crime scene was compared with the DNA of a suspect, Colin Pitchfork. The match between the crime scene DNA and the suspect not only solved the case, but also marked the inception of a revolutionary forensic tool.

The Process involved

In DNA fingerprinting, instead of looking at the whole sequence of a person's DNA, looks at the presence or absence of common marker that can be quickly and easily identified. **DNA fingerprinting typically relies on *short tandem repeats* (STRs), which are unique to individuals.** These sections of DNA can be compared between two different samples. If they show the same pattern after gel electrophoresis, it indicates that the samples are from the same source.

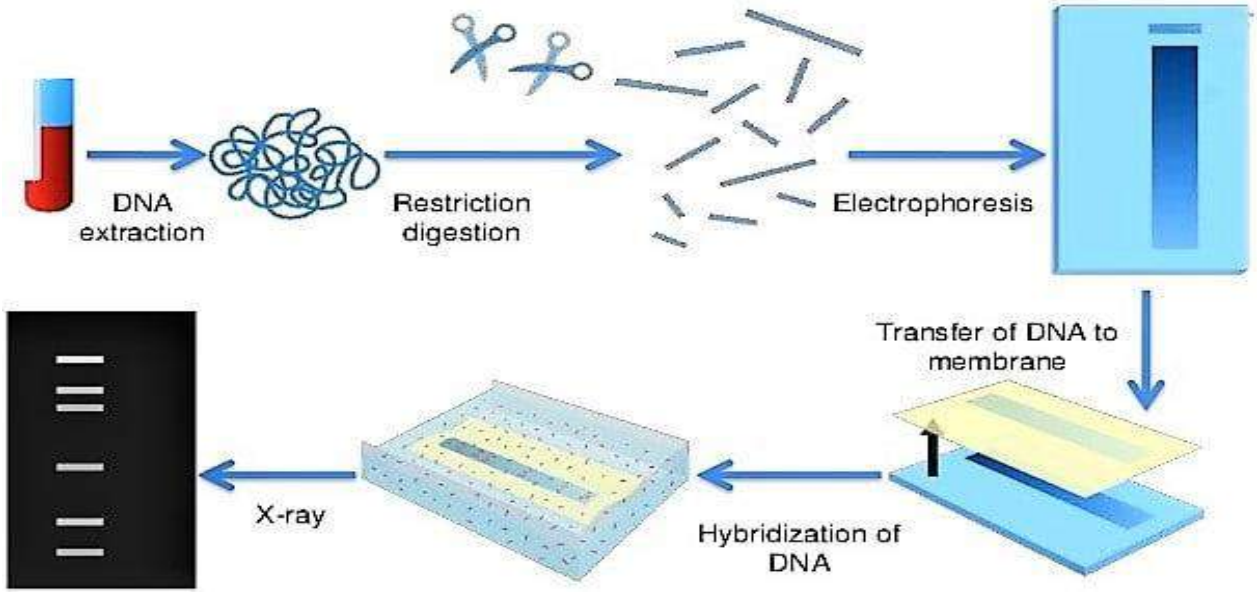
The procedure for getting a DNA fingerprint consists of

- First obtaining a sample of cells, such as skin, hair, or blood cells, which contain DNA.
- The DNA is extracted from the cells and purified.
- The method originally used by Jeffreys was based on restriction

> "What we had was a rare thing in science and that was my eureka moment when we first stumbled upon the whole idea of DNA fingerprinting"- **Sir Alec Jeffreys**

fragment length polymorphism (RFLP) technology, in which the DNA was then cut at specific points along the strand, with proteins known as restriction enzymes.

- Fragments of varying lengths that were produced were sorted by placing them on a gel and then subjecting the gel to an electric current (electrophoresis)
- They were split into single strands and transferred to a nylon sheet.
- The fragments underwent auto-radiography
- Radioactive DNA bound to the minisatellites.
- The fragments were then exposed to an X-ray film; the resultant pattern of marks could then be analyzed. A pictorial representation is given below.



DNA fingerprinting process (Credit: worldpress.com)

The **Modern method** is based on the use of the polymerase chain reaction (PCR).

- This is an automated procedure that requires only small amounts of DNA as starting material and can work even with partially degraded DNA.
- In this process microsatellites have shorter repeat units (typically 2 to 4 base pairs in length) than minisatellites (10 to more than 100 base pairs in length).
- With the help of PCR thousands of copies of the fragment can be created.
- Once an adequate amount of DNA has been produced with PCR, the exact sequence of nucleotide pairs in a segment of DNA can be determined by using one of several biomolecular sequencing methods.

Applications

The applications of DNA in forensic investigations are many. It serves as an essential tool in solving criminal cases, from identifying victims and linking suspects to crime scenes, to exonerating the innocent.

DNA is the fingerprint of the 21st century-**John Walsh**

In cases where traditional evidence falls short, DNA analysis can provide the much-needed breakthrough.

The FBI and other law enforcement agencies use the CODIS index, which compares 13 sections of DNA and can accurately identify criminals based on a DNA sample. The U.K. established its National DNA Database in 1995; by 2023, it has over 5.9 million registered people. According to discover magazine, at the end of 2022, in the U.S., the National DNA Index System has DNA information for more than 15.7 million offenders and more than 4.8 million arrestees. Since 2002, an international DNA database has also existed — INTERPOL's DNA database — which currently has more than 280,000 people profiled from almost 90 countries.

One of the famous criminal cases involving the technique of DNA fingerprinting was that of O.J Simpson, a former National Football League (NFL) player, broadcaster and actor in the USA.

The O.J. Simpson case, also known as the *People of the State of California v. O.J. Simpson*,

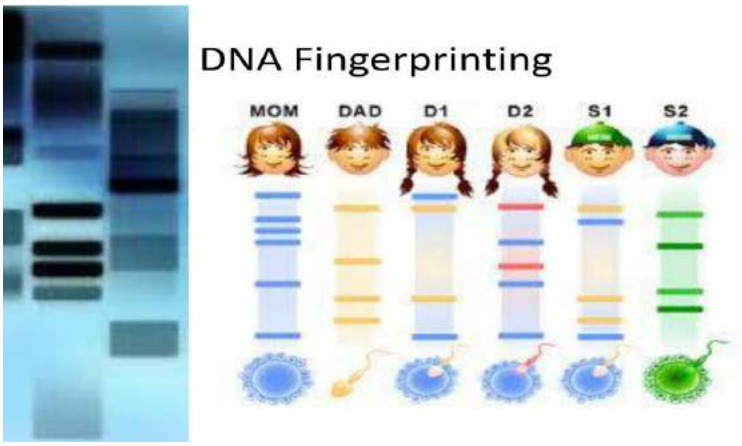
O.J. Simpson (Credit: wtlcfm.com)

was a high-profile criminal trial in 1995. O.J. Simpson, a former American football star, was accused of the murders of his ex-wife, Nicole Brown Simpson, and her friend, Ron Goldman. One significant aspect of the case was the use of DNA fingerprinting, also known as DNA profiling or DNA testing. The prosecution presented DNA evidence that linked O.J. Simpson to the crime scene. They found blood samples at the crime scene, in Simpson's car, and at his home. DNA testing was performed on these samples, and the results showed that the blood found at these locations matched O.J. Simpson's DNA profile.

The DNA evidence played a crucial role in the trial and was a major factor in Simpson's eventual acquittal. The defense team raised questions about the way the evidence was collected and handled, creating reasonable doubt in the minds of the jurors. As a result, O.J. Simpson was found not guilty of the murders in a highly publicized verdict.

Moreover, DNA plays a significant role in reuniting families separated by conflict, disaster, or adoption. Through advanced techniques, individuals can trace their genetic heritage, uncover long-lost relatives, and reconstruct their family trees. This not only provides solace to those yearning to connect with their roots but also highlights the remarkable humanitarian aspect of DNA technology.

"DNA fingerprinting: where science becomes the silent witness, speaking the truth in every cell."**-Unknown**



The unique DNA fingerprints of the individual members of the same family (Credit: Slide Serve)

In science, DNA fingerprinting is used to determine how closely related species and populations are to other species and populations. Further, it can track their spread over time. This ability to look directly at an organism's gene markers has revolutionized our understanding of zoology, botany, agriculture, and even human history.

Challenges and Ethical Considerations

While DNA technology has revolutionized forensic investigations, it is not without challenges. Issues of privacy, consent, and the responsible use of genetic information loom large. Striking a delicate balance between solving crimes and protecting individual rights remains a pressing concern. Ethical guidelines and stringent protocols are vital to ensuring the responsible use of DNA evidence, safeguarding both justice and privacy.

Looking Ahead

The combination of DNA science and forensic investigation stands as a testament to human ingenuity and perseverance. From the laboratories to the courtroom, DNA analysis has become an indispensable tool in crime investigation.

As technology continues to advance, the future of forensic DNA analysis appears promising. Rapid DNA testing, portable sequencing devices, and enhanced databases are reshaping the landscape of forensic investigations. These innovations hold the potential to expedite identifications, solve cold cases, and further refine our understanding of human genetics. With the advancement in Genetics, the application of DNA technology in the field of crime investigation, as also in other fields, is expected to become more and more sophisticated.

Ref: en.wikipedia.org; www.britannica.com**; biologydictionary.net; microbenotes.com; ChatGPT**

Along with the CCTV camera and the tapping of emails and phone calls, the DNA fingerprint has become part of a civic apparatus that can follow the movements of individuals with unprecedented accuracy-**The Guardian**

ECONOMICS: GENE ECONOMY

Gene therapy has a profound impact on world economy. It is one of the fastest growing fields today and gene therapy companies have been among the hottest in the stock market. The World Economic Forum points out that the global gene therapy market is expected to increase from $ 5.3 billion in 2022 to $ 19.11 billion by 2027.

Here, we discuss the impact of the fast- growing gene therapy market on global health care. Besides, we also briefly discuss bio- economy, a product of the third phase of genomic revolution.

1. Gene Therapy & Healthcare

According to nature.com 'gene therapy is at an inflection point'. Although the gene therapy industry is still in the early stage of development, 'early clinical successes and substantial funding have generated enormous momentum'.

