



**Deccan Education Society's
Fergusson College (Autonomous), Pune**

Department of Biotechnology



Biographia

Volume II: Molecular Mosaic



"The more we know, the more we realise there is to know"
-Jennifer Doudna

March 2024 Issue

In this issue of Biographia...

Welcome to the latest edition of our science magazine, where we dive into the fascinating realm of molecular biology, a field that unravels the mysteries of life at its most fundamental level. Within the pages of this issue, we embark on a captivating journey that correlates this fundamental field to other disciplines of life sciences like cellular and developmental biology, human physiology and analytical techniques.

Molecular biology is the basis of our understanding of life itself, diving deep into the genetic code, the machinery of cells, and the networks that precisely govern biological processes. It offers insights into the origins of life, the mechanisms of diseases, and the potential for groundbreaking technologies.

In these pages, you will encounter a rich tapestry of topics that showcase the diversity and complexity of molecular biology in a systemic approach. From the elegant simplicity of its rich history and discovery to the bewildering complexity of autoimmune diseases, from the tiny world of telomers and mRNAs to the vast landscape of genomics and gene editing, and a few puzzles to tease your brain, our magazine is a celebration of the marvels of molecular biology.

As we go into the latest advances and discoveries in molecular biology, we invite you to join us on this journey of exploration and discovery. There is something within these pages to inspire, inform, and ignite your passion for Science and Biotechnology.

So, let us embark together on this voyage into the heart of molecular biology, where each new discovery brings us closer to understanding the intricate machinery of life itself.



-The Editors:

**Siddhesh Gavali, Yash Wankhede,
Arjun Suley, Yashvi Shah, Manasi
Mahajan & Mandar Tijare**

TIMELINE

MOLECULAR BIOLOGY



1665

Robert Hooke

Observe "cells" in cork using a microscope, laying the ground work for cell theory.

publishes "On the Origin of Species," laying the foundation for genetics.

1859

Charles Darwin



1866

Gregor Mendel

Discovers the basic principles of heredity through his work with pea plants, later known as Mendelian genetics.

Isolates "nuclein" from white blood cells, the first identification of nucleic acid.

1869

Friedrich Miescher



1910

Thomas Morgan

Experimental research with fruit fly (*Drosophila*) by which he established the chromosome theory of heredity.

Demonstrate the "transforming principle" in bacteria (*Pneumococcus*) suggesting DNA role in heredity.

1928

Frederick Griffith



1944

Oswald Avery, Colin MacLeod, and Maclyn McCarty

Identify DNA as the "transforming principle" or chemically suggest that DNA is genetic material.

Discovers Chargaff's rules, revealing specific base-pairing ratios in DNA, hinting at its structure.

1950

Erwin Chargaff



1952

Rosalind Franklin

Obtained X-ray diffraction images of DNA, providing crucial clues about its structure.

Publish the double helix model of DNA, revolutionizing our understanding of genetics.

1953

James Watson and Francis Crick



1958

Matthew Meselson and Franklin Stahl

Conduct the Meselson-Stahl experiment, verifying DNA semi-conservative replication.

Deciphers the first codon in the genetic code, opening the door to understanding protein synthesis (UCU for serine).

1961

Marshall Nirenberg



1972

Paul Berg

Recombination DNA technology emerges, enabling manipulation of genes for various purposes. Recombinant DNA's - splices SV40 and E coli.

Develops rapid DNA sequencing technology, facilitating large-scale genome sequencing.

1977

Frederick Sanger



1983

Kary Mullis

Invents the polymerase chain reaction (PCR), a technique for amplifying DNA segment.

The Human Genome Project is launched, aiming to sequence the entire human genome.

1990

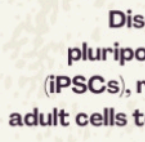
Francis Collins



1997

Ian Wilmut and Keith Campbell

Dolly the sheep become the first mammal cloned from an adult somatic cell.



2007

Shinya Yamanaka



2012

Jennifer Doudna and Emmanuelle Charpentier

The CRISPR-Cas9 system is developed, revolutionizing gene editing with its precision and efficiency.

mRNA technology contributes to COVID-19 mRNA vaccine development.

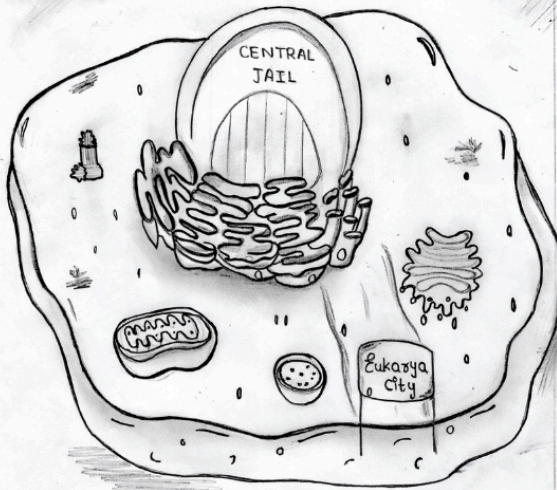
2021

Katalin Kariko and Drew Weissman's

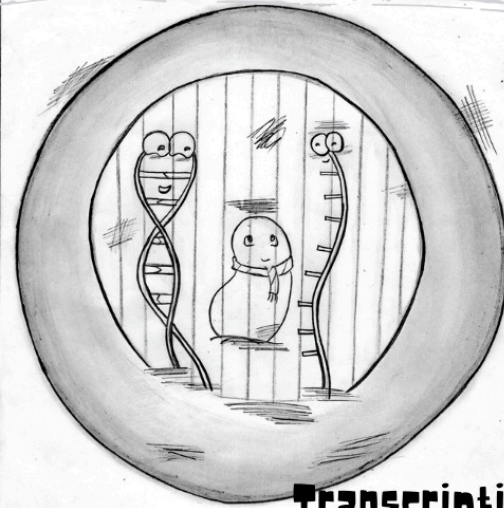


The Twisted Tale of mRNA Maturation

Once Upon a time, in a city called "Eukarya"; existed a jail called "Nucleus".

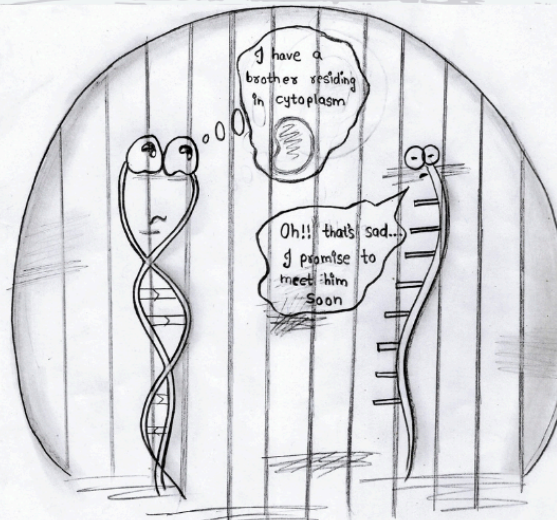


Three friends DNA, mRNA, RNA Polymerase were imprisoned.

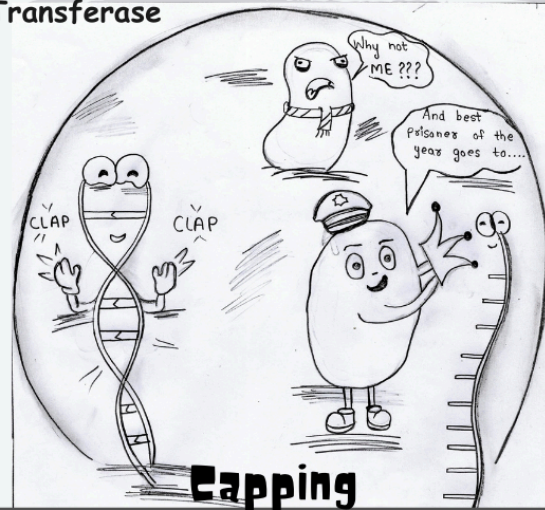


Transcription

DNA talks about his family (Ribosome) to mRNA

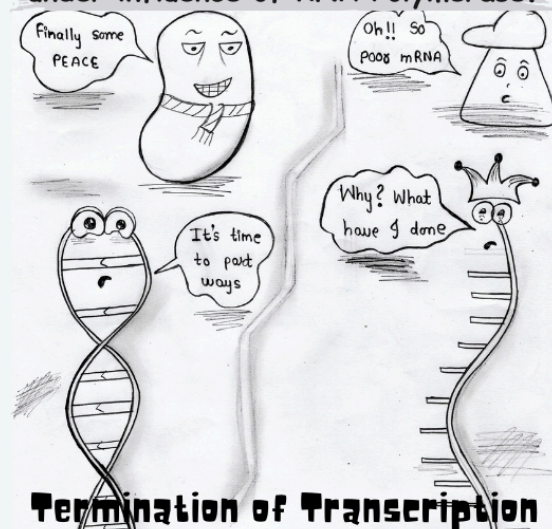


The "Best Prisoner of the Year" is awarded to the most diligent and disciplined mRNA molecule by Guanylyl Transferase



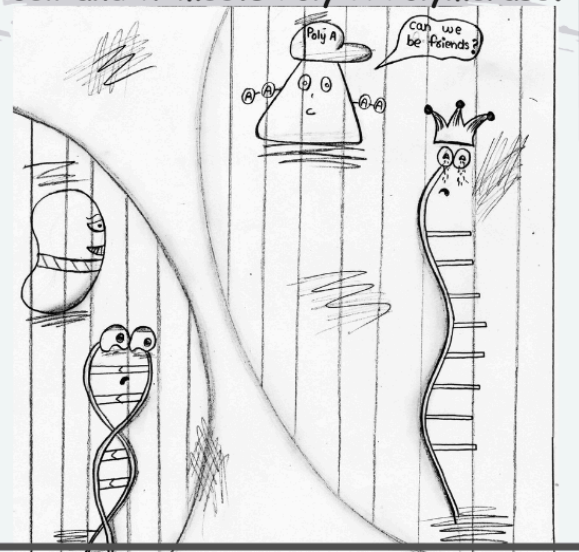
Capping

DNA and mRNA's friendship becomes sour due to the Termination factor under influence of RNA Polymerase.

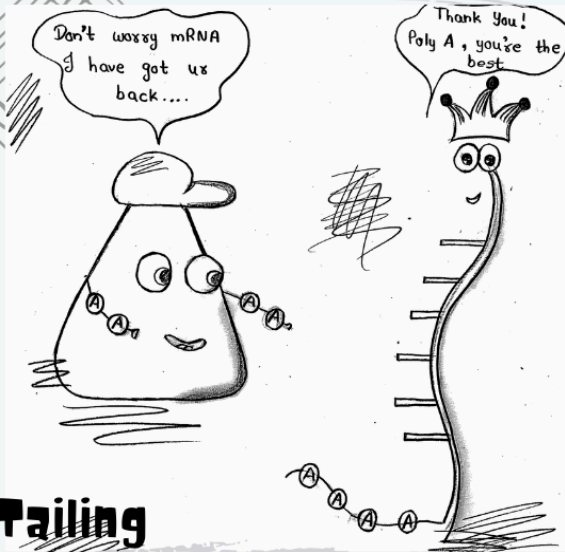


Termination of Transcription

The sad mRNA moves out to another cell and it meets Poly A Polymerase.