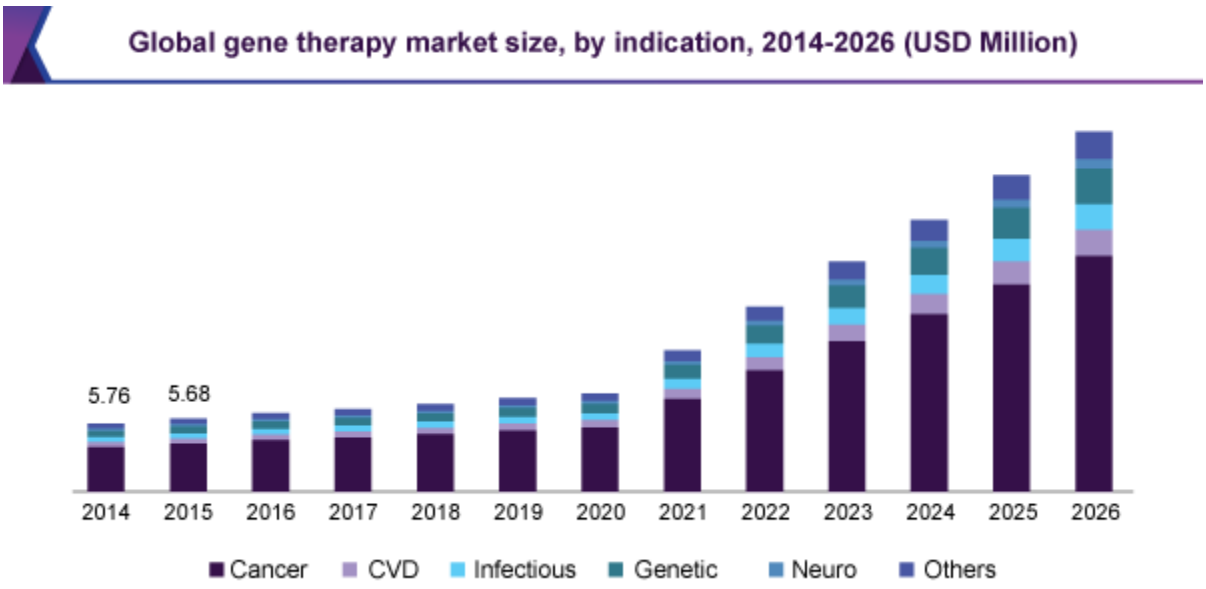
Currently over 2000 therapies are reportedly in development, globally and the number of gene therapies is growing exponentially. This scientific explosion is translating into economic gains.

The development of new tools and technology has led to the emergence of new companies. WEF reports that in 2021 the number of developers reached 1308, raising a record of $ 22.7 billion, 57% higher than previous two years.

A simulation model proposed by www.medrxiv.org suggests that a total of 1.09 million patients are expected to be treated by gene therapy from January 2020 to December 2034. The expected peak annual spending on these therapies is estimated at $25.3 billion, and the total spending from January 2020 to December 2034 will be $306 billion.

(Credit: psmarketresearch.com)

Applications of gene drives will have profound economic implications, comparable to the Green Revolution or crop biotechnology.**www.tandfonline.com**



(Credit: pinterest.com)

High cost of therapies

Once they receive approvals, gene therapies enter the market with record price-tags. It costs $ 850,000/-to treat Leber congenital amaurosis, a rare eye disease that could lead to blindness; $ 2.8 million to treat beta thalassemia, a rare blood disorder. The Economist reports that the cost of a shot of Zolgensma, a gene therapy for spinal-muscular atrophy, comes to $2.1m. It is one of a new generation of ultra-expensive medicines. Treatments for beta-thalassemia and Hemophilia, two blood disorders, cost $2.8m and $3.5m, respectively. Their prices may be overtaken by gene therapies for sickle-cell disease, and one for Duchenne muscular dystrophy, which are yet to be approved. The high prices are due to high manufacturing cost, high investments and market factors (See box below).

Impact The high cost of therapies has led to high inequity in treatment -- patients being mostly confined to rich countries, while in Low- and Medium-Income Countries (LMICs), where disease burden is high, they are totally neglected.

Diversity Genomic research (Credit: NIH)

Developing new anti-aging therapy in China (credit flipboard.com)

Currently, only 5% of the roughly 7000 rare diseases have an FDA-approved drug, leaving thousands of conditions without a cure—**World Economic Forum**

Trade Name (Proper Name)	Cost	Indication and type of therapy	Manufacturer	Patient Population
Kymriah (tisagenlecleucel)	$475,000	CAR-T cell therapy for treatment of patients up to 25 years old with B-cell acute lymphoblastic lymphoma	Novartis	1.6 per 100,000 (6500 new cases per year in the US)
Yescarta (axicabtagene ciloleucel)	$373,000	CART-T cell therapy for treatment of adult patients with non-Hodgkin's lymphoma	Kite Pharma (bought by Gilead)	3.8 per 100,000 (7500 new cases per year in the US)
Luxturna (voretigene neparvovec-rzyl)	$850,000 ($425,000 per eye)	AAV therapy for patients with biallelic RPE65 mutation-associated retinal dystrophy	Spark Therapeutics, Inc	1 in 50,000 worldwide
Strimvelis (GSK2696273)	$648,000 (594,000 Euros)	CAR-T cell therapy for patients with severe combined immunodeficiency (ADA-SCID)	Glaxosmithkline	Between 1 in 200,000 to 1 in 1 million per year
Glybera (alipogene tiparvovec)	$1.2 million (1 million Euros) Withdrawn	AAV therapy for Lipoprotein lipase deficiency	uniQure	1 in 1 million in the US per year

(Credit: Medium)

Making gene therapy efficient and equitable

The full potential of gene therapy can be realized only if it is made affordable and accessible to all people suffering genetic disorders, instead of only to few. NIH-National Center for Biotechnology Information points out that numerous obstacles to efficient market access prevail. They range from resource-consuming manufacturing processes to reimbursement and funding challenges.

The World Economic Forum and other expert bodies have come out with suggestions to decentralize research and manufacturing, improve quality, reduce costs and inequities and to involve local population.

- To make changes in innovation and policy at individual, institutional, national, continental and global levels.
- To continue to develop cost-effective ways of gene therapies wherein the private sector has to play an important role.
- Instead of expensive *ex vivo* procedures that require removal of a patient's cells from their body, opt for novel *in vivo* methods to simplify the procedure to a single injection directly into the patient, saving time and money.
- Payers, providers and gene therapy companies to work out better payment and reimbursement models, by spreading costs over time, and linking payments to patient outcomes.

> Gene editing products seem to follow a much faster development rate from bench to Market-**NIH**

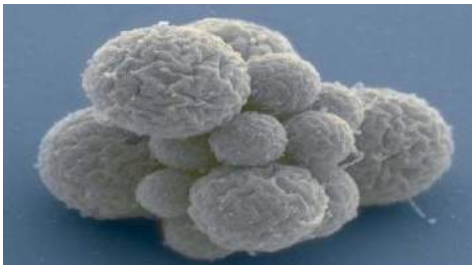
- To establish policy and regulation gene therapy frame works by individual countries as per R&D guided by recommendations from the World Health Organization, on safety, efficacy and ethics.
- To move manufacturing locally and to "point of care" settings (within hospitals) which can both significantly reduce the cost and improve accessibility.
- LMICs to enter the global market, prioritizing the needs of communities carrying the highest disease burdens. Many LMICs have weak systems to support the emergence of new companies or to have collaborations with multinational companies. Stronger private sector involvement will be critical for penetration into emerging markets.
- Re-organize infrastructure developed during the COVID pandemic to produce gene therapies.
- Information, Communication and Education activities (IEC) to be made accessible to a broad range of stakeholders as patient and public support is critical for the successful adoption of any new technology.
- A patient-centered approach will ensure that the community is involved in research and will have a say in receiving a particular health intervention when it is available.
- Direct investment to institutions in Africa; increasing the level of investment through funding partnerships; and longer periods of investment could help to reduce inequality
- Regulations in one country must also converge with the frameworks of other countries to make it easier for companies to operate efficiently.

11. The Gene Economy

i. Gene editing is having huge impacts not only on healthcare, but also on agriculture and many other fields (For details pl see the Food & Diet section of this issue of Life Stream)

ii. Synthetic Biology- What happens when biology becomes technology?

We saw how the first two phases of gene therapy-gene sequencing and gene editing -led to advancements in healthcare. According to experts, the 'third phase of the genomic revolution



The first synthetic bacterial cell (Credit: youngmindsonline.org)

will involve synthetic biology, which encompasses *the creation of new genomes and the manipulation of genes to manufacture a wide range of products, from fertilizers to cosmetics to medicine'*. Synthetic biology is in wide use to construct viruses, bacteria, eukaryotic cells with synthetic genomes.

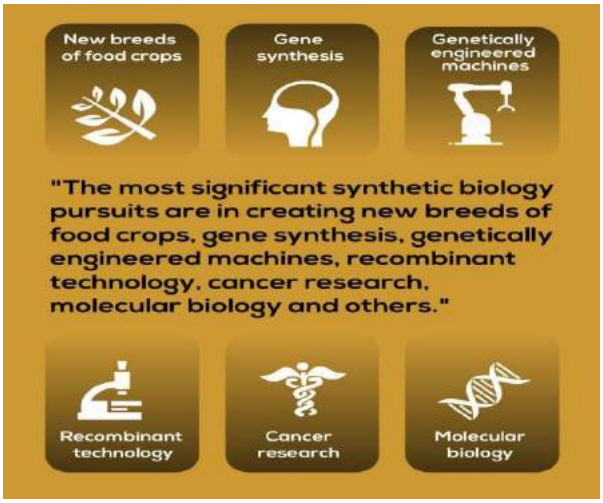
Synthetic **Genomics** is a nascent field of synthetic biology. When biology becomes technology, 'it breaks

> It is time to rethink intellectual property and pricing practices that prevent global access to genetic therapies.

down the boundaries between science, society, nature and technology that can lead us to imagine different possible futures'

What started in the healthcare industry is expanding into many sectors. The bioeconomy covers all sectors and systems that rely on biological resources (animals, plants, microorganisms, and derived biomass, including organic waste) as well as their functions and principles. The revolutionary technology of synthetic biology is poised to make a profound impact on the way a vast array of products is manufactured, from lab-grown meat to cosmetics to biodegradable packaging.

Synthetic genomics is now making a huge impact on personalized medicine, life sciences and chemical industries.



(Credit: boldbusiness.com)

Economic Impact According to a report in marketsandmarkets.com. the global synthetic biology market is projected to reach $30.7 billion by 2026 from $9.5 billion in 2021, at a compound annual growth rate of 26.5% during the forecast period. 'Factors favoring the market's growth include a wide range of applications of synthetic biology, the rising R&D funding and growing initiatives in synthetic biology, the declining costs of DNA sequencing and synthesis, and the increasing investments in the market'. However, experts point out that biosafety, biosecurity, and ethical concerns related to synthetic biology could slow growth. Lessons learned from Covid-19 vaccines could advance synthetic biology. Despite its huge potential, presently, the research coverage is not considered at the desired levels. Some experts point out that investors are paying relatively little attention to its enormous business potential.