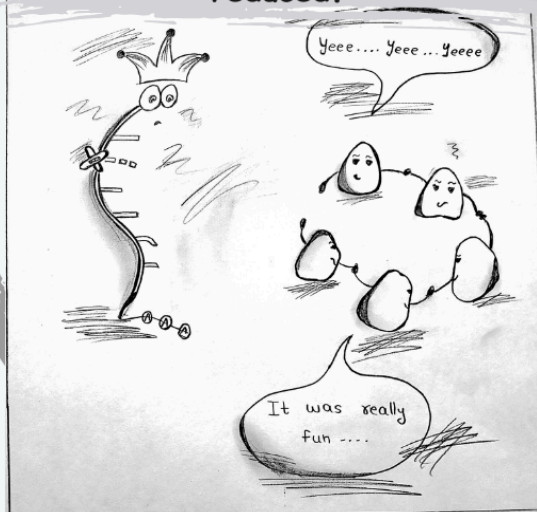


Poly A polymerase tries to befriend mRNA.

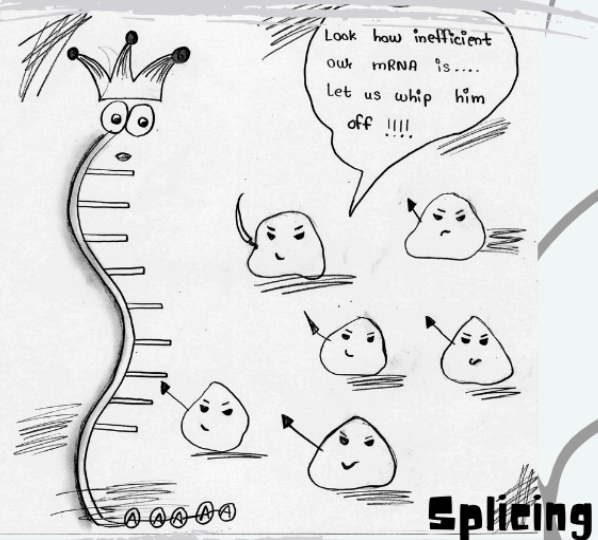


Tailing

The mRNA is now all bandaged due to the mocking and his size gets reduced.



Group of Bully torments mRNA.



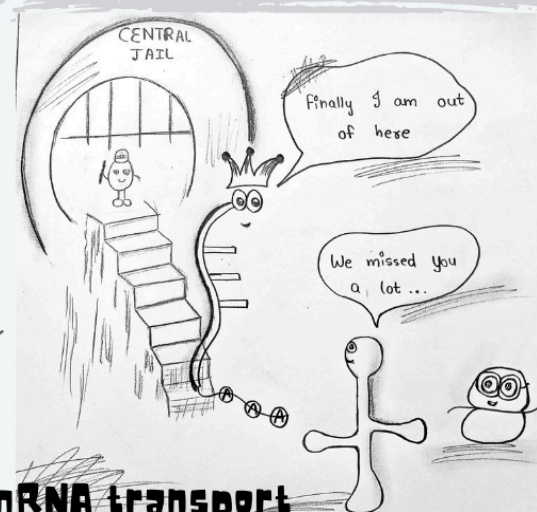
Splicing

As time passes, mRNA gets used to all the humiliation and becomes Stronger & Mature.



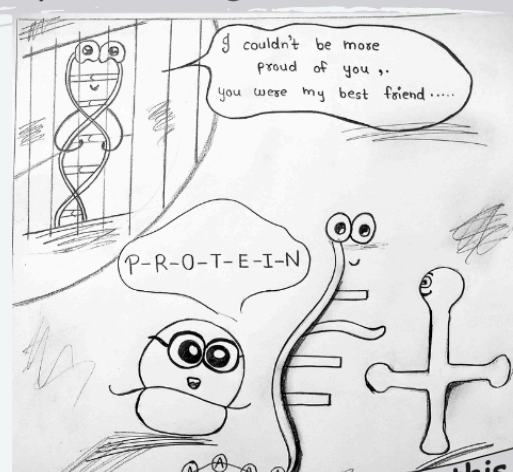
Matured mRNA

mRNA has served his sentence and gets released out of the jail as his period of punishment is over.



mRNA transport

mRNA meets his brother tRNA and Ribosome (DNAs Family) and writes up the message P-R-O-T-E-I-N.



Translation

And in this way the story continues...

UNVEILING THE DARK LEGACY

Horrific Experiments in the past: What carved the need for ethical experimentation

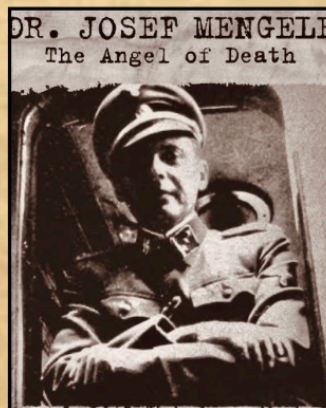
DURING WORLD WAR II, VARIOUS UNETHICAL EXPERIMENTS WERE CONDUCTED BY MILITARY FORCES, MOST NOTABLY BY NAZI GERMANY AND IMPERIAL JAPAN. SOME OF THE MOST NOTORIOUS EXAMPLES ARE HUMAN EXPERIMENTATION UNDER THE GUISE OF MEDICAL RESEARCH, DOCTORS AND SCIENTISTS CONDUCTED HORRIFYING EXPERIMENTS ON PRISONERS IN



CONCENTRATION CAMPS. THESE EXPERIMENTS INCLUDED FREEZING, HYPOTHERMIA STUDIES, STERILIZATION EXPERIMENTS, INFECTIOUS DISEASE RESEARCH, AND BRUTAL SURGICAL PROCEDURES WITHOUT ANESTHESIA. UNIT 731 WAS A COVERT BIOLOGICAL AND CHEMICAL WARFARE RESEARCH AND DEVELOPMENT UNIT OF THE IMPERIAL JAPANESE ARMY.

THE DARKEST CHAPTERS IN THE HISTORY OF MILITARY SCIENCE

N AZI HUMAN EXPERIMENT WAS A SERIES OF MEDICAL EXPERIMENT ON LARGE NUMBERS OF PRISONERS, INCLUDING CHILDREN, BY NAZI GERMANY IN ITS CONCENTRATION CAMPS HEADED BY JOSEF MENGELE IN THE EARLY TO MID 1940S, DURING WORLD WAR 2 AND THE HOLOCAUST. MANY EXPERIMENTS SUCH AS EXPERIMENTS ON TWINS, BONE MUSCLE AND NERVE TRANSPLANTATION, MALARIA EXPERIMENT, IMMUNISATION EXPERIMENT, EPIDEMIC JAUNDICE, MUSTARD GAS EXPERIMENT AND STERILIZATION AND FERTILITY EXPERIMENT. THE USE OF BACTERIAL INJECTION IN BONE MARROW WAS DONE. EXPERIMENT RESULTS IN DEATH, TRAUMA, DISFIGUREMENT, PERMANENT DISABILITY AND SUCH ARE CONSIDERED EXAMPLES OF MEDICAL TORTURE. AROUND 1200 TO 1500 PEOPLE WERE USED IN THESE EXPERIMENT AND MORE THAN HALF DIED AS A RESULT.



BIOETHICS FOR JUSTICE



BIOETHICS IS CRUCIAL BECAUSE IT PROVIDES A FRAMEWORK FOR ADDRESSING MORAL DILEMMAS AND ETHICAL CONSIDERATIONS ARISING FROM ADVANCEMENTS IN BIOLOGY, MEDICINE, AND TECHNOLOGY. ACTS AND LAWS PLAY A CRUCIAL ROLE IN MAINTAINING BIOETHICS. SOME KEY ONES INCLUDE:

THE NUREMBERG CODE: ESTABLISHED IN RESPONSE TO THE NAZI MEDICAL EXPERIMENTS, IT LAYS DOWN PRINCIPLES FOR ETHICAL MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS, INCLUDING VOLUNTARY CONSENT AND MINIMIZING HARM.

THE DECLARATION ON BIOETHICS AND HUMAN RIGHTS: ADOPTED BY UNESCO, IT ADDRESSES ETHICAL ISSUES ARISING FROM ADVANCES IN BIOLOGY, MEDICINE, AND BIOTECHNOLOGY, EMPHASIZING RESPECT FOR HUMAN DIGNITY AND HUMAN RIGHTS.



U NIT 731 WAS A BIOLOGICAL & CHEMICAL WARFARE RESEARCH & DEVELOPMENT UNIT OF THE IMPERIAL JAPANESE ARMY THAT UNDERTOOK LETHAL LUMAN EXPERIMENTATION DURING THE 2ND SINO- JAPANESE WAR (1937-1945) WORLD WAR II. ISHII HAD PROPOSED THE CREATION OF A JAPANESE BIOLOGICAL & CHEMICAL RESEARCH UNIT IN 1930. TEST SUBJECTS WERE GATHERED FROM THE SURROUNDING POPULATION WERE SELECTED TO GIVE A WIDE CROSS SECTION OF POPULATION INCLUDING CRIMINALS AND POLITICAL PRISONERS. THOUSANDS OF MEN WOMEN AND INFANTS INTERNED AT PRISONERS OF WAR CAMPS WERE SUBJECTED TO VIVISECTION, OFTEN WITHOUT ANAESTHESIA AND USUALLY ENDING UP WITH THE DEATH OF VICTIMS. AN ATTACK ON CHANGDA IN 1941, REPORTEDLY LED TO APPROX. 10000 BIOLOGICAL CAUSALITIES AND 1700 DEATHS AMONG ILL- EQUIPPED JAPANESE TROOPS, WITH MOST CASES DUE TO CHOLERA. THE RESULTING CHOLERA, ANTHRAX AND ESTIMATED TO HAVE KILLED CHINESE CIVILIANS , AT LEAST 400000.

UNVEILING THE DARK LEGACY

Horrific Experiments in the past: What carved the need for ethical experimentation

DESIGNED BY THE SBS TIMES

UNIT 731

DETACHMENT 731, THE KAMO DETACHMENT, ISHII UNIT, ISHII DETACHMENT OR THE ISHII COMPANY, WAS A COVERT BIOLOGICAL AND CHEMICAL WARFARE RESEARCH AND DEVELOPMENT UNIT OF THE IMPERIAL JAPANESE ARMY THAT UNDERTOOK LETHAL HUMAN EXPERIMENTATION DURING THE SECOND SINO-JAPANESE WAR (1937-1945) OF WORLD WAR II.

FOUNDER

IN 1932, SURGEON GENERAL SHIRŌ ISHII CHIEF MEDICAL OFFICER OF THE JAPANESE ARMY WAS PLACED IN A COMMAND OF THE ARMY EPIDEMIC PREVENTION RESEARCH LABORATORY (AEPRL). ISHII HAD PROPOSED THE CREATION OF A JAPANESE BIOLOGICAL AND CHEMICAL RESEARCH UNIT IN 1930. IT WAS DIVIDED AT THE SAME TIME INTO THE "ISHII UNIT" AND "WAKAMATSU UNIT" WITH A BASE IN HSINKING. FROM AUGUST 1940, THE UNITS WERE KNOWN COLLECTIVELY AS THE "EPIDEMIC PREVENTION AND WATER PURIFICATION DEPARTMENT OF THE KWANTO" OR "UNIT 731".

HUMAN EXPERIMENTS

PRISONERS WERE INJECTED WITH DISEASES, DISGUISED AS VACCINATIONS, TO STUDY THEIR EFFECTS. PRISONERS WERE ALSO REPEATEDLY SUBJECT TO RAPE BY GUARDS.

THOUSANDS OF MEN, WOMEN, CHILDREN, AND INFANTS INTERNED AT PRISONER OF WAR CAMPS WERE SUBJECTED TO VIVISECTION, OFTEN WITHOUT ANESTHESIA AND USUALLY ENDING WITH THE DEATH OF THE VICTIM.

UNIT 731 WERE INVOLVED IN RESEARCH, DEVELOPMENT AND EXPERIMENTAL DEPLOYMENT OF EPIDEMIC-CREATING BIOWARFARE WEAPONS IN ASSAULTS AGAINST THE CHINESE POPULACE (BOTH CIVILIAN AND MILITARY) THROUGHOUT WORLD WAR II.

AT LEAST 12 LARGE-SCALE FIELD TRIALS OF BIOLOGICAL WEAPONS WERE PERFORMED, AND AT LEAST 11 CHINESE CITIES WERE ATTACKED WITH BIOLOGICAL AGENTS.

AN ATTACK ON CHANGDA IN 1941 REPORTEDLY LED TO APPROXIMATELY 10,000 BIOLOGICAL CASUALTIES AND 1700 DEATHS AMONG ILL-PREPARED JAPANESE TROOPS, WITH MOST CASES DUE TO CHOLERA.

DURING BIOLOGICAL BOMB EXPERIMENTS, RESEARCHERS DRESSED IN PROTECTIVE SUITS WOULD EXAMINE THE DYING VICTIMS.



Above: Vivisection being performed on a Chinese by a Japanese biological warfare doctor.

上圖：日本細菌戰醫學博士正在進行的一場活體解剖。



Above: A Chinese woman, raped and impregnated by a Unit 731 researcher, Koseki, is vivisected along with her fetus in the laboratory at Pingfang.

上圖：一個由七三一部隊的成員小島桂子強姦而懷孕的中國婦女，在該地戰中的胎兒一起被活活解剖。



UNVEILING THE DARK LEGACY

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DESIGNED BY THE SBS TIMES

THE NAZIS EXPERIMENTS

NAZI HUMAN EXPERIMENTATION WAS A SERIES OF MEDICAL EXPERIMENTS ON LARGE NUMBERS OF PRISONERS, INCLUDING CHILDREN, BY NAZI GERMANY IN ITS CONCENTRATION CAMPS IN THE EARLY TO MID 1940S, DURING WORLD WAR II AND THE HOLOCAUST. CHIEF TARGET POPULATIONS INCLUDED ROMANI, SINTI, ETHNIC POLES, SOVIET POWs, DISABLED GERMANS, AND JEWS FROM ACROSS EUROPE.

TYPICALLY, THE EXPERIMENTS RESULTED IN DEATH, TRAUMA, DISFIGUREMENT OR PERMANENT DISABILITY, AND AS SUCH ARE CONSIDERED EXAMPLES OF MEDICAL TORTURE. AFTER THE WAR, THESE CRIMES WERE TRIED AT WHAT BECAME KNOWN AS THE DOCTORS' TRIAL.



HUMAN EXPERIMENTS

BONE, MUSCLE, AND NERVE TRANSPLANTATION EXPERIMENTS: FROM ABOUT SEPTEMBER 1942 TO ABOUT DECEMBER 1943 EXPERIMENTS WERE CONDUCTED AT THE RAVENSBRÜCK CONCENTRATION CAMP, FOR THE BENEFIT OF THE GERMAN ARMED FORCES, TO STUDY BONE, MUSCLE, AND NERVE REGENERATION, AND BONE TRANSPLANTATION FROM ONE PERSON TO ANOTHER. SECTIONS OF BONES, MUSCLES, AND NERVES WERE REMOVED FROM THE SUBJECTS WITHOUT USE OF ANESTHESIA. AS A RESULT OF THESE OPERATIONS, MANY VICTIMS SUFFERED INTENSE AGONY, MUTILATION, AND PERMANENT DISABILITY.

PRISONERS WERE ALSO EXPERIMENTED ON BY HAVING THEIR BONE MARROW INJECTED WITH BACTERIA TO STUDY THE EFFECTIVENESS OF NEW DRUGS BEING DEVELOPED FOR USE IN THE BATTLE FIELDS.

EXPERIMENTS ON TWINS: EXPERIMENTS ON TWIN CHILDREN IN CONCENTRATION CAMPS WERE CREATED TO SHOW THE SIMILARITIES AND DIFFERENCES IN THE GENETICS OF TWINS, AS WELL AS TO SEE IF THE HUMAN BODY CAN BE UNNATURALLY MANIPULATED. THE CENTRAL LEADER OF THE EXPERIMENTS WAS JOSEF MENGELE, WHO FROM 1943 TO 1944 PERFORMED EXPERIMENTS ON NEARLY 1,500 SETS OF IMPRISONED TWINS AT AUSCHWITZ. ABOUT 200 PEOPLE SURVIVED THESE STUDIES. OFTEN TIMES, ONE TWIN WOULD BE FORCED TO UNDERGO EXPERIMENTATION, WHILE THE OTHER WAS KEPT AS A CONTROL. IF THE EXPERIMENTATION REACHED THE POINT OF DEATH.

THE SYMPHONY OF SCHIZOPHRENIA

SCI BUZZ >

A REAL-LIFE CASE: THE ROAMING PARANOIA

PATIENT PROFILE:

NAME: MR. X (A PSEUDONYM)

BACKGROUND: A GAINFULLY EMPLOYED YOUNG AFRICAN MALE ADULT WITH NO HISTORY OF SUBSTANCE ABUSE.

SYMPTOMS: ROAMING AROUND TOWN, MOVING FROM ONE BANK TO ANOTHER, EXHIBITING SIGNS OF PARANOIA

The Scenario: Imagine being Mr. X, your mind a kaleidoscope of fragmented thoughts. You're convinced that unseen forces conspire against you. The bank tellers? They're spies, whispering coded messages. The streets? A maze of hidden traps. Your footsteps echo like secrets, and the sun casts shadows that morph into menacing shapes.

Symptoms Unveiled:

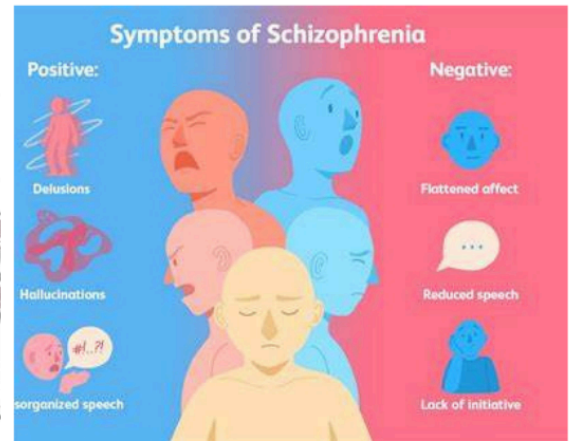
Hallucinations: You hear voices—sinister whispers that curl around your consciousness. They're not mere echoes; they're vivid, insistent. The bank manager's voice? It's a serpent, urging you to flee.

Delusions: The world is a puzzle, and you're the missing piece. The bank's security cameras? They track your every move. The ATM? A portal to another dimension.

Disorganized Thinking: Your thoughts ricochet, colliding like bumper cars. Sentences fragment, meanings blur. You're a poet of chaos, crafting verses only you can decipher.

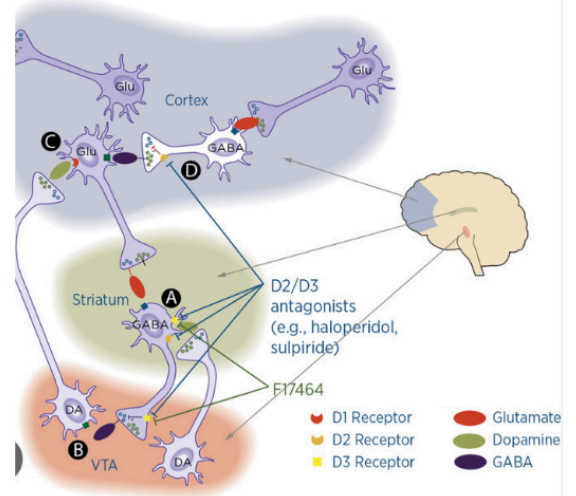
Emotional Turmoil: Fear clings to you like damp clothes. Paranoia gnaws at your sanity. You're a tightrope walker, balancing between dread and despair.

SYMPTOMS >



WHAT MOLECULAR PATHWAYS DRIVE THE VIVID HALLUCINATIONS AND PARANOID DELUSIONS EXPERIENCED BY MR. X?

DETAIL >



FiguDamine D2/D3 receptors targeted

MOLECULAR PATHOPHYSIOLOGY

Schizophrenia is a complex mental disorder with a multifaceted etiology involving both genetic and environmental factors. Schizophrenia is known to have a significant genetic component, with heritability estimates ranging from 60% to 80%. However, it is not caused by a single gene but rather by a combination of multiple genetic variations, each contributing a small amount to the overall risk. Many of the genes implicated in schizophrenia are involved in neurodevelopmental processes, including synaptic pruning, neuronal migration, and synaptic plasticity. Genes such as DISC1 (Disrupted in Schizophrenia 1), NRXN1 (Neurexin 1), and COMT (Catechol-O-methyltransferase) have been linked to schizophrenia and are involved in synaptic function and neurotransmission.

Defects at the genetic level cause dysregulation of receptor proteins and enzymes that interfere with neurotransmission and synaptic plasticity. Three major hypotheses involved in schizophrenia are:

1. Dopaminergic Pathway:

- **Role:** Dopamine, the brain's conductor, orchestrates pleasure, motivation, and cognition.
- **Dysregulation:** In schizophrenia, the mesolimbic pathway floods with dopamine, leading to amplified perceptions, heightened emotions, and auditory hallucinations.
- **Prefrontal Cortex:** Meanwhile, the prefrontal cortex suffers.
- **Its dopamine receptors (D1-D3) whimper,** impairing cognition and reality-checking.

SUCEPTIBLE GENES IN SCHIZOPHRENIA VISUALISED IN A MODEL SYNAPSE

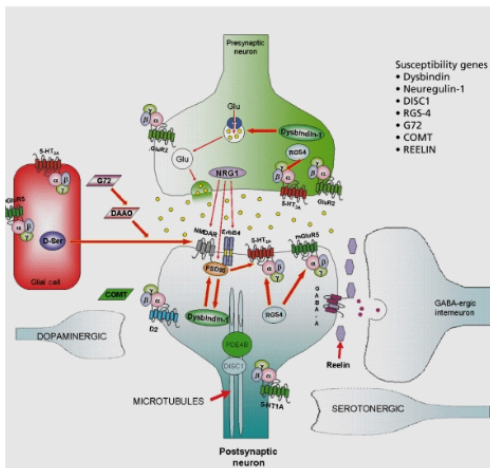
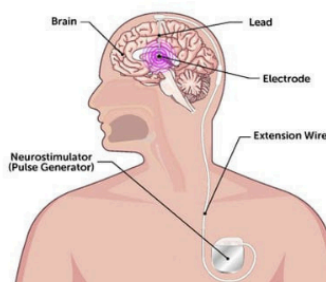


Figure:
Schizophrenia susceptibility genes are localized in overlapping neuronal pathways. Shown in diagrammatic form are the presumed localizations of various schizophrenia susceptibility gene products in a model synapse in the prefrontal cortex. As shown, a typical pyramidal neuron fiber receives inputs from dopaminergic, serotonergic, glutamatergic, and GABA-ergic neurons. The various susceptibility genes indicated may modulate pre- or postsynaptic glutamatergic functioning. Antipsychotic drugs mainly affect biogenic amine receptor activities which may be either pre- or postsynaptic in nature. GABA, γ -aminobutyric acid

#INDIA'S LEAP IN 'PSYCHOSURGERY': WHAT IS DEEP BRAIN STIMULATION (DBS), RECENTLY USED TO TREAT SCHIZOPHRENIA & DEPRESSION?