Future McKinsey estimated in a May 2020 report that as much as 60% of the global economy's physical inputs could be made using synthetic biology, resulting in direct economic benefits of at least US$1.7 trillion between 2030 and 2040. The World Economic forum points out that biological innovations have the potential to address 45% of the current disease burden of the world and to produce 60% of our physical inputs into the global economy in the next 10-20 years. ----------

Ref: en.wikipedia.org; www.cell.com; www.genome.gov;marketsandmarkets.com;www.genengnews.com;www.alliance Bernstein.com;

At the intersection of an aging population, climate change and environmental degradation lies the bioeconomy, increasingly underpinned by advances in synthetic biology-**World Economic Forum**

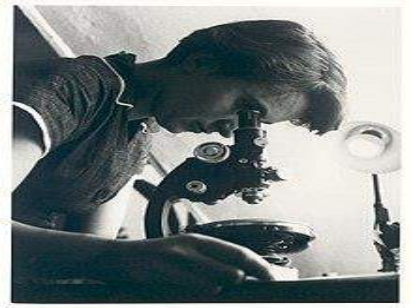
PERSONALITIES: WOMEN IN GENETICS & MOLECULAR BIOLOGY

When we read the history of Genetics, we find that male contributors have dominated the field. Barring one or two, women hardly entered the field. Today, the scenario has changed. More and more women are making significant contributions to modern genetics and molecular biology. Some are even Nobel Prize winners.

Here, we mention the story of two dedicated women scientist of earlier times. We also note the contributions of two modern women scientists, who shared the Nobel Prize in 2020, for developing a new gene-editing technology.

Like all other disciplines in science, genetics too has been dominated by male scientists. It is only after a double-helix model was proposed for DNA that the names of women scientist started emerging in modern genetics and molecular biology. The first name that comes to mind is that of Rosalind Franklin who provided the critical Proof for the DNA double helix-model, proposed by Watson and Crick.

1. Rosalind Franklin-The Dark Lady of DNA



Franklin at work (Ref: Wikipedia) **Rosalind Elsie Franklin** (1920 -1958) was a British chemist and X-ray crystallographer 'whose work was central to the understanding of the molecular structures of DNA, RNA (ribonucleic acid), viruses, coal, and graphite'. Her life history is summarized as follows: -

- Born in Notting Hill, London, into an affluent and influential British Jewish family.
- Father, Ellis Arthur Franklin was a politically liberal London merchant banker; Mother- Muriel Frances Waley.
- Graduated in 1941 with a degree in natural sciences from Newnham College, Cambridge.
- Worked on the physical chemistry of coal and earned a PhD from Cambridge in 1945
- Moved to Paris in 1947 as a post-doctoral researcher and became an accomplished X-ray crystallographer.
- Joined King's College London in 1951 as a research associate. Discovered some key properties of DNA, which eventually facilitated the correct description of the double helix structure of DNA.
- Owing to disagreement with her director, John Randall, and her colleague Maurice Wilkins, Franklin was compelled to move to Birkbeck College in 1953.
- Best known for her work on the X-ray diffraction images of DNA while at King's College London
- Photo 51, taken by her student Raymond Gosling, led to the discovery of the DNA double helix
- Francis Crick, James Watson, and Maurice Wilkins shared the Nobel Prize in Physiology or Medicine in 1962.Her name was excluded, as the Nobel Committee generally did not make posthumous nomination

> While the biological properties of de-oxy pentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here...show the basic molecular configuration has great simplicity."– **Rosalind Franklin**

- Working under John Desmond Bernal, Franklin led pioneering work at Birkbeck on the molecular structures of viruses.
- On the day before she was to unveil the structure of tobacco mosaic virus at an international fair in Brussels, Franklin died of ovarian cancer at the age of 37 in 1958.
- Her team member Aaron Klug continued her research, winning the Nobel Prize in Chemistry in 1982.

Although her works on coal and viruses were appreciated, Franklin's contributions to the discovery of the structure of DNA were largely not recognized during her life-time. In April 2023, scientists, based on new evidence, concluded that Rosalind Franklin was a contributor and "equal player" in the discovery process of DNA, rather than other way.

A musical, titled "Double Helix", based on Franklin's contribution to the discovery opened on 30 May 2023 at the Bay Street Theater in Sag Harbor, NY.

2. Barbara McClintock & the "Jumping genes"

Barbara McClintock (ref: Wikipedia)

Not many outside the fields of genetics and molecular biology might have heard the name of **Barbara McClintock (1902 –1992)** an American scientist and cyto-geneticist who was awarded the 1983 Nobel Prize in Physiology or Medicine.

- Born Eleanor McClintock on June 16, 1902, in Hartford, Connecticut, to Homeo-physician Thomas Henry McClintock and Sara Handy McClintock
- Began her studies at Cornell's College of Agriculture in 1919 receiving a BSc in 1923; MSc and PhD in 1925 and 1927, respectively in botany
- Part of a group that studied the new field of cytogenetics in maize, the focus of her research for the rest of her life.
- In 1936 appointed Assistant Professorship in the Department of Botany at the University of Missouri in Columbia.
- In early 1941, a visiting Professorship at Columbia University
- In December 1941,took up a research position in the Department of Genetics, Cold Spring Harbor Laboratory;
- In 1944 undertook a cytogenetic analysis of *Neurospora crassa* which became a model species for classical genetic analysis.
- Recognized as among the best in the field, awarded prestigious fellowships, and elected a member of the National Academy of Sciences in 1944.
- During the 1940s and 1950s, discovered transposition ("jumping genes,")
- Due to unfair criticism of her research, she stopped publishing her data in 1953.Later, study of the cytogenetics and ethnobotany of maize races from South America.
- In the 1960s and other 1970s, scientists confirmed the

> Science, for me, gives a partial explanation for life. In so far as it goes, it is based on fact, experience and experiment— **Rosalind Franklin**

mechanisms of genetic change and protein expression that she had demonstrated in her maize research.

- Awards and recognition followed, including the **Nobel Prize for Physiology or Medicine in 1983** for the discovery of genetic transposition; the first woman to win that prize unshared.

McClintock's contribution to cytogenetics

McClintock chose *Zea mays* (maize), as the subject of her research, particularly those plants that produce variably colored kernels. 'Maize is an ideal organism for genetic analysis because each kernel is an embryo produced from an individual fertilization. Hundreds of offspring can be scored on a single ear'.

Labelled maize. Barbara McClintock discovered that genes could "jump" by studying generational mutations in maize. *Courtesy of Cold Spring Harbor Laboratory.*

She developed the technique for visualizing maize chromosomes and used microscopic analysis to demonstrate many fundamental genetic ideas.

From the late 1920s, McClintock studied chromosomes and how they change during reproduction in maize.

During the 1940s and 1950s, she demonstrated **that genes are responsible for turning physical characteristics on and off.**

She developed theories to explain **the suppression and expression of genetic information from one generation of maize plants to the next**.

She produced **the first genetic map for maize**, linking regions of the chromosome to physical traits.

She demonstrated the **role of the telomere and centromere**, regions of the chromosome that are important in the conservation of genetic information.

Genetic recombination -a mechanism by which chromosomes exchange information takes place by crossing-over during meiosis. **McClintock discovered transposable elements (TEs), also known as "jumping genes." *It suggested that an organism's genome is not a stationary entity, but rather is subject to alteration and rearrangement.***

Because McClintock felt like an outsider within her field, she was able to look at her

> "If you know you are on the right track, if you have this inner knowledge, then nobody can turn you off... no matter what they say"-**Barbara Mclintock**

scientific subjects from a perspective different from the dominant one, leading to several important insights.

McClintock made discoveries far beyond the understanding of the time. But her concepts were met with criticism from the scientific community at that time. *McClintock was awarded the Nobel Prize in 1983 more than 30 years after, in recognition of this and her many other contributions to the field of genetics.*

She was compared to Gregor Mendel in terms of her scientific career by the Swedish Academy of Sciences when she was awarded the Prize.

McClintock giving her Nobel Lecture (Wikipedia)

Awards & Honors

McClintock received many awards and honors including the National Medal of Science by Richard Nixon in 1970- the first woman to receive it; the Benjamin Franklin Medal for Distinguished Achievement in the Sciences. In all she was awarded 14 Honorary Doctor of Science degrees and an Honorary Doctor of Humane Letters in 1986; elected a Foreign Member of the Royal Society in 1989 and inducted into the National Women's Hall of Fame.

Last Years

McClintock died of natural causes in Huntington, New York, on September 2, 1992, at the age of 90; she never married or had children.

3. Women in Gene Editing

A mention may be made about two distinguished women scientists who developed the gene-editing technique called CRISPR that has revolutionized genetics. They have been awarded the 2020 Nobel Prize in Chemistry for developing "one of gene technology's sharpest tools: the CRISPR/Cas9 genetic scissors", the tools to edit the DNA.

Emmanuelle Charpentier, is a microbiologist from Paris and currently with the Max Planck Unit for the Science of Pathogens in Berlin, and **Jennifer Doudna,** a biochemist at the University of California, Berkley, USA.

> It might seem unfair to reward a person for having so much pleasure over the years, asking the maize plant to solve specific problems, and then watching its responses-
> **Barbara McClintock**

"By utilizing this technology, researchers can change the DNA of animals, plants and microorganisms with extremely high precision. This technology has had a revolutionary impact on the life sciences, is contributing to new cancer therapies, and may make the dream of curing inherited diseases come true" (Nobel Prize Press Release, 2020 para. 1)

Jennifer Doudna & Emmanuelle Charpentier began a formidable partnership in 2011- Credit: Vilnius University; Laura Morton Photography

NOTE: We have seen how two women geneticists -Rosalind Franklin and Barbara McClintock --had to fight against all odds and faced discrimination in establishing themselves as accomplished scientists. During her life time Rosalind did not get due credit for her path-breaking work; McClintock had to wait for 30 long years to get her work recognized.
But today things have greatly changed. Women face less discrimination and are able to carry on their work with courage and confidence. The coming days will find more and more women attracted to the field of genetics.