Deep Brain Stimulation (DBS)



India's first surgery for schizophrenia took place recently at Marengo hospital Gurugram. A 28-year-old African patient suffering from schizophrenia since age 13 was resistant to all drugs and cognitive therapies, DBS successfully helped him recover. Deep Brain Stimulation (DBS) is a neurosurgical procedure that involves implanting electrodes into specific areas of the brain to modulate neural activity. These electrodes are connected to a pulse generator device, which delivers electrical impulses to the targeted brain regions. By modulating neural circuits, DBS can alleviate symptoms and improve quality of life for patients who have not responded adequately to medication or other treatments.

2. Glutamatergic Pathway:

- Role: Glutamate, the brain's chatterbox, connects neurons like a thousand phone lines.
- NMDA Receptors: These receptors dance to glutamate's tune. In schizophrenia, some NMDA receptors falter, disrupting communication. It's like static on a radio channel.
- Hypofunction: Thoughts fragment, and the mind's orchestra loses harmony.

3. GABAergic Pathway:

- Role: GABA, the calming pianist, inhibits neural activity.
- Imbalance: In schizophrenia, GABA's rhythm falters. The symphony becomes discordant.
- Circuit Dysfunction: Neural circuits misfire, amplifying chaos.

Apart from the defects in neurotransmitter signaling, there are some other molecular abnormalities that can interfere with cognitive functioning in schizophrenia such as:

- Methyl Tags: They hush or amplify gene expression. Trauma, stress compose these notes.
- Shifted Brain Score: Epigenetics whispers in the DNA.

Oxidative Stress and Inflammation: Increasing evidence suggests that oxidative stress and neuroinflammation play a role in schizophrenia. Imbalance between reactive oxygen species (ROS) and antioxidant defenses, as well as dysregulation of inflammatory cytokines and microglial activation, may contribute to neurotoxicity and neuronal dysfunction in schizophrenia.

RECENT THERAPEUTIC INTERVENTIONS

THIRD GEN ANTIPSYCHOTIC DRUGS

Third-generation antipsychotics, such as Aripiprazole, Brexpiprazole, and Cariprazine, have a unique mechanism of action compared to first and second-generation antipsychotics.

These drugs are D2 receptor partial agonists, meaning they can both activate and antagonize dopamine D2 receptors depending on the extracellular dopamine concentration.

Aripiprazole, for example, acts as a dopamine stabilizer by inhibiting cAMP accumulation through the dopamine D2 receptor and competing with dopamine in high extracellular concentrations, resulting in partial antagonism and clinical benefits. Third-generation antipsychotics also interact with other G protein-coupled receptors (GPCRs) and can have agonist or antagonist effects on these receptors.

The precise molecular mechanisms of action of third-generation antipsychotics are still being studied, but their unique properties allow for a more nuanced modulation of dopamine signaling and potentially reduce side effects associated with D2 receptor antagonism.

These advancements aim to address the limitations of first and second-generation antipsychotics, such as limited efficacy for all symptoms, significant side effects, and lack of selectivity for specific dopamine pathways. Unlike gen 1 antipsychotics these cater to the negative and cognitive symptoms as well along with the positive symptoms which were the only ones targeted by gen 1 antipsychotics. Clinical use of Aripiprazole includes besides schizophrenia bipolar disorder, major depression, obsessive-compulsive disorder, and autism.

One of the distinguishing features of third-generation antipsychotics is their affinity for serotonin (5-HT) receptors, particularly the 5-HT_{2A} receptor subtype. By antagonizing 5-HT_{2A} receptors, these medications help to restore the balance between dopamine and serotonin neurotransmission in key brain regions implicated in schizophrenia pathology.

Growing evidence suggests that glutamatergic dysfunction plays a crucial role in schizophrenia, particularly in cognitive impairment. Some third-generation antipsychotics, such as aripiprazole, exhibit partial agonist activity at glutamate receptors, including the N-methyl-D-aspartate (NMDA) subtype. By modulating glutamatergic neurotransmission, these medications may improve cognitive function and alleviate negative symptoms associated with schizophrenia.



The Neuroquiz

CAN YOU GUESS THE NEUROLOGICAL DISORDER ?

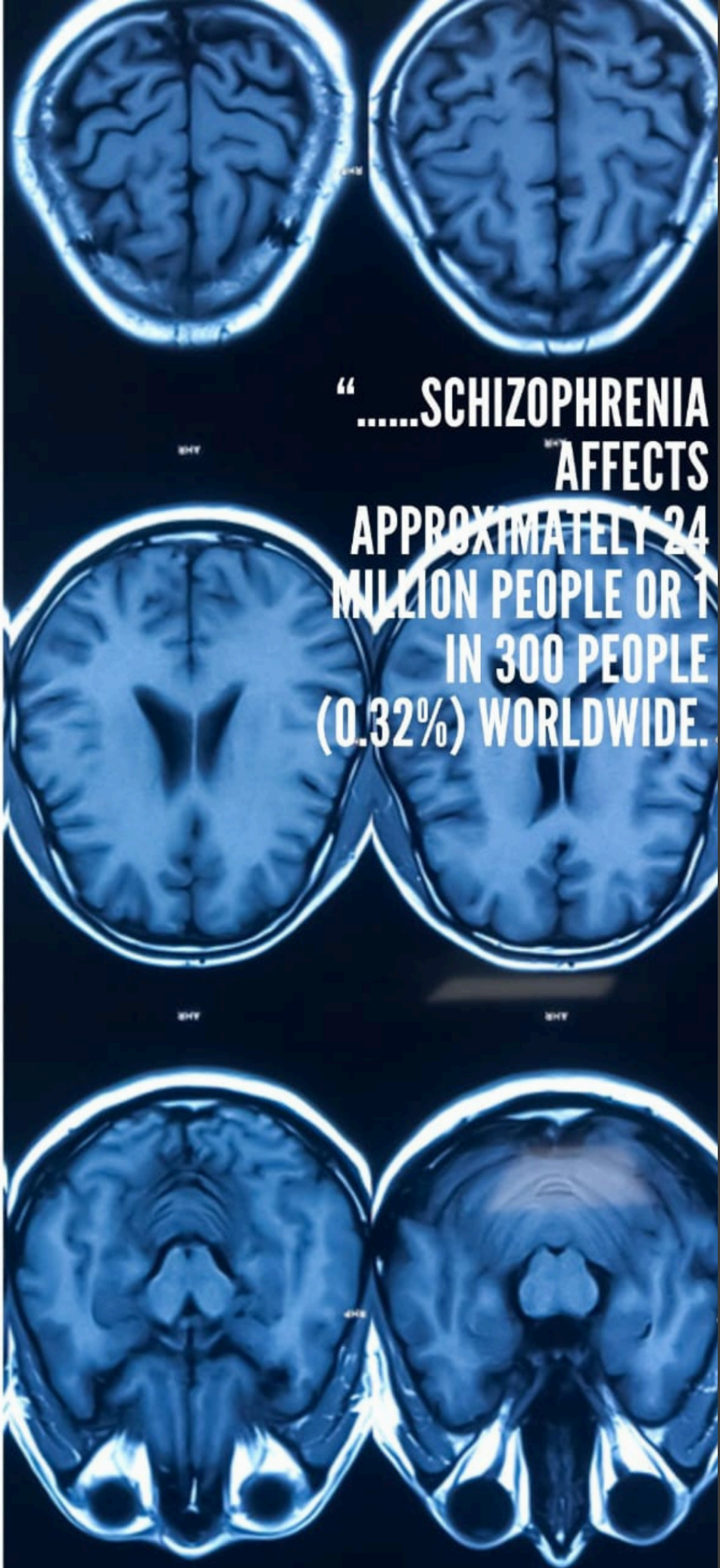
Use the details given in the question

1) Mr. A is a 65-year-old male who was referred to a neurologist for evaluation of his symptoms. He had been experiencing tremors, stiffness and difficulty with balance and coordination for the past two years. He also reported difficulty with fine motor tasks such as buttoning his shirt and writing. He had been diagnosed with hypertension and was taking medication for it, but had no other significant medical history.

- a) Parkinson's disease
- b) Alzheimer's' disease
- c) Huntington's disease
- d) Bell's palsy

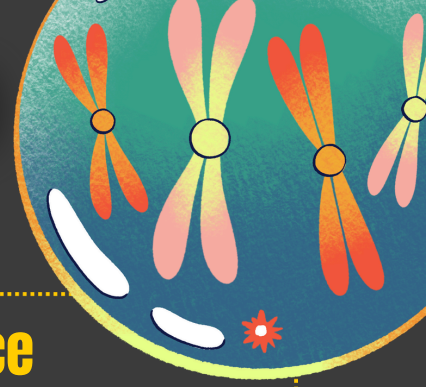
2) A 16-year-old female got admitted with the complaints of decreased sleep, irritable and excessively happy, irrelevant and increased speech, use of abusing words to her parents Her onset of symptoms is sudden with 6 months of duration. During assessment her vitals were stable, and she had a previous history of catatonia for which she received treatment. She was not under regular treatment and follow-up, and then she developed the symptoms of feeling sad, not interacting with her family members, and not able to maintain her activities of daily living (ADL).

- a) Bell's palsy
- b) Epilepsy
- c) Alzheimer's disease
- d) Bipolar disorder



“.....SCHIZOPHRENIA AFFECTS APPROXIMATELY 24 MILLION PEOPLE OR 1 IN 300 PEOPLE (0.32%) WORLDWIDE.

Telomere: Key to Ageing



Introduction and Significance

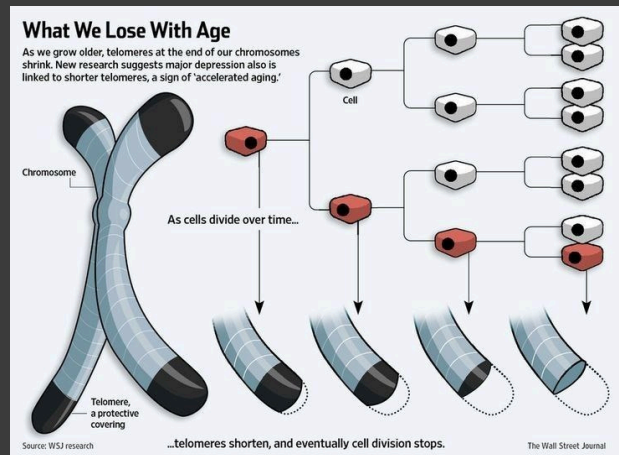
Telomeres are repetitive DNA sequences located at the ends of chromosomes that play a crucial role in maintaining genomic stability and cell viability. They protect the genetic material from degradation and fusion with neighboring chromosomes during cell division. Telomeres shorten with each cell division, eventually leading to cellular senescence and aging. Understanding the mechanisms underlying telomere maintenance and regulation is of great significance in the field of aging research, as telomere length has been linked to various age-related diseases, including cancer, cardiovascular disease, and neurodegenerative disorders.

Working and Principle

The enzyme telomerase is responsible for maintaining telomere length by adding repetitive DNA sequences to the ends of chromosomes. Telomerase activity is tightly regulated in normal cells, with somatic cells typically exhibiting low levels of telomerase expression. In contrast, cancer cells often upregulate telomerase activity to overcome cellular senescence and achieve immortality. The balance between telomere shortening and telomerase-mediated elongation is critical for cellular homeostasis and longevity.

A Dna damage response (DDR) is triggered when genomic DNA damage takes place. But this alone is not sufficient to initiate senescence. When irreparable DNA damage on telomere takes place an unceasing DDR is initiated. This activates a complex set of post- inflammatory cytokines, which mediate inflammation and fibrosis. All this compiled together is impactful in impairing stem cell function and alter differentiation thus contributing organismal ageing.

Human cells such as male germ cells, activated lymphocytes, and certain types of stem cell populations contain the enzyme telomerase, which helps in telomeric regeneration. TERT (telomerase reverse transcriptase) gene in it's active state, helps maintain the telomeric structures. Another RNA component, TERC, provides template for telomere formation. These together help in telomeric regeneration. If we can slow down the process of telomere shortening by developing vectors and gene therapies that can induce activation of the telomerase enzyme in normal somatic cells; this along with a better lifestyle just might be the key to slow down ageing.



Research

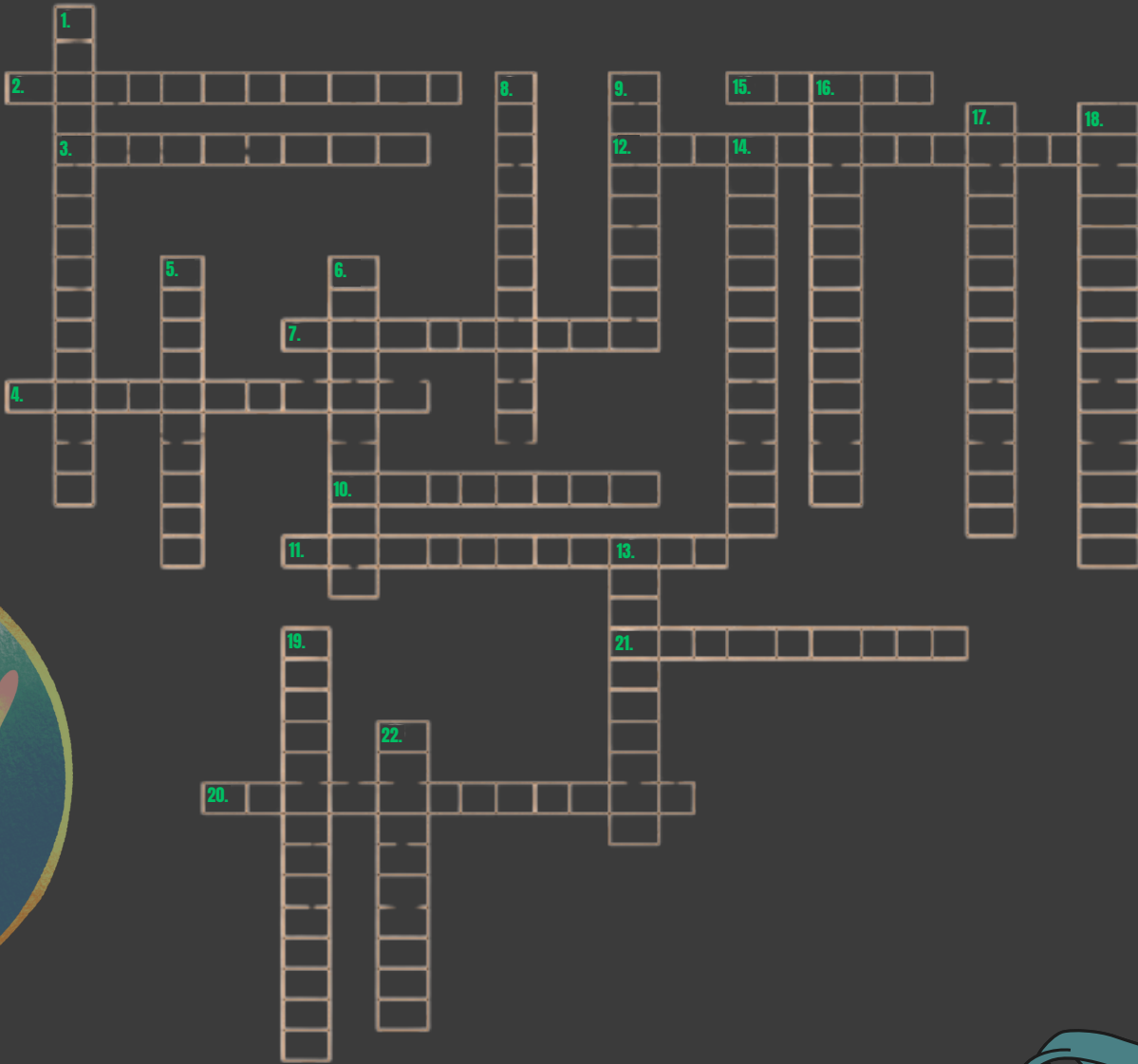
The very first use of telomerase gene therapy on humans is quite controversial. Development of Adeno-Associated virus (AAV) was going on which could express human TERT (telomerase reverse transcriptase). The CEO of a particular company self-experimented with this virus. Interestingly enough, the company published positive results of this self-experimentation. Luckily, more and more researchers are publishing good amounts of experimental results that talk about transfer of essential genes that are essential maintaining telomeric sections, providing hope that we might just be able to turn anti-aging into a reality.

Applications & Conclusion

The field of telomere biology has scope in wide range of applications in personalized medicine, regenerative therapy, and anti-aging interventions. Therapeutic approaches targeting telomeres and telomerase are being actively investigated in preclinical and clinical studies for their potential to combat age-related diseases and enhance longevity.

It's Game time!!!

Cellular Scrabble

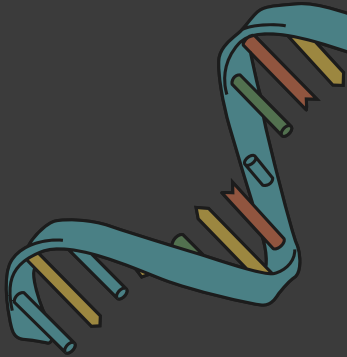
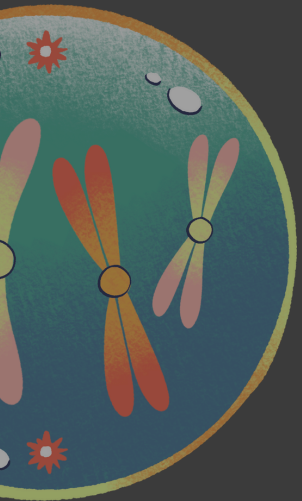


Across:

- 2). Primary physical shape of double-stranded DNA molecules
- 3). What's the study of the origin and history of words, including how words have evolved over time and across languages?
- 4). The sum of all chemical reactions that occur in an organism
- 7). An array of all the Chromosomes found in an organism
- 10). Molecule catalyzes the formation of peptide bonds during translation?
- 11). It is a synonym for "translator" that starts with an "I"?
- 12). States that DNA from and cell all organisms should have 1:1 ratio of Pyrimidine and purine bases
- 15). What is the three-letter abbreviation for a unit of genetic code that specifies an amino acid?
- 20). The process of transporting a substance or cellular entity to a specific location within or on the membrane of a cell.
- 21). What is the term for sequence of nucleotides on mRNA that is complementary to a codon?

Down

- 1). The process of making proteins.
- 5). Major metabolic mechanism.
- 6). Which Molecule responsible for carrying amino acids to the ribosome during protein synthesis.
- 8). The process by which the information in a strand of DNA is copied into a new molecule of messenger RNA.
- 9). Often masked in genes.
- 13). What is the term for a person who translates written language?
- 14). Enzyme is responsible for transcribing DNA into RNA.
- 16). To copy DNA
- 17). DNA sequence where RNA polymerase binds to initiate transcription.
- 18). Only shows if there are two of them.
- 19). Type of mutation.
- 22). Unwinders..





Healthline

<https://www.healthline.com/health/diabetes-and-wound-healing>



National Institutes of Health (NIH) (.gov)

<https://www.nih.gov/news-events/nih-research-matters>

Poor immune response impairs diabetic wound healing

Diabetes and Wound Healing: Why Is It Slower?



Geisinger Health System

<https://www.geisinger.org/2017/11/08/3-reasons-diabetic-wounds-are-slow-to-heal>

3 Reasons Diabetic Wounds are Slow to Heal



West Coast Wound & Skin Care

<https://westcoastwound.com/why-does-diabetes-impair-wound-healing/>

Why Does Diabetes Impair Wound Healing?

miRNAs dysregulation in wound repair

Chronic skin wounds and scars result from aberrant wound healing processes such as deficient restoration of the epidermal barrier, vascular insufficiency, diabetes mellitus, and local-pressure effects, with underlying mechanisms indicating long term inflammation, impaired keratinocyte migration, and dysregulated microRNA expression.

miRNAs and their proposed role in impairing diabetic tissue repair

Besides significant alteration in the expression of inflammatory cytokines, such as Tumor Necrosis Factor (TNF)- α , Interleukin (IL)-6, IL-8 and growth factors that coordinate wound repair, it has been documented that

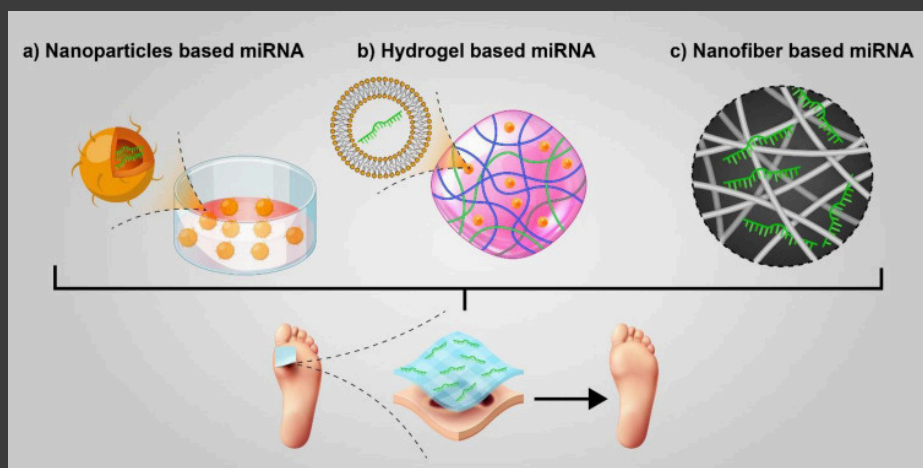
hyperglycemia changes the profile and action of microRNAs (miRNA).