Emmanuell Charpentier & Jennifer Doudna proudly holding their Nobel Prizes (Credit: Oxford Academy)
Ref: en.wikipedia.org; www.nature.com;www.ncbi.nlm.nih.gov; www.britannica.com; www.bbcnews.com;www.nobelprize.com

> ""We could create a gene gap that would get wider with each new generation," **Jennifer Doudna**

ART & ARCHITECTURE: GENETIC ART

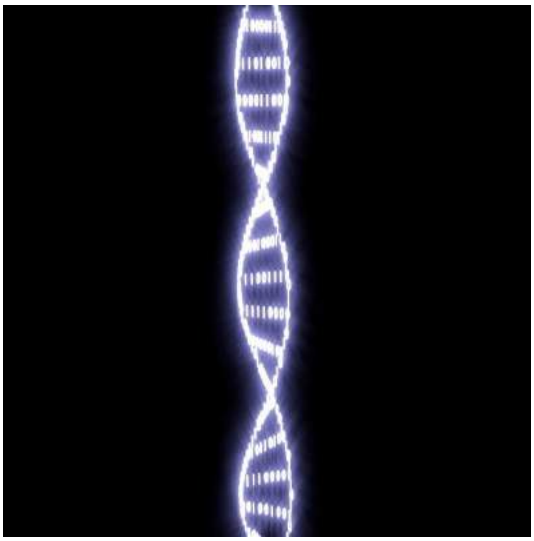
In this section we try to explain how artists take inspiration from concepts in Genetics, including the double-helix model of DNA and Gene/genome editing

Scientists are usually type-casted as 'responsible guardians of knowledge and artists as irreverent humanists. Art is born out of creativity and abstract thoughts and seemingly open set of rules, whereas, science is a practice rooted in laws of logic, facts, and structure'. While scientists apply logic and reason in their search for truth, artists depict a range of human emotions thorough their creations. Although art and science may appear incompatible, we now know that such divisions are artificial.

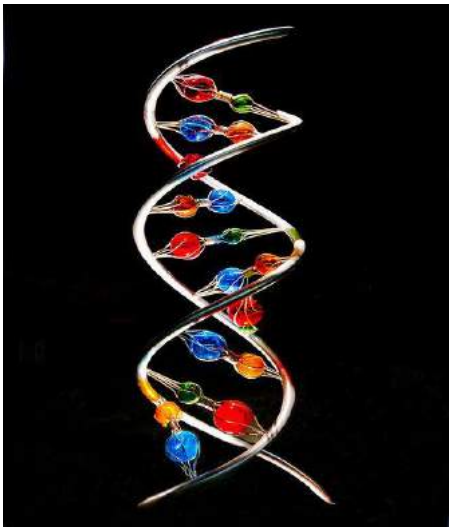
Genetic Art One area in which we can witness the interplay of science and art is **Genetic Art** which artistically depict the design, structure and beauty of the genetic material -DNA and DNA- based technology like gene editing. As someone noted, a new era of art may be upon us, as one that finds beauty and aesthetics in biology.

According to the science journal Nature "Contemporary visual artists are incorporating genetic concepts into their work, and this work has become prominently featured in numerous museum and gallery exhibitions. Such art uses visual images that represent the language of genomics, the values affected by genetic understanding of the body and the implications of bioengineering".

The Double Helix has caught the imagination of artists more than any other object in genetics. The visual representation of the life molecule, with two strands coiling around each other, radiating potential power, energy and beauty is a favorite theme of artists. One can find the depiction of DNA in wall papers, wall posters, art pieces, models etc. Here are a few samples: -



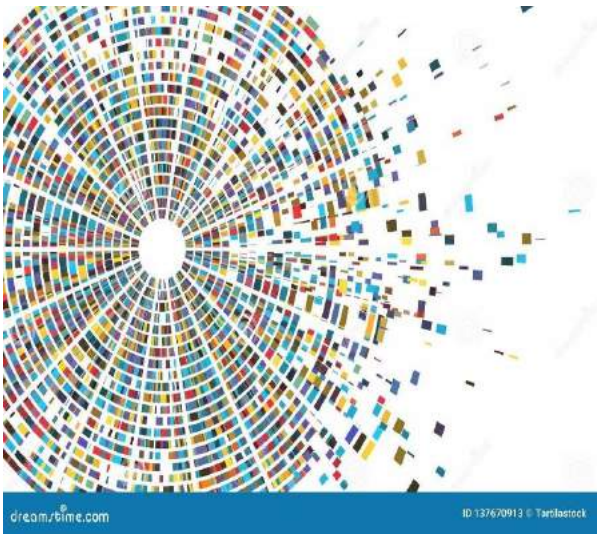
(Credit: (wallpapersafari.com)



(Credit: pintrest.com)

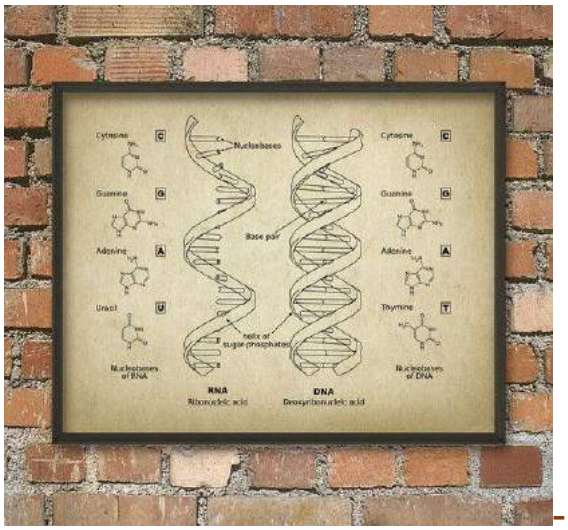
Up to now, art has viewed science as a source of inspiration, passive and beautiful, like a languid nude. Art hasn't really understood science yet- **www.materialstoday.com**

Double helix wall papers (Credit: **wallpaperaccess.com**)

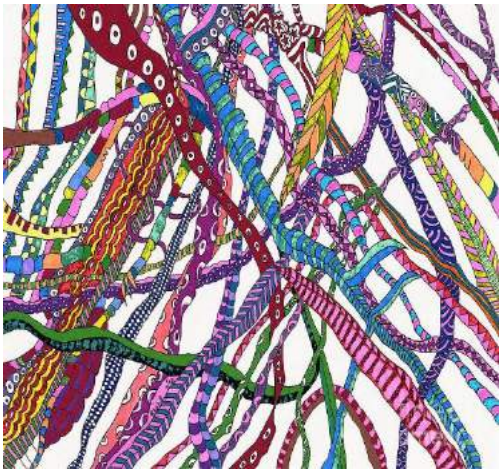


Genome sequence map, chromosome architecture and genetic sequencing chart

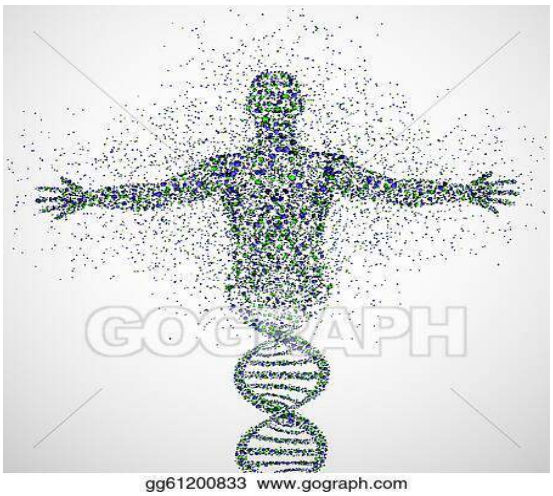
(Credit: bernardbeneito.com)



(Credit:wallpaperaccess.com)



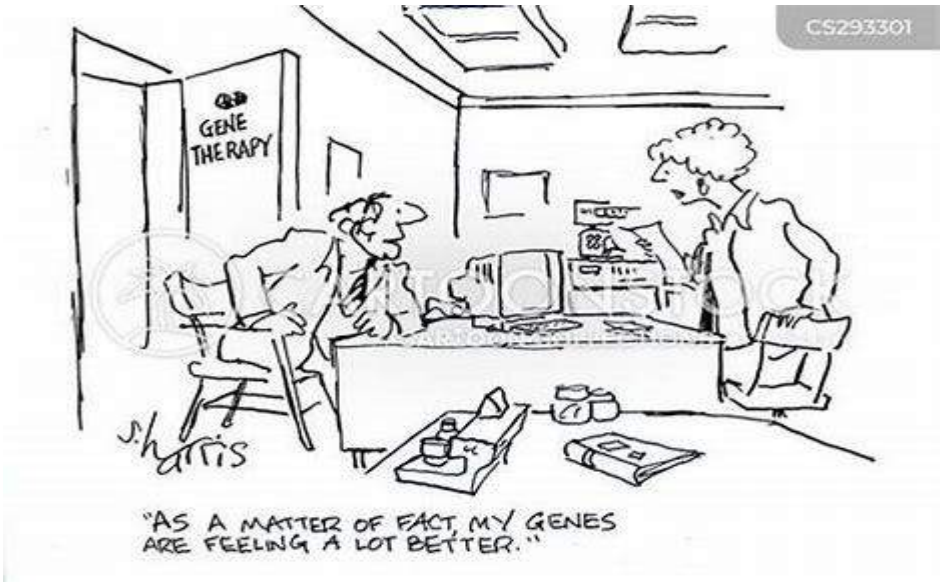
Dancing DNA-painting by Rheba McMichael-Fine Art America



Prototype of man

Only art and science make us suspect the existence of life to a higher level, and maybe also instil hope thereof. – **Ludwig van Beethoven**

Gene/Genome editing Cartoons are a separate genre of Gene Art. In the net one can find many cartoons illustrating the funny aspects of gene editing and creation of new genomes. Satirical and humorous and speaking in a distinct language, these cartoons often evoke serious thinking on the impact of gene technologies on humans, animals and plants. See how funny are some of them.



(Credit: cartoonstock.com)

(Credit: cartoon stock.com)

(Credit: scoopnest.com)

Ref: www.nature.com; Ekac.org; www.materialstoday.com;www.cartoonstock.com;ekac.org;www.sciencedirect.com;www.geneart.org.uk

There is an art to science, and a science in art; the two are not enemies, but different aspects of the whole-**Issac Asimov**

POEM: GENE POEMS

1. POEM BY THOMAS HARDY

Heredity Poem by Thomas Hardy

Heredity

I am the family face;
Flesh perishes, I live on,
Projecting trait and trace
Through time to times anon,
And leaping from place to place
Over oblivion.

The years-heired feature that can
In curve and voice and eye
Despise the human span
Of durance-that is I;
The eternal thing in man,
That heeds no call to die.