In contrast to acute wounds that progress through the various phases of wound healing linearly in healthy individuals, diabetic wounds become stalled

Variations in the levels of circulating and tissue miRNAs show encouraging potential for diagnosing and treating chronic wounding

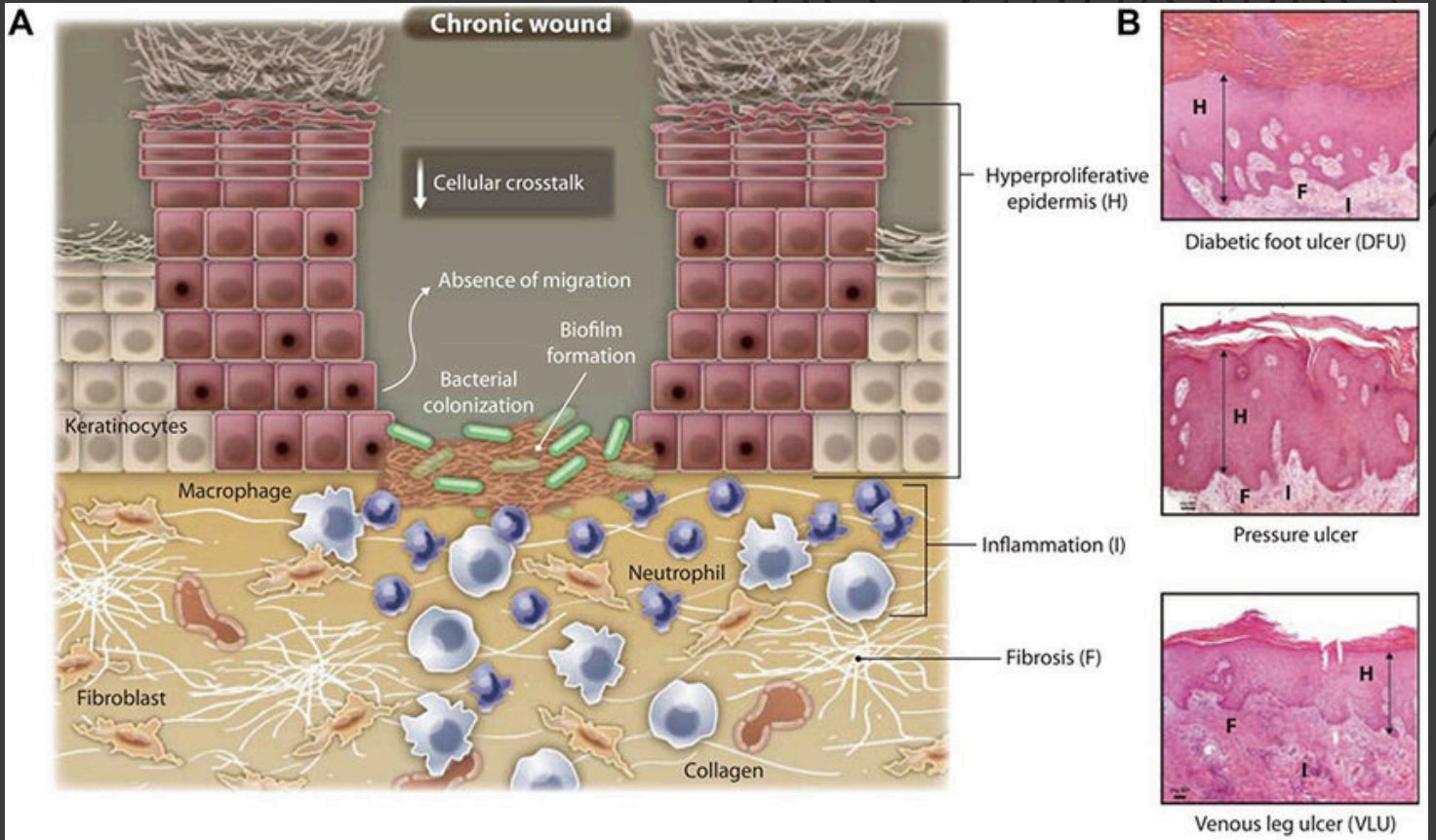
Among the myriad functions as controllers of gene expression, miRNAs have been shown to play a role in various skin conditions like prolonged inflammation or abnormal scar formation.

- miRNAs have been known to decrease pro-inflammatory responses
- Reduced levels of many miRNAs following injury in diabetic wounds might contribute to the atypical inflammatory reaction noted in such wounds.
- miRNA dysregulation also interferes with macrophage maturation
- miRNAs have also been involved in preventing wound re-epithelization in diabetic wounds
- miRNAs dysregulation downregulates the growth and differentiation of keratinocytes
- change in miRNA levels also prevents cell migration involved in wound healing



Representations of miRNAs conjugated with bioactive dressings, including nanoparticles (a), hydrogels (b), and nanofibers (c). Integration of miRNAs into bioactive materials can accelerate the healing of diabetic wounds

Molecular pathology of chronic wounds



Decoding Oncology: A Molecular Perspective on Diverse Gene Targets

In the intricate landscape of oncology, molecular biology plays a pivotal role in unraveling the complexities of cancer development and progression. Various gene targets have emerged as focal points for therapeutic interventions, each offering unique insights into the molecular basis of malignancies.

TP53 (Tumor Protein 53):

At the forefront stands TP53, a tumor suppressor gene orchestrating cellular integrity. Acting as the "guardian of the genome," TP53 regulates the cell cycle, DNA repair, and apoptosis. However, mutations in TP53 are prevalent in diverse cancers, disrupting its tumor-suppressive functions. These alterations not only drive uncontrolled cell growth but also confer resistance to conventional therapies, posing a significant challenge in cancer treatment.

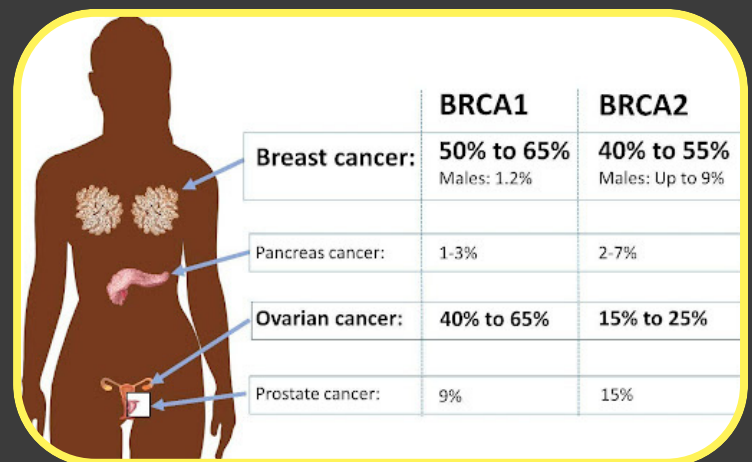
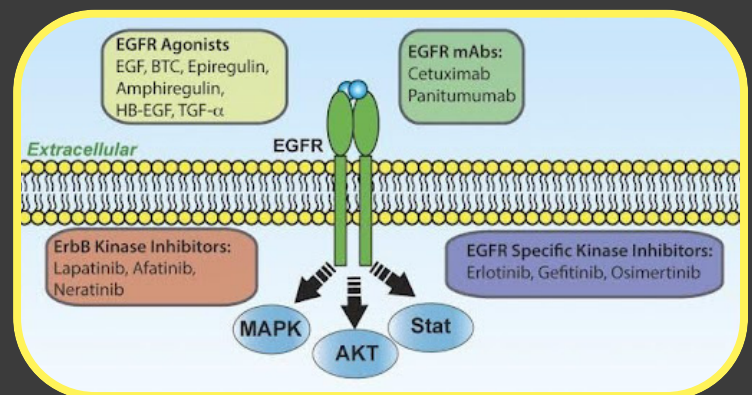
EGFR (Epidermal Growth Factor Receptor):

EGFR, a receptor tyrosine kinase, is pivotal for cellular growth and survival. Aberrations in EGFR signaling through mutations or overexpression, contribute to the pathogenesis of several cancers. Lung, breast, and colorectal cancers frequently harbor EGFR abnormalities, making it an attractive target for therapeutic intervention. Inhibitors such as gefitinib and erlotinib have demonstrated efficacy in subsets of patients with EGFR-driven malignancies.

BRCA1 and BRCA2:

The BRCA genes, essential for DNA repair mechanisms, have gained prominence due to

their association with hereditary breast and ovarian cancers. Mutations in BRCA1 and BRCA2 compromise the cell's ability to repair DNA damage, leading to genomic instability. Targeting these vulnerabilities with Poly (ADP-ribose) polymerase (PARP) inhibitors has emerged as a promising strategy, exploiting synthetic lethality in BRCA-mutant tumors.



HER2 :

HER2, a member of the epidermal growth factor receptor family, is implicated in breast and gastric cancers. Amplification or overexpression of HER2 drives aggressive tumor growth. Targeted therapies, exemplified by monoclonal antibodies like trastuzumab, have revolutionized the treatment landscape for HER2-positive cancers, illustrating the power of precision medicine.

KRAS:

KRAS mutations are recurrent in various cancers, particularly pancreatic and colorectal. Despite

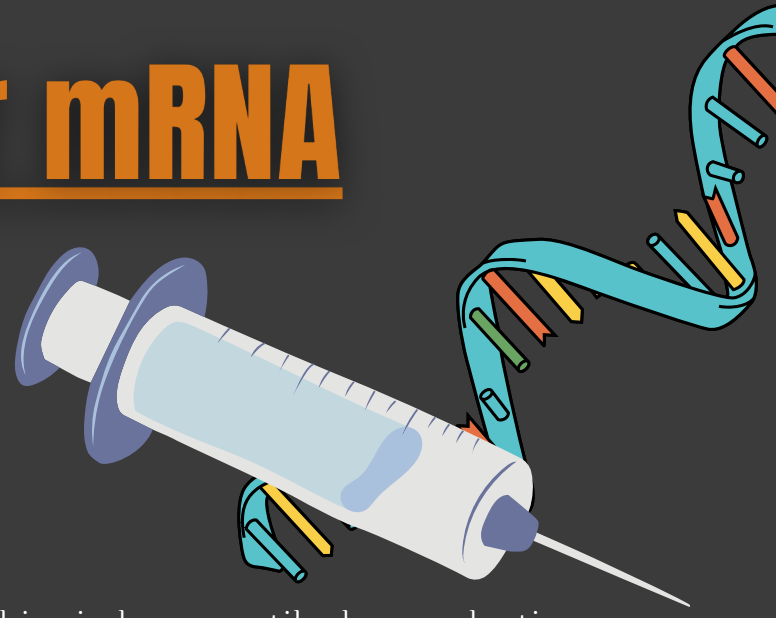
being historically challenging to target directly, recent advancements in drug development aim to inhibit mutated KRAS, holding promise for overcoming this long-standing therapeutic obstacle.

In conclusion, a molecular biology perspective on gene targets in oncology unravels the intricate mechanisms underpinning cancer. As our understanding deepens, the potential for developing targeted therapies tailored to specific genetic alterations brings us closer to a new era of precision medicine, where individualized treatments based on molecular profiles hold the key to more effective cancer management.

Nobel prize for mRNA

Vaccines

Katalin Karikó and Drew Weissman won the Nobel Prize in Physiology or Medicine for their work on mRNA-based vaccines. Their Modified discoveries on nucleotide bases enabled the rapid development of effective mRNA vaccines during one of the greatest public health emergencies in modern times as mRNA vaccine against COVID-19. This discovery fundamentally changed our understanding of how mRNA interacts with the immune system. Vaccines are potent tools against viruses, providing the immune system with targeted training. Early versions used weakened viruses, while modern ones leverage molecular biology to train the immune system using viral genome snippets.



This induces antibody production or an immune response, depending on the approach, researchers want to find a faster and more efficient way to produce mRNA for vaccines. So in the 1980s, they developed a cell culture-free system called in vitro transcription, which uses the body's natural ability to transform nucleic acids into proteins. However, there were some challenges with stability and limited protein production. Overall, it was a promising approach that needed some improvements.



Dr. Katalin Karikó and Dr. Drew Weissman

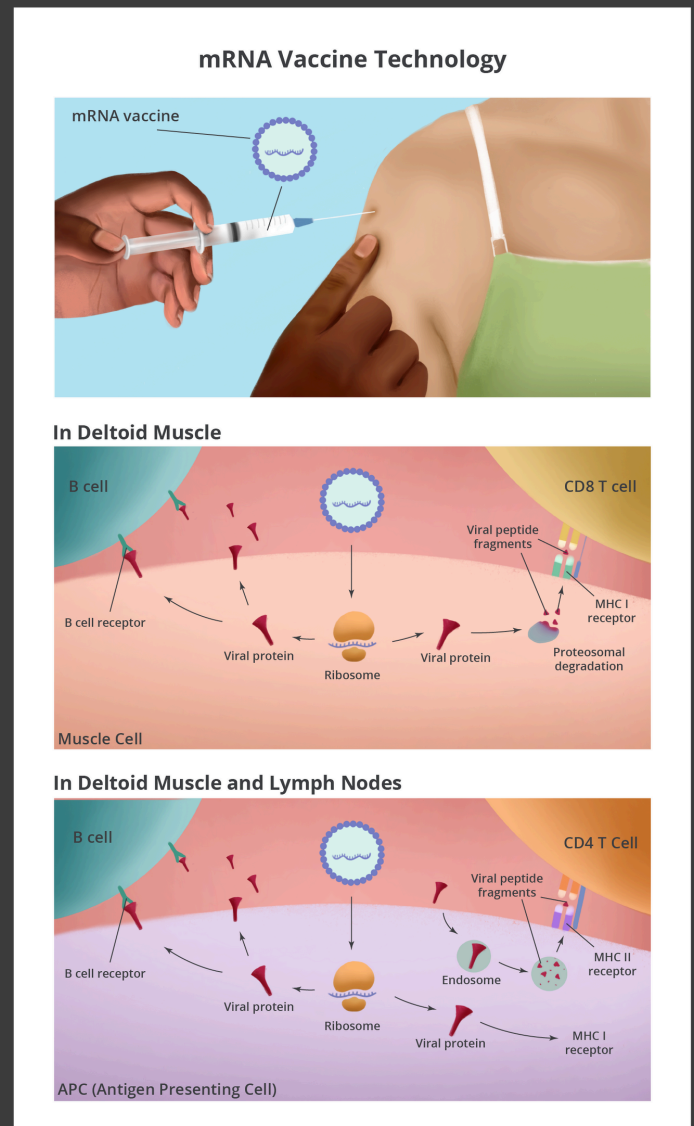
“THE PROMISE OF mRNA VACCINES”

Karikó and Weissman teamed up in 1997 at UPenn. They wanted to develop mRNA-based therapeutics and an HIV-1 vaccine. With Karikó's RNA biochemistry expertise and Weissman's immunology knowledge, they aimed to understand how mRNA interacts with the immune system. Their focus was on unravelling the molecular mechanisms behind the inflammatory response to in vitro transcribed mRNA.

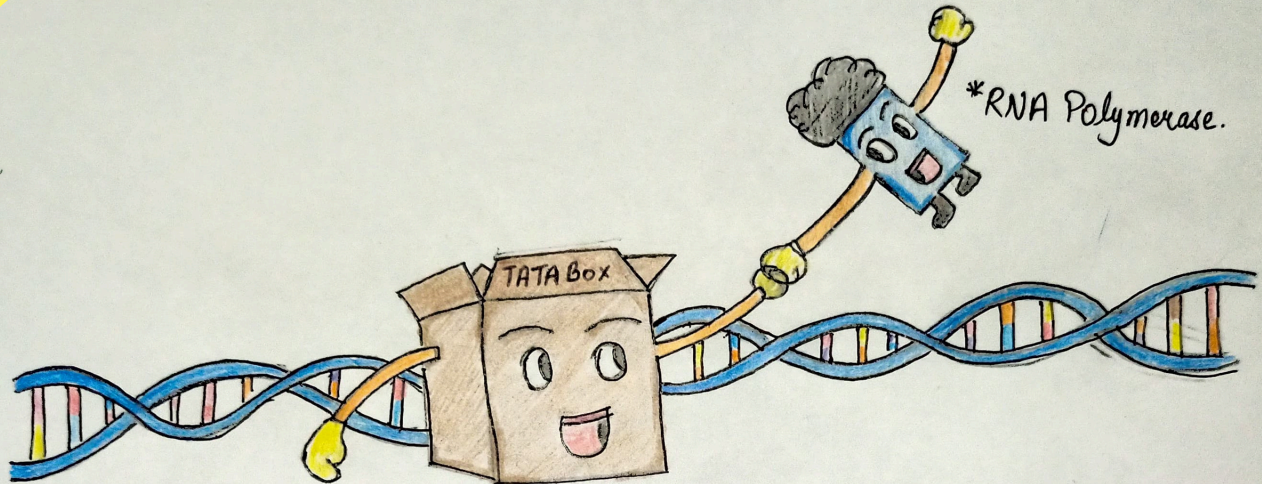
When the researchers delivered in vitro transcribed mRNA to immune cells, it triggered a strong immune response. They discovered that specific patterns of nucleic acids activated Toll-like receptors (TLRs), leading to a cytokine response. In 2005, Karikó and Weissman had a breakthrough. They wondered if the lack of chemical modifications in in-vitro transcribed mRNA caused the immune reaction. By introducing modifications, they reduced inflammatory signalling and increased protein yield. Their experiments in mice showed therapeutic potential.

Karikó and Weissman's discoveries on base modifications in mRNA have revolutionized vaccine development. Their findings allow for quick adaptation to new viral strains, making mRNA vaccines flexible and fast.

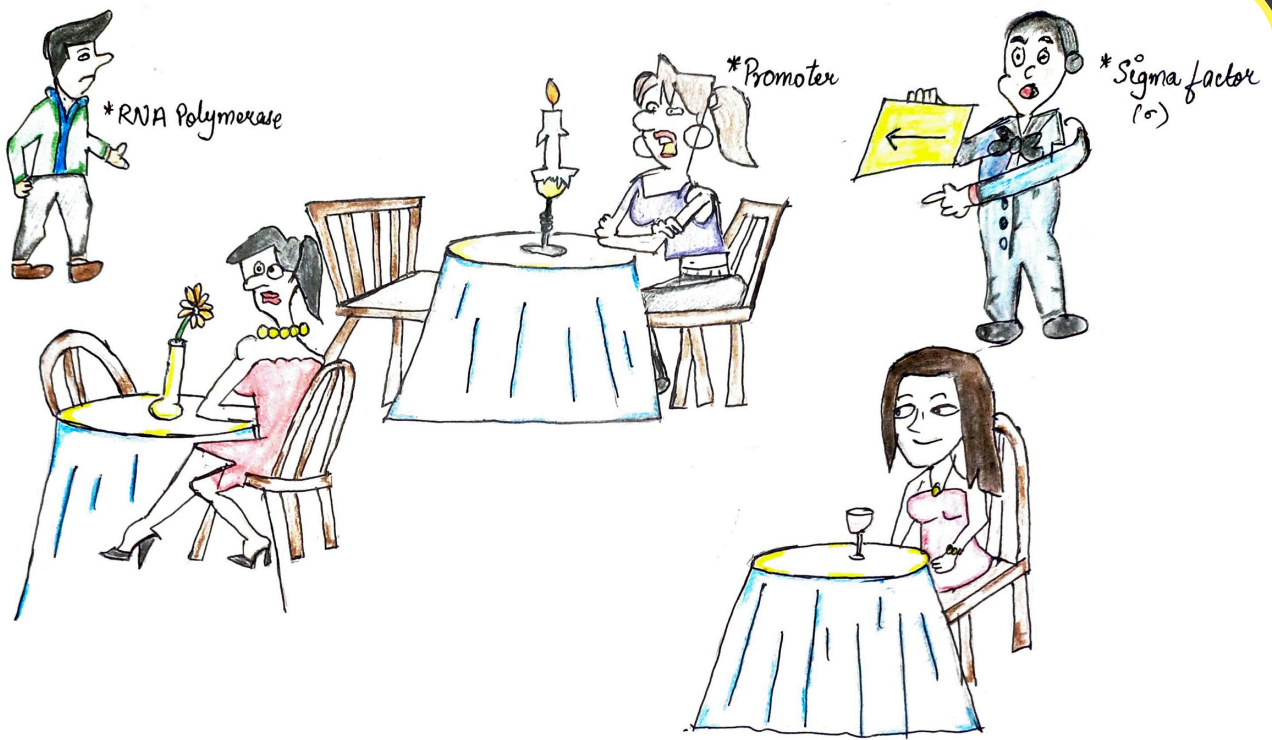
These advancements extend beyond COVID-19 including those targeted to SARS-CoV-2, Zikavirus and MERS-CoV Vaccine development. mRNA technology is being explored for cancer vaccines and other infectious diseases. The future of mRNA holds great promise for therapeutic protein delivery. Karikó's journey to develop mRNA therapeutics was met with challenges, but her persistence paid off. She joined BioNTech in 2013 and partnered with Pfizer to create an RNA vaccine against COVID-19. Thanks to their efforts, over 13 billion vaccine doses have been administered worldwide. Their vision has truly shaped the world we live in today.



TALE-O-MERS 1.0



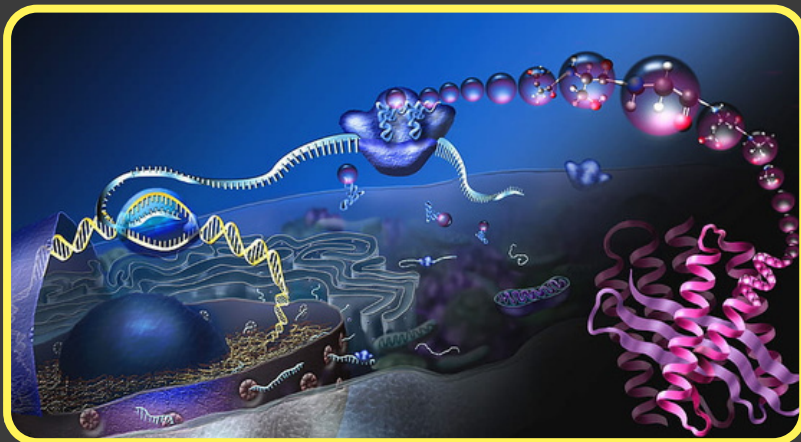
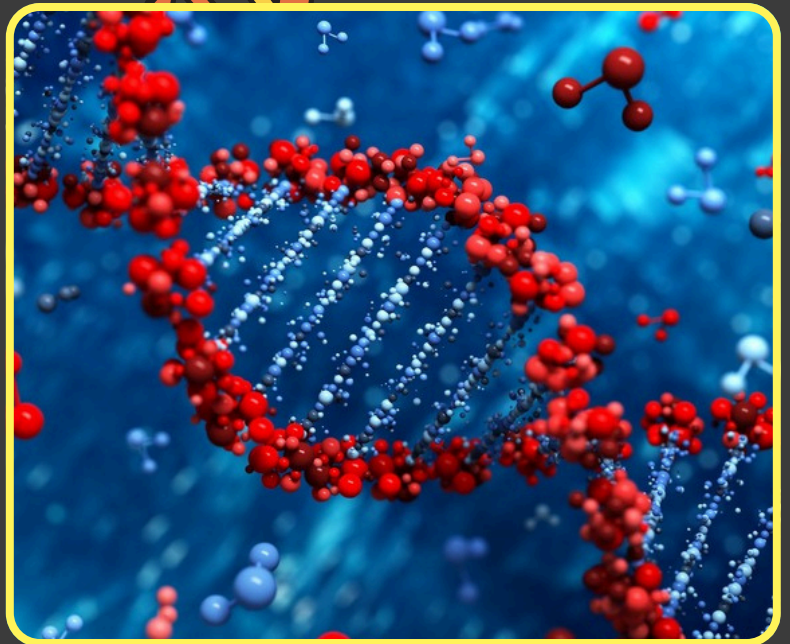
TATA Motors : "Connecting aspirations"
TATA Box : "Connecting RNA Polymerase"



RNA Polymerase goes on a blind dates and always manages to get the perfect match which promotes him further. Don't get encouraged by this. He has his Sigma friend to help him out. You don't.