Thomas Hardy

internetPoem.com

POEM-2

THE GENES SAYS IT ALL	***- Sudha Shrotria***
At a restaurant one day, *As I made my way,* *A lady dignified and refined* *Walked up to me;* *'Can I ask you something?' said she,* *Wondering what she had in mind,* *"Sure, go ahead," I said;* *She took my father's name,* *And asked if my surname was the same;* *"Aren't you his daughter," she said,* *Seeing my puzzled look* *She went on with her narration* *Recalling the location,* *And the name of the place* *Twin houses at the army base,*	*Neighbors of yesteryears,* *She was nine* *My kid brother's friend I hear;* *Recalling they played around* *Games new-found* *Scampering through the garden door* *Playing hide and seek* *Shouting sore.* *Forgotten as it was so long ago,* *In recollection I was slow-* *'As I saw you walk in today,' she said* *I remembered your father ahead* *'Same face, Same smile* *Same walk and demeanor,"* *The image stood out so tall,* ***The gene says it all.*** ***(Ms. Sudha Shrortria is a former civil servant and a prize-winning poet. She is also the Associate Editor of Life stream)***

Poetry is a matter of life, not just a matter of language-
Lucille Clifton

TRAVEL: CIMMYT

Today, there are many institutions across the world which are engaged in genetic research. Among them CIMMYT is unique, for, it was the seat of green revolution only a few decades ago.

One of our team members looks back at her visit to CIMMYT and writes about its past and present.

(Credit: Wikipedia)

The International Maize and Wheat Improvement Center, better known by its Spanish acronym **CIMMYT** (***Centro Internacional de Mejoramiento de Maíz y Trigo***), with its headquarters in Mexico, is a non-profit research-for-development organization that develops improved varieties of wheat and maize, with the goal of attaining world food security. CIMMYT is the global leader in publicly-funded maize and wheat research and related farming systems.

I visited CIMMYT sometime in 1980. Located in El Batán, near Texcoco, at a distance of 25-30 kms from the Mexican airport, it takes about half an hour to forty minutes (depending on the traffic) to reach it. It was then famous for breeding short varieties of high-yielding wheat varieties that created the agriculture revolution in the 1970's and 80's. My visit was supported by the FAO (Food & Agricultural Organization), as a part of a project.

While going towards it by road, I imagined CIMMYT to be a large complex, having huge colonial style buildings. Instead, I found an array of buildings designed for functionality and convenience.

The people at the CIMMYT treated me as an honored guest. I was accommodated in one of their guestrooms which too was simple, elegant and functional. I remember that the room was full of natural air and light. It had minimum furniture.

Breakfast was provided in a large open space. Breakfast was indeed a treat for a

> Food is the moral right of all who are born into this world. ~ **Norman Borlaug**

vegetarian like me - apart from fruit juices, several types of local fruits like banana, water melon, musk melon (cantaloupe), different kinds of bread, boiled beans etc. were spread out.

Norman Borlaug It was on the second morning of my visit that I met late **Norman Ernst Borlaug (1914 –2009),** famous for his contributions to the development of

(Credit: cropforlife.com)

high-yielding short varieties of wheat, which revolutionized world agriculture. Borlaug was an American agronomist who took up an agricultural research position with CIMMYT, where he developed semi-dwarf, high-yielding, disease-resistant wheat varieties. During the mid-20th century, Borlaug led the introduction of these high-yielding varieties combined with modern agricultural production techniques to Mexico, Pakistan, and India. “As a result, Mexico became a net exporter of wheat by 1963. Between 1965 and 1970, wheat yields nearly doubled in Pakistan and India, greatly improving the food security in those nations .Borlaug was often called "the father of the Green Revolution", and is credited with saving over a billion people worldwide from starvation”.

Apart from Nobel prize in 1970, he was also awarded the Presidential Medal of Freedom and the Congressional Gold Medal in the United States.

Of course, there were criticism directed at the capital-intensive green revolution. However, it remains a reality that countries like India could attain self- sufficiency in food production only due to it.

The great scientist was having his breakfast, when I was introduced to him by one of the Indian scientists, Junagad from Gujarat. Ever-smiling, Borlaug looked genteel and serene. He politely invited us to join him at the table. He patiently answered our questions and explained to us the nature of his work. He also posed for a photograph with us. I have always cherished those moments spent in the company of the great scientist.

CIMMYYT- history

One of the researchers acted as my guide and took me around

> The green revolution has an entirely different meaning to most people in the affluent nations of the privileged world than to those in the forgotten world---**Norman Borlaug**

CIMMYT. She briefed me on how CIMMIT was set up and what were its activities.

CIMMYT was born out of the cooperative efforts of the Mexican government and the Rockefeller Foundation that led to the founding of the Office of Special Studies, an organization within the Mexican Secretariat of Agriculture in 1943. The project involved research in genetics, plant breeding, plant pathology, entomology, agronomy, soil science, and cereal technology. The goal of the project was to boost wheat production in Mexico, which at the time was importing a large portion of its grain, through selective plant breeding and crop improvement.

The project developed into a collaboration between Mexican and international researchers. It established global networks to test experimental crop varieties. The program was renamed as CIMMYT in 1963, though it was still under the Secretariat of Agriculture's jurisdiction.

Main founders include Bill & Melinda Gates Foundation, CGIAR, Foundation for Food and Agriculture Research (FFAR), OCP Group and the national governments of Australia, Britain, Canada, China, Germany, Mexico, Norway and the United States. Historically, CIMMYT received funding from the European Commission and the Rockefeller Foundation. Today CIMMYT innovates agricultural practices to help boost production, prevent crop disease, and helps to improve livelihoods of smallholders.

Though its headquarters are in Mexico, the center operates through 12 regional offices (Afghanistan, Bangladesh, China, Colombia, Ethiopia, India, Kazakhstan, Kenya, Nepal, Pakistan, Turkey, and Zimbabwe), as well as number of experimental stations. with more than 400 partners in over 100 countries.

Germplasm Collection

CIMMYT hosts the largest collection of maize and wheat in the world: 28,000 unique kinds of maize and 150,000 types of wheat. I am glad that I was able to visit it.

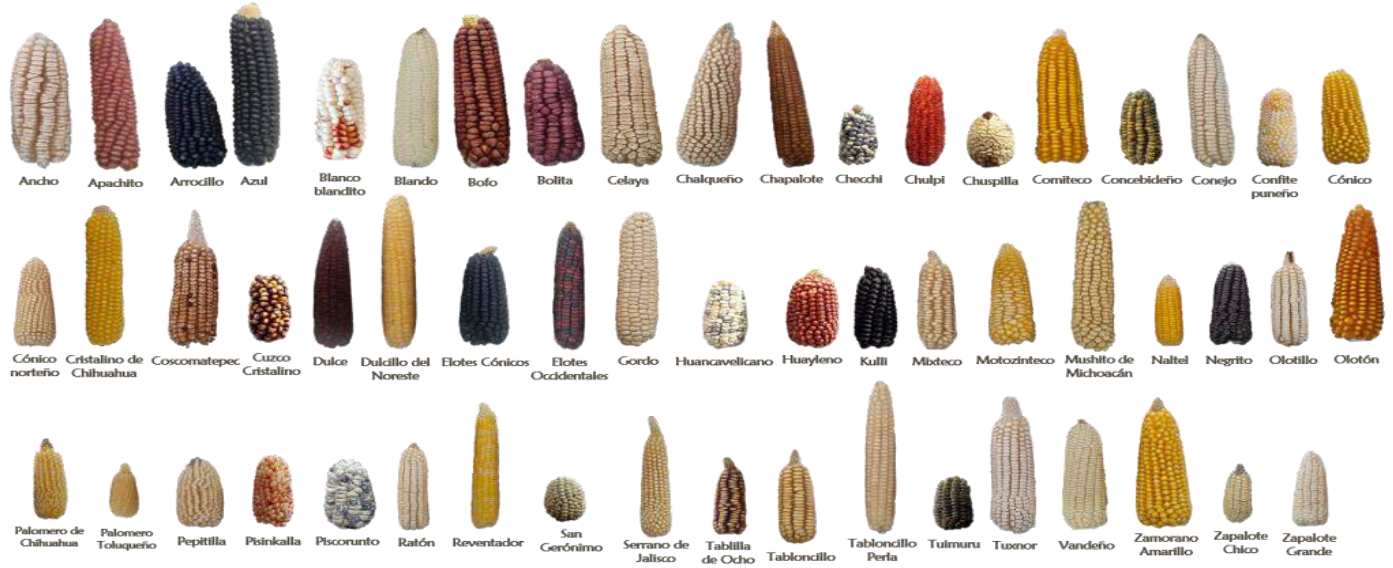
CIMMYT's germplasm bank, also known as a seed bank, is at the center of CIMMYT's crop-breeding research.

cimmyt.org

> Green Revolution technologies are scale-neutral but not resource-neutral ~ **M. S. Swaminathan.**

Maize is the most widely cultivated crop in the world. It is

believed to have originated in Mexico, which is home to a rich diversity of varieties that has evolved over thousands of years of domestication. According to CIMMYT, “These collections represent and safeguard the genetic diversity of unique native varieties and wild relatives and are held in long-term storage. The collections are studied by CIMMYT and used as a source of diversity to breed for traits such as heat and drought tolerance and resistance. CIMMYT’s germplasm is freely shared with scientists and research and development institutions to support maize evolution and ensure food security worldwide”.



Examples of some of the 59 native Mexican maize landraces. Photo courtesy of CIMMYT Maize Germplasm B

Field visits

(Credit: CIMMYT.com) After acquainting myself with various activities undertaken by CIMMYT, I spent the next two days visiting the fields. Coming from India, I was familiar with paddy, maize and wheat fields owned by small and large farmers. But never have I witnessed such large extents of wheat and maize fields before.

My guide explained to me the Plant breeding techniques employed. Looking back, I realize that during these three days at the Center, I learned more about genetics and plant breeding than I ever learned in my master’s classes.

> There doesn't seem to be any other way of creating the next green revolution without GMOs. ~ **E. O. Wilson**

Junagad and his Mexican girlfriend Conchita took me on a tour or of the

local tourist attractions. Conchita even got the closed church at Chapingo open late in the evening, so that I could see the world- famous wall paintings of Diego Rivera! We had dinner at one of the local Mexican restaurants, which was a jail once upon a time. I tasted Tortillas and the sauce made of hot chillies. They reminded me of our food back at home. After spending three days at CIMMYT I returned to Mexico City.

New varieties

According to CIMMYT, its centers do not release any "variety". Partners (public /private) release CIMMYT/CGIAR products (hybrids or improved OPVs) as "Varieties", following national rules and regulations. CIMMYT/CGIAR responsibility is to develop improved germplasm (inbred lines, hybrids, improved OPVs) and deploy these through partners (public/private).

CIMMYT is the largest contributor of improved maize germplasm annually as international public goods. *Over 54% of publicly bred maize varieties released in the developing world are reported to have CIMMYT's elite maize germplasm*. *CIMMYT scientists have developed 70% of wheat varieties presently planted globally and about half of the world's corn, or maize, varieties.* By CIMMYT's own accounts, the pedigrees of about half of the maize and wheat varieties sown in low- and middle-income countries carry contributions from its breeding research.

Recently, I read with interest some of the recent achievements of CIMMYT**.**

Maize is a crop grown on over 38 million hectares in sub-Saharan Africa, accounting for 40% of cereal production in the region and providing at least 30% of the population's total calorie intake. A ten-year partnership led by CIMMYT and International Institute of Tropical Agriculture **(**IITA) tackles climate-induced risks in maize production, developing and deploying new climate-adaptive varieties benefiting over 8 million households in sub-Saharan Africa.

Ten new CIMMYT-developed maize varieties released in Pakistan in 2020

New Technologies

Back at home I often wondered whether CIMMYT has adopted genomics and gene editing tools for crop improvement. I learnt from their newsletters that no current CIMMYT-derived maize or wheat variety sown by farmers is a product of genome editing. CIMMYT believes that 'Genome editing, like every tool, is selectively useful'; it will be used for developing new varieties with specific traits or characteristics for which the tool is suited.

CIMMYT would like to maintain the capacity to use both transgenic and genome editing techniques to help ensure that these options remain available to benefit

> For Mexicans, the "children of corn," maize is entwined in life, history and tradition. It is not just a crop; it is central to their identity -CIMMYT News Letter

smallholder, resource-poor farmers.

CIMMYT at 50- 2016 (cimmyt.org)

CIMMYT is trying to use of genome editing techniques to improve resistance to maize lethal necrosis (MLN), a disease that devastated maize crops in eastern Africa (Ethiopia, Kenya, Uganda, Rwanda, Tanzania, and DR Congo), while maintaining the productivity of elite varieties. It is also exploring how to improve resistance to other diseases that affect wheat and maize globally. Enhancing the nutritional value of wheat or maize is another area of its interest. However, I felt that the use of new genetic tools could be perhaps on a larger scale by it, of course, using them judiciously to solve specific problems, region-wise.

Safety CIMMYT is concerned about human and animal health or environmental safety. It does not support the work of institutions that do not show proper regard for those concerns and national biosafety regulations and procedures. The CIMMYT Biotechnology Research Oversight Committee, comprising senior management including the Director General, approves and oversees all research using genome editing technologies at CIMMYT.

Importance

The pack of buildings nestled by green wheat and maize fields often appear in my mind's eye. In this age of globalization, it is remarkable that CIMMYT continues to remain as an institution with public commitment.

My visit was very brief. However, from my visit to CIMMYT I learned that advancements in genetics ought not be confined to the laboratories alone, but need to be transferred to the field, wherein lies the action; the knowledge gained should not remain in the exclusive domain of the scientists, but need to be translated to the multitude of people who may benefit from it.

> Whether we or our politicians know it or not, Nature is party to all our deals and decisions, and she has more votes, a longer memory, and a sterner sense of justice than we do— **Wendell Berry**

FOOD & DIET: GENES & FOOD

In this section we discuss how gene/genome editing and synthetic biology are influencing food production in a big way. We also explore how the food we eat influence our genes.

1. **Gene Editing** In the Section on Economy (Gene Economy) of this issue of Life stream, we introduced gene/genome editing and showed how it is revolutionizing the treatment of cancer and other chronic diseases, as well as various genetic disorders. Today gene/genome editing is transforming the field of agriculture too.

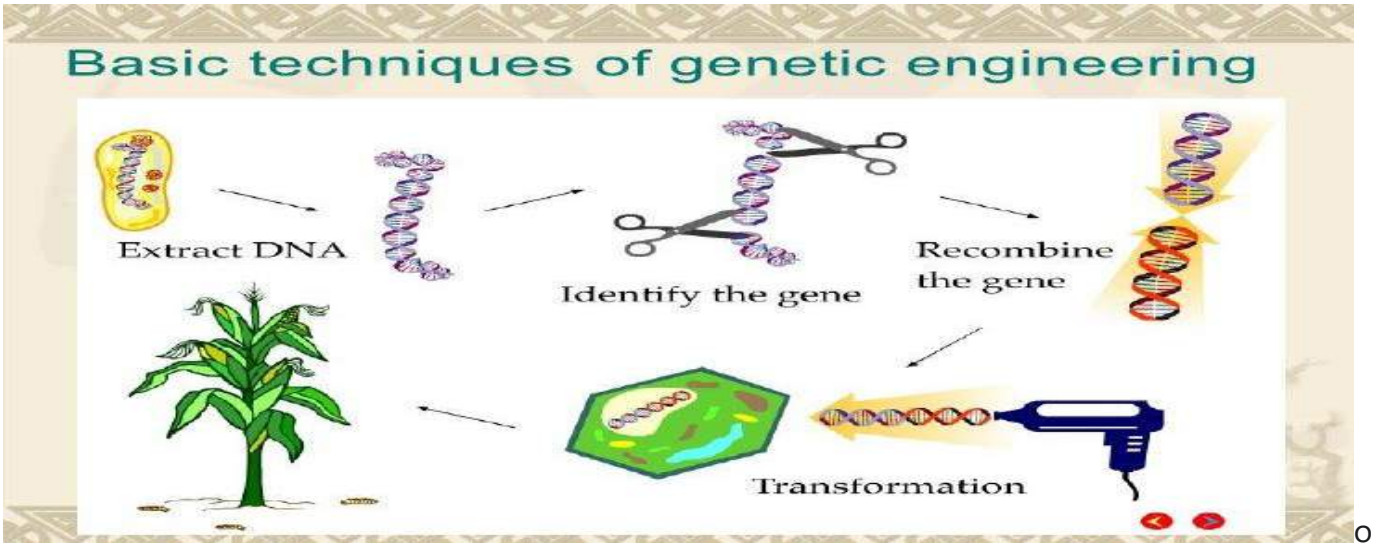
Evolution of farming techniques

Plant breeding For many years, farmers produced new varieties through traditional cross-breeding techniques. But this process can take a long time to get a desired offspring. Further, it is a matter of trial and error.

Genetic modification (GM), involves adding genes to a plant's DNA from a different species of plant - or even an animal.

Cis-genesis is like GM, but involves adding genes from the same or very closely-related species.

Gene-editing (GE), which is a much newer technique in which specific genes are targeted. As opposed to genetic engineering, which inserts a segment of DNA at random, the various genome editing methods identify *a specific genetic sequence at a specific location* in the organism's genome and modify the genome of an organism with precision and efficiency *Genetic editing removes the random element in conventional breeding.*

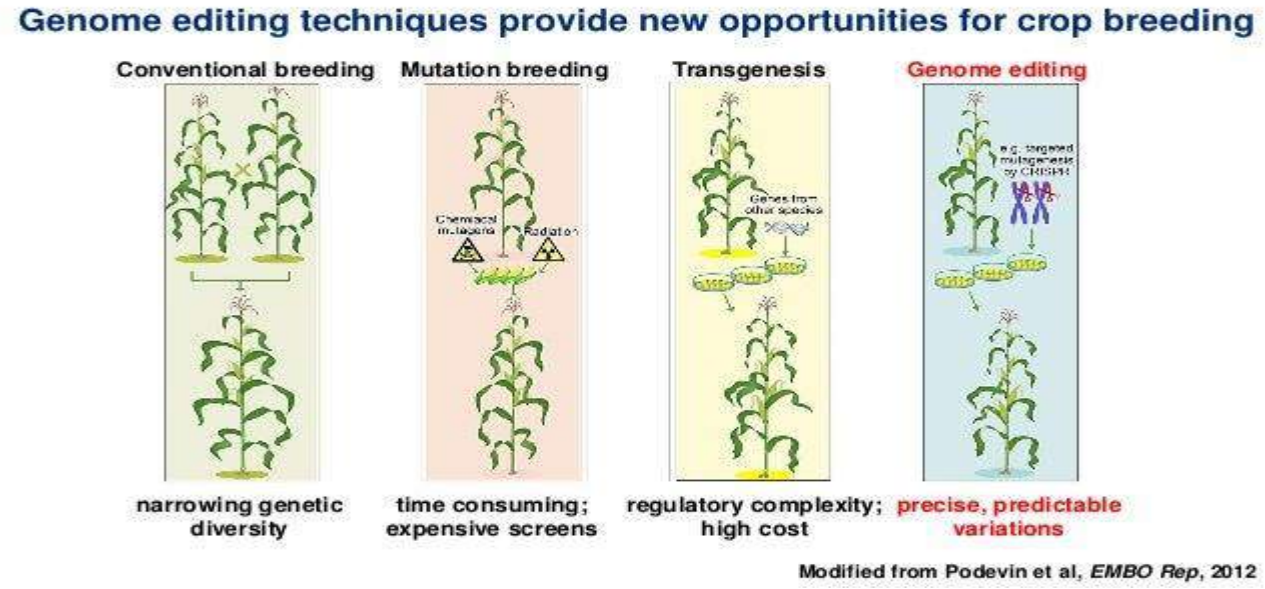


Genetic engineering (Credit: slideshare.net)

Genome editing offers the fundamental advantages of faster trait development, lower research and development costs, technical versatility, the development of novel traits, high precision. It apart from

> There is enormous power in this genetic tool (CRISPR), which affects us all. It has not only revolutionized basic science, but also resulted in innovative crops and will lead to ground-breaking new medical treatments," - **Claes Gustafsson**, chair of the Nobel Committee for Chemistry.

can greatly enhance productivity and broaden the scope of crop improvement, with high economic advantages.



(Credit: SlideShare)

Tools & techniques

- Most commonly used tools in GE include the **CRISPR-Cas system, TALENs, and Zinc finger nucleases.**
- **CRISPR-Cas system** is based on a simplified version of the bacterial CRISPR-Cas9 anti-viral defence system. By delivering the Cas9 nuclease complex with a synthetic guide RNA (gRNA) into a cell, the cell's genome can be cut at a desired location, allowing existing genes to be removed and/or new ones added in vivo.
- The newly-developed transcription activator-like effector nucleases **(TALENs**) comprise a nonspecific DNA-cleaving nuclease fused to a DNA-binding domain that can be easily engineered.
- Zinc finger nucleases **(ZFNs)** are artificial enzymes that can cut DNA at specific sequences.

GE-Products

Genome editing has revolutionized biotechnology. 140 genome-edited variants of 36 crops that improve yields and nutrition, control infections and pests, produce varieties that are resilient to climate change are reportedly on the way.

Genetically edited farm animals(bbcnews.com)

Gene edited corn usually has nutrients found in meat (Ref: Digital Trends)

Instead of producing new varieties of food, the food industry is mainly interested in the development of new varieties of existing crops and to introduce traits that improve yields. In Japan, one can already buy tomatoes rich in a neuro transmitter called GABA, with calming effect, and modified sea bream with more flesh, suitable for sushi. Seedless blackberries and stoneless cherries are being developed by a US firm. In the UK, tomatoes that contain vitamin D have been developed. Scientists in UK have also been experimenting with gene-edited wheat.

Are gene-edited foods safe? We have already dealt with safety concerns regarding GE, especially relating to the field of medicine. Safety concerns have been expressed about GE crops too. The pros and cons are listed below.

PROS &	CONS
• Scientists insist that the food produced through GE is safe to eat as all food is rigorously tested. • GM crops consumed by billions of consumers in North and South America and Asia for more than 25 years with no ill-effects. • No evidence that GM crops have harmed human health or damaged ecosystems; same to be true for GE crops. • Gene-edited produce is indistinguishable from natural varieties; face less opposition than GM food.	• No distinction between GE foods and those produced by the earlier GM technology. • Fear that GE foods will not require additional testing. • Adverse impact GE on the environment • Genome editing by countries with less stringent regulatory or ethical standards probably increases the risk of the creation of harmful biological agents or products.

The Guardian newspaper reported a recent unpublished polling by YouGov for the Department for Food and Rural Affairs (Defra) which is interesting

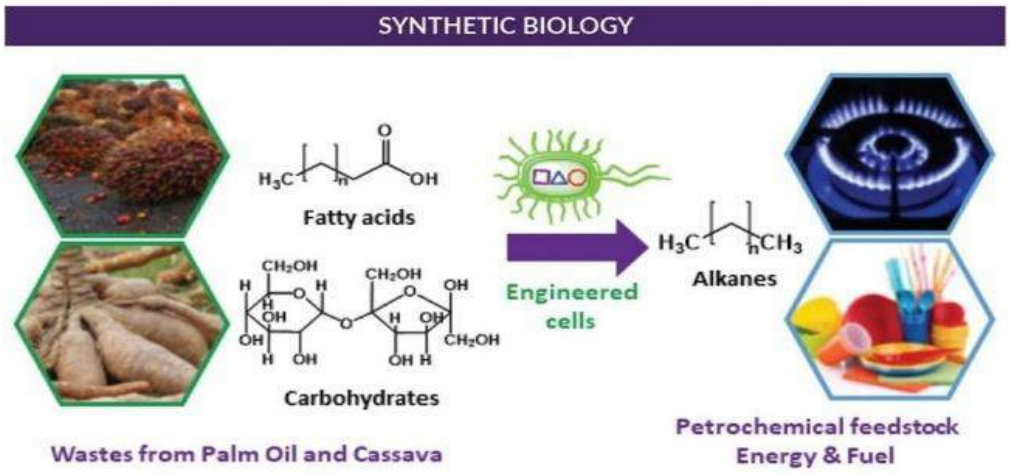
- 54% said GE crops were "acceptable"
- 28% said they were "unacceptable"
- The polling also found that 78% were in favour of some environmentally-beneficial applications of GE, such as the reduced use of pesticides and herbicides
- But ther technology might cause s

All the food we eat, whether Brussels sprouts or pork bellies, has been modified by mankind. Genetic engineering is only one particularly powerful way to do what we have been doing for eleven thousand years- **Michael Specter**

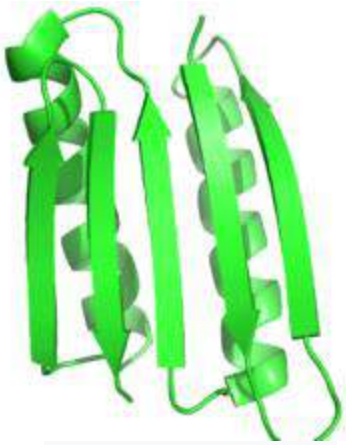
11. Synthetic Biology

In the Section Gene Economy in this issue of Life Stream we saw how Synthetic biology (in which the concepts in biology and engineering are combined) is transforming the world economy. It will also impact how we grow food and what we eat. Products from synthetic biology are rapidly entering the food markets and by 2030 "It is highly likely that you will have eaten, worn, used or been treated with one". The next decade will see more products that derive their superior performance and affordability from engineered biology.

How it works



(Credit: vistec.ac.th)



The Top7 protein was one of the first proteins designed for a fold that had never been seen before in nature. Ref: Wikipedia

Synthetic Biology Research at NASA Ames Research Center (Ref: Wikipedia)

Synthetic genomics, unlike genetic modification, *does not use naturally occurring genes in its life forms, but makes use of custom designed base pair series.*

Scientists are Th at sin celerating ing that now

> "I think the biggest innovations of the 21st century will be at the intersection of biology and technology. A new era is beginning." — **Steve Jobs**
>
> **Brand**

able to construct long base pair chains cheaply and accurately on a large scale. They perform experiments on genomes *that do not exist in nature*.

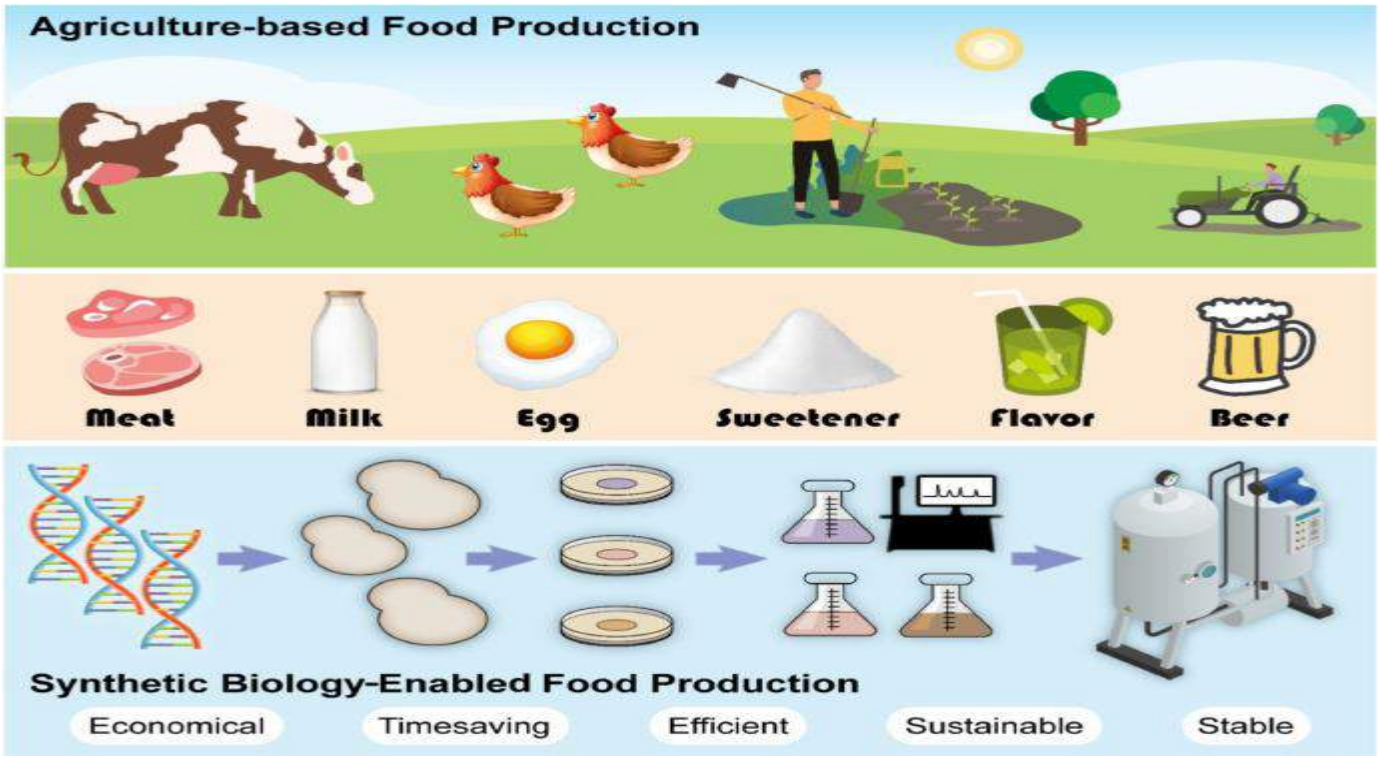
Examples

- The yeast *Pichia pastoris* was engineered to produce soy *leghemoglobin*, which improves meaty flavors and aromas when added to a plant-based burger
- Compared to a beef patty, the *Impossible Burger (brand name)* requires 96% less land and 89% fewer greenhouse gases. Worldwide, their products are available in over 30,000 restaurants and 15,000 grocery stores. It offers consumers a new generation of plant-based proteins that look, act, and taste far more like the real thing than ever before.
- The palate of food additives that are obtained from engineered yeast is growing rapidly, with products emerging that contain Vitamin E (DSM), Stevia (Amyris and DSM) and milk whey (Perfect Day).

Photograph: Mike Licht/flickr (theguardian.com)

Advantages

Synthetic biology can improve the traditional food production and manufacturing, food nutrition or add new features. Further, it can transform the traditional fermented food production.



Consumer response

The Guardian newspaper points out that 'the technology has rapidly outstripped consumer interest". According to a Pew Research Centre poll, only two out of 10 Americans are willing to give lab meat a go."

111. Genes & Food

While on the one hand scientists are employing new technologies for crop improvement and food production, on the other they are studying the influence of food on our genes.

In an earlier issue of Life Stream, we explored how various food items influence the functioning of our brains. Here, we consider the influence/impact of food items on our genomes.

The food-gene connection We usually think of food in terms of calories, energy and sustenance. However, the latest evidence suggests that food components affect the genome, and that in turn, may affect our health, physiology and longevity. The study of this process is called **Nutrigenomics**. It is a discipline still in its infancy.

An article in the website conversation.com explores the link between food and our genomes. It brings out the astonishing fact that food can drive biological processes by interacting with the genomes. A perfect example cited is that of the honey bee.

The Honey Bee Mystery

"Your genetics load the gun. Your lifestyle pulls the trigger." - **Mehmet Oz**

't -

(Ref: pinterest.com) A bee-hive is a proven example of how food reacts with genes. Worker bees labor hard, are sterile and live only a few weeks. 'The queen bee, sitting deep inside the hive, has a life span that lasts for years and a fecundity so potent she gives birth to an entire colony'. And yet, worker and queen bees are genetically identical. They acquire two different life forms because of the kind of food they eat.

The queen bee feasts on royal jelly; worker bees feed on nectar and pollen. Both foods provide energy, but royal jelly can unlock the genetic instructions to create the anatomy and physiology of a queen bee. How does this happen? Food is composed of carbohydrates or sugars, proteins, fat and micronutrients such as vitamins and minerals. When the jelly breaks down into these compounds and products, they can trigger genetic switches that reside in the genome (Ref: www.conversation.com)

'Depending on the type of nutritional information, the genetic controls activated and the cell that receives them, the messages in food can influence wellness, disease risk and even life span'.

Some interesting facts

- Traditional systems like Ayurveda, in India, recognized the connection between food and our body/mental make-up. Ayurveda identifies three body types based on a person's physical and mental make-up. Each body type is prescribed a separate set of food items, to keep the system in balance. Ayurveda also advocates that a pregnant woman should eat only certain type of food, not others.
- Modern medical researchers also say that a human mother's diet changes the levels of fatty acids as well as vitamins such as B-6, B-12 and folate that are found in her breast milk. This could alter the type of nutritional messages reaching the baby's own genetic switches. Whether or not this has an effect on the child's development is, not clear at the moment.
- In humans and mice, by-products of the amino acid methionine, which are abundant in meat and fish, are known to influence genetic dials that are important for cell growth and division.
- Vitamin C helps protect the genome from oxidative damage by affecting the function of cellular pathways that can repair the genome.

- Grass-fed cows and grain-fed cattle have different amounts and types of fatty acids and vitamins C and A . So, when we drink the two types of milk, different nutritional messages are received by the cells.
- The food we eat also affects the microorganisms living in our guts, skin and mucosa. For example, in mice, the breakdown of short-chain fatty acids by gut bacteria alters the levels of serotonin, a neurotransmitter that inter-alia regulates mood, anxiety and depression.
- Added ingredients in food can also alter the flow of genetic information inside cells. Breads and cereals enriched with folate, in the absence of other naturally occurring micronutrients such as vitamin B-12, could contribute to the higher incidence of colon cancer, possibly by affecting the genetic pathways that control growth.
- Chemicals found in food packaging like Bisphenol A, or BPA, turns on genetic dials in mammals that are critical to development, growth and fertility.
- Studies show that in humans and animals, the diet of grandparents influences the activity of genetic switches and the disease risk and mortality of grandchildren.
- The genetic information in food could arise also from the agricultural, environmental and economic policies of a country, or the lack of them.

The science of decoding the genetic food messages and their role in health and disease is still in infancy. Scientists are yet to find how nutrients act on genes, what the underlying principles are, and, how the diets of past generations influence their progeny. Many of these studies have so far been done only in animal models. However, there is no doubt that nutria-genomics is going to play a vital role in our lives. ----------

Ref: www.bbc.com Ref: Theophthalmologist.com; Geneticliteracyproject.org; acsess.onlinelibrary.wiley.com; www.researchgate.net; sciencedirect.com; theconversation.com

GENES & SPACE TRAVEL

Studying the effects of spaceflight on gene expression is indeed very challenging

Ever since astronauts started visiting outer space, scientists were concerned about genetic changes, due to exposure to a variety of factors in space. Therefore, NASA scientists have been exploring 'how gene expression changes in response to the environment inside the International Space Stations (ISS) and how each astronaut's unique DNA will determine their response to the space station environment'.

Epigenetic studies explore mechanisms through which environmental factors, like microgravity, high carbon dioxide levels and radiation alter the way DNA is read. According to NASA, 37 studies under way in the space station, of which three focus specifically on genetic research.

Twin Studies NASA carried out a study to assess how space travel can affect gene expression in different organs of the human body, using twins. Astronaut Scott Kelly was aboard the ISS from 2015 to 2016

> Food contains information that speaks to our genes not just calories for energy-**Dr. Markhyman**

continuously for 340 days, while his twin brother Mark stayed on Earth. NASA found that although Scott's basic genetic code was not altered," the environment of the space station affected the way in which this code was converted into tissue", especially, the important biological pathways relating to bone formation and the immune system.

Scott and Mark Kelly. NASA

Scott Kelly (left) and Mikhail Kornienko right) on board the ISS during their year in space. Credit: NASA

NASA categorized gene expression based on possible risk such as low, medium or high. Low-risk changes to gene expression (approximately 93 per cent of all the changes) became normal when Scott returned to Earth. Possible medium- to high-risk changes that lead to the immune system being on high alert did not reverse even after six months.

Research also showed that the rate of gene mutation during spaceflight could *never* produce a 7% change in the genome in a year. But the media the reports erroneously claimed that 7% of it changed. NASA then had to clarify that the 7% difference referred to "gene expression," rather than the entirety of the DNA.

The findings in the Kelly case need to be validated through other similar studies. Although the study of identical

twins provide the best evaluation effects of space on gene expression, it is difficult to find ideally suited twins for this purpose.

"Some of the most exciting things that we've seen from looking at gene expression in space is that we really see an explosion, like fireworks taking off, as soon as the human body gets into space" -**Chris Mason,** Principal investigator, Twins Study

2. Flight Engineer Christina Koch works on the Genes in Space-6 experiment 2. NASA astronaut Nick Hague works on the Genes In Space-6 experiment that is aimed at studying radiation damage to DNA.

Study of blood samples Scientists also conducted studies on how chemical differences in blood samples before flights affect genetic changes during space travel. Analysis of blood samples from seventy-two astronauts showed that each astronaut's genetic background plays a role in determining his/her epi-genetic response in the space station.

Mitochondrial studies

Mitochondria is the powerhouse of the cell. The first clue about the connection between mitochondria and spaceflight came from research using rodents in a comprehensive study by Afshin Beheshti and his colleagues published in the journal Cell recently.

The team compared the tissues from mice flown on separate space missions and noticed mitochondrial dysfunction. The study suggests mitochondrial stress leads to changes in gene regulation, metabolism, and the immune system in both mice and humans, after time spent in space. It may be the root cause of symptoms so diverse as bone problems, vision issues, muscle wasting and increased oxidative stress. NASA's data on humans backed this hypothesis up. The changes identified in astronaut Scott Kelly's immune system during his space flight may be explained by the changes observed in the activity of his mitochondria as well.

Why should humans adapt to live in space?

"It's a sense of duty. Humans have a unique duty that no other species have.

As far as we know, we're the only species that have this unique awareness of extinction.

It's only humans who can understand what it means for a species, or even for all of life, to go away. That means it's only us that can prevent it. Our track record on this is mixed as humanity goes. I think life is very precious and so I'd like it to last longer than just the lifespan of this planet or the Solar System"- **Professor Chris Mason** who is a space geneticist and author of **The Next 500 Years**, published by The MIT Press

The Japanese Space Exploration Agency also reported whole genome gene expression changes observed in a group of ten astronauts in 2016.

Impact of the studies The preliminary data suggests significant changes including alterations in genes associated with the response to oxygen and carbon dioxide levels, reduced ability to make energy and bone and an increased ability to fight infection and maintenance of DNA, most likely due to

"We were able to verify for the first time that CRISPR/Cas9 does successfully cut in space and establish this amazing gene editing tool in space for the first time" (ref: space.com)

astronauts being in an enclosed environment. The increased expression of DNA repair genes could be a result of increased levels of radiation in space that causes DNA damage and genome changes.

The gene expression changes in humans could be compared to gene expression changes in animals and on Earth-based analogues. Now, scientists have gathered the largest set of data about space biology to date based on astronauts including the Kelly twins, mice and insects that have flown on the space station.

The 30 studies, authored by more than 200 researchers from around the world, represent the largest body of information on the risks of space flight to the human body. The studies identify six molecular changes that may have an impact on the astronaut's health, including DNA damage, oxidative stress, alterations of the length of telomeres, shifts in micro-biomes, mitochondrial dysfunction and gene regulation.

According to NASA, the changes on a cellular and molecular levels may impact the astronaut's health during and after the missions on cardio-vascular, central nervous, Musculo-skeletal, immune and gastro-intestinal systems as well as causing disruptions to circadian rhythms and changes in vision.

Making space flights safer

If astronauts are to go all the way to Mars, they will suffer even higher doses of radiation and an even higher numbers of changes in the genome. Scientists are looking into possibilities of using genetic engineering to enable a person to better survive in space or on another planet. There are multiple possible approaches being explored.

The use of gene-editing technology in space

- For the first time, astronauts onboard the ISS used CRISPR-Cas9 technology to edit DNA in space.
- The student-led experiment, awarded through the Genes in Space competition, used CRISPR-Cas9 gene editing technology to create targeted breaks in the yeast genome that imitate damage to DNA caused by radiation.
- It may help us understand DNA repair mechanisms and to improve the current methods to protect astronauts against cosmic radiation during space travel **(Ref: ISS National Laboratory)**

Benefits

Genetic and epigenetic studies in astronauts promise to provide astronauts with personalized medical interventions, while in space. Those of us on Earth could also benefit from potential therapies. The ongoing animal studies could lead to identification of drugs that counteract harmful effects of gene expression. Hopefully, these will work not just in animals, but also in astronauts.

Ref: theconversation.com; www.space.com;www.britannica.com; www.genesinspace.org; www.cnn.com

The ability to sequence the DNA of living organisms in space opens a whole new world of scientific and medical possibilities-**NASA**

LIFE STREAM

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LIFE SCIENCE FOUNDATION

Service in Trusteeship

ABOUT US

The Life Science Foundation is a Not- for- Profit Public Charitable Trust registered on 30th December, 2009. It is a unique initiative by two officers belonging to the Indian Administrative Service (Bihar cadre) namely S. Jalaja and A.N.P. Sinha (IAS-1974) who have retired as Secretaries to Government of India. Their long experience with Governments at the National and State levels have instilled in them the will to continue to serve people, although from a different platform. Service through the medium of a public charitable Trust is in keeping with the Gandhi's ideal of Trusteeship.

OUR VISION

The term Life science encompasses all aspects of life from Right to life- an inalienable right of every human being- to the interconnectedness of the entire web of life. Our vision, therefore, is to promote holistic understanding of life and its purpose, and improvement of quality of life of all.

OUR MISSION

Our mission is to improve quality of life through policy formulation, applied research and real-life action. The Gandhian ideals of Sarvodaya and Trusteeship will be the guiding spirit.

OUR AIMS AND OBJECTIVES

To accomplish the above vision and mission, the Foundation will initially have the following aims and objectives. In course of time, more could be included:

1. To promote strategic thinking and suggest policy interventions on holistic and sustainable development.

2. To promote holistic health care system based on simple living, preventive healthcare, and both modern and traditional health systems.

3. To undertake studies, research and action-oriented projects pertaining to holistic life

4. To undertake pilot projects of good governance including e-governance and eventually support the governments in adopting and up scaling successful pilots.

5. To work towards promoting quality of life of vulnerable sections of population, including women and children.

6. To promote all- round human resource development.

7. To design self- sustaining livelihood projects which minimize subsidies and donor dependency