NAVIGATING THE DEPTHS THROUGH MOLECULAR ODYSSEY

Within the extensive realm of biological sciences, molecular biology has undergone tremendous changes, driven by revolutionary discoveries, technological advancements, and interdisciplinary collaborations. Commencing from the important milestone of discovering a DNA structure to molecular cloning, we have progressed significantly. Ancient molecules offer a direct window into the biological past and allow us to follow evolutionary processes in real time.



It all starts with the discovering of DNA's double helix by Watson and Crick, which completely transformed the field and led to the comprehension of genetic replication and function. It illustrates the complexities of gene structure and function that emerged in the late 1970s, challenging the once-simple link between DNA and protein.

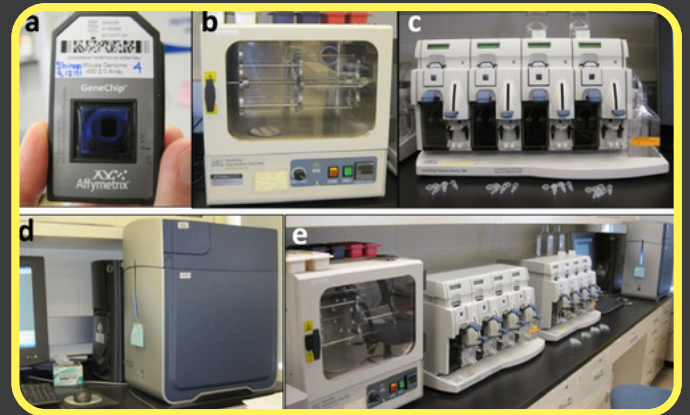
PCR

The idea of PCR, a crucial technique in molecular biology, was suggested by Kjell, Kleppe and colleagues in 1971. Expanding on the concept of DNA replication in nature, Kleppe envisioned a method for amplifying specific DNA sequences in vitro. The development of PCR drastically transformed the field of molecular biology, allowing researchers to amplify and analyze DNA with unparalleled precision and efficiency.

PCR (Polymerase Chain Reaction) amplifies DNA segments in vitro. It entails three steps: denaturation, where DNA strands are separated at high temperature; annealing, where primers bind to complementary sequences; and extension, where DNA polymerase synthesizes new DNA strands using nucleotides. This process is repeated multiple times exponentially amplifying the target DNA, making PCR a powerful tool in molecular for various applications such as diagnostics and research.



Micro Array



The origin and methodology of microarrays was initially introduced and described in antibody microarrays (also referred to as antibody matrix) by Tse Wen Chang in 1983 in a scientific publication and a series of patents.

Microarrays are a two-dimensional layout of biological samples with samples placed in spots numbering in the thousands and organized into columns and rows. They allow for efficient of genetic material and the most common type, DNA microarrays, have been utilized for large-scale studies of expression.

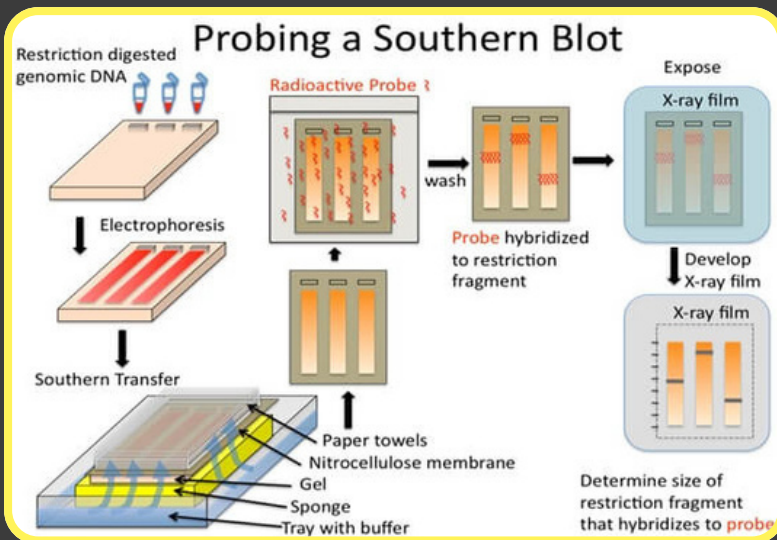
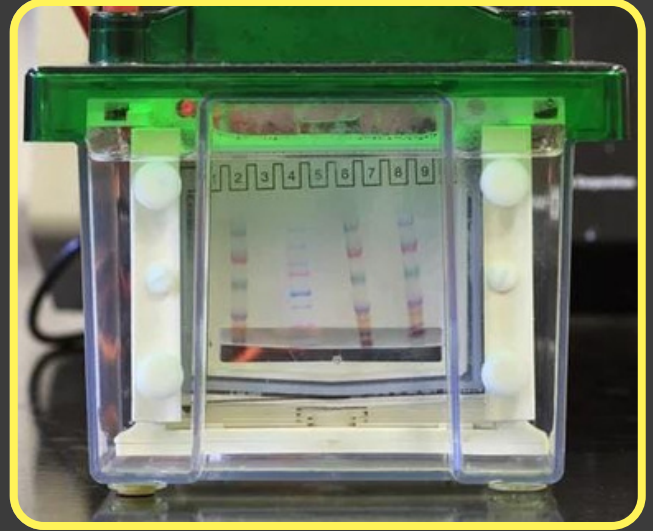
Microarray technology has grown from a pioneering method applied by researchers at the cutting edge to an omnipresent technique helping in advancement of biology. This technology has brought about a major revolution.

SOUTHERN BLOTTING

Southern invented Southern blot after combining three innovations, the first one is the restriction endonucleases used to cut the DNA at a particular sequence, second is the gel electrophoresis that is based on separation of mixtures of DNA, RNA, or proteins according to molecular size, and third is blotting-through methods.

Southern blot was invented in 1973 but was published later in 1975. It entails the transfer of DNA fragments from a gel onto a solid support membrane, followed by the detection of specific sequences using labeled probes. This technique refashioned the field by enabling the visualization of specific DNA fragments within a complex mixture.

and was awarded the Nobel Prize in 1948 for his work, was a pioneer in the creation of gel electrophoresis.



GEL ELECTROPHORESIS

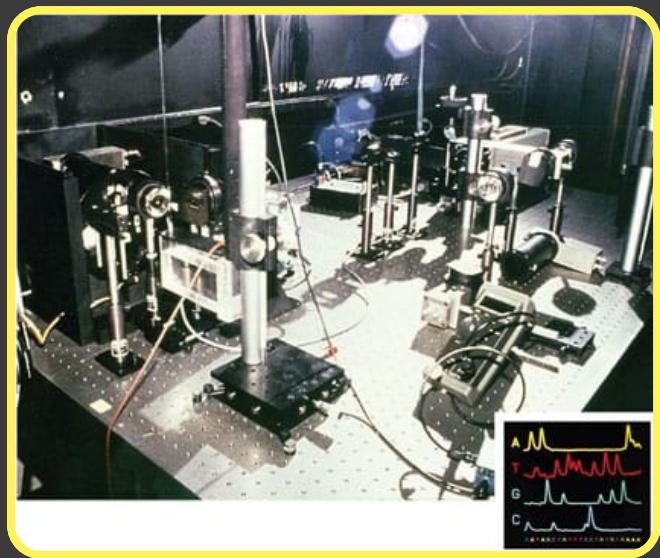
Arne Tiselius, a Swedish scientist who published his first study on electrophoresis, in 1937, in the publication, "A New Apparatus for Electrophoretic Analysis of Colloidal Mixtures",

The name "electrophoresis" was derived from the Greek word "phoresis," which means "being carried," and originally referred to the mobility of charged particles inside an electrical field.

Today, electrophoresis remains a cornerstone in molecular biology laboratories worldwide. It is commonly employed for various applications, including DNA analysis, protein purification, and drug development. Gel electrophoresis, utilizing agarose or polyacrylamide gels, is routinely used to separate DNA fragments by size, essential for tasks such as DNA fingerprinting and genetic analysis. Additionally, protein electrophoresis techniques, such as SDS- PAGE, are essential for analyzing protein composition and purity in biochemistry and biotechnology research.

DNA Sequencing

The Sanger sequencing method, developed by Frederick Sanger and colleagues in the late 1970s, revolutionized the field of genomics by enabling the determination of DNA sequences with unprecedented accuracy. Sanger sequencing relies on the incorporation of chain-terminating deoxynucleotides during DNA synthesis, allowing for the stepwise determination of nucleotide sequences. This technique laid the foundation for the Human Genome Project and paved the way for modern high-throughput sequencing technologies.



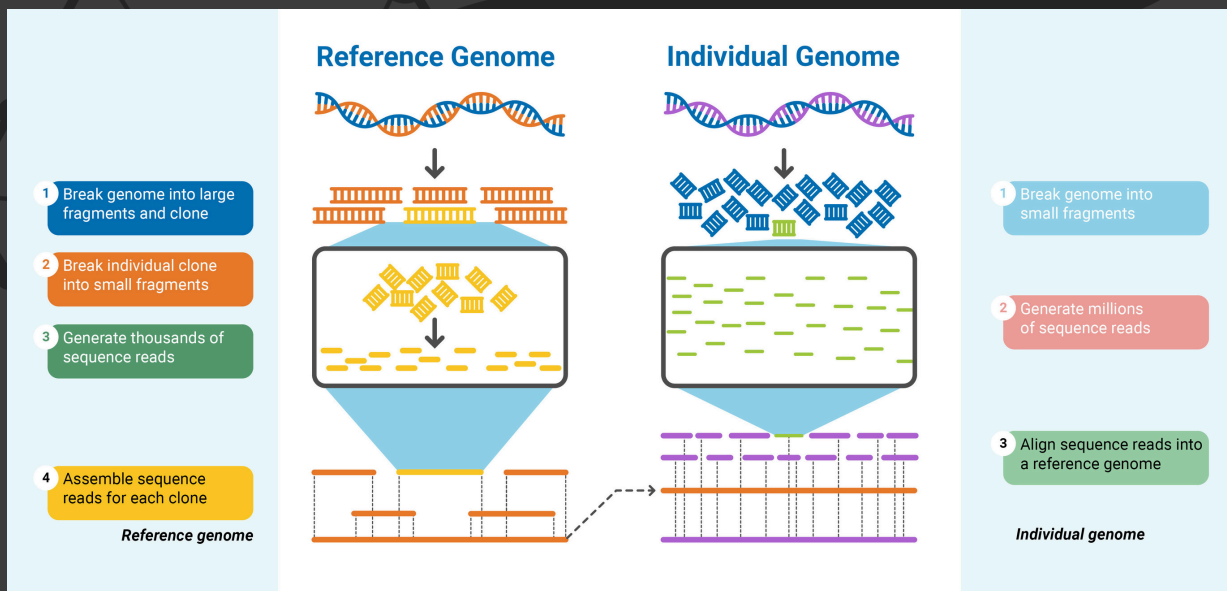
HOW DOES WHOLE GENOME SEQUENCING WORK?

Whole genome sequencing (WGS) is becoming the preferred method for molecular genetic diagnosis of rare and unknown diseases and for identification of cancer targets. Compared to other molecular genetic methods, WGS captures most genomic variation and eliminates the need for sequential genetic testing.

DNA sequencing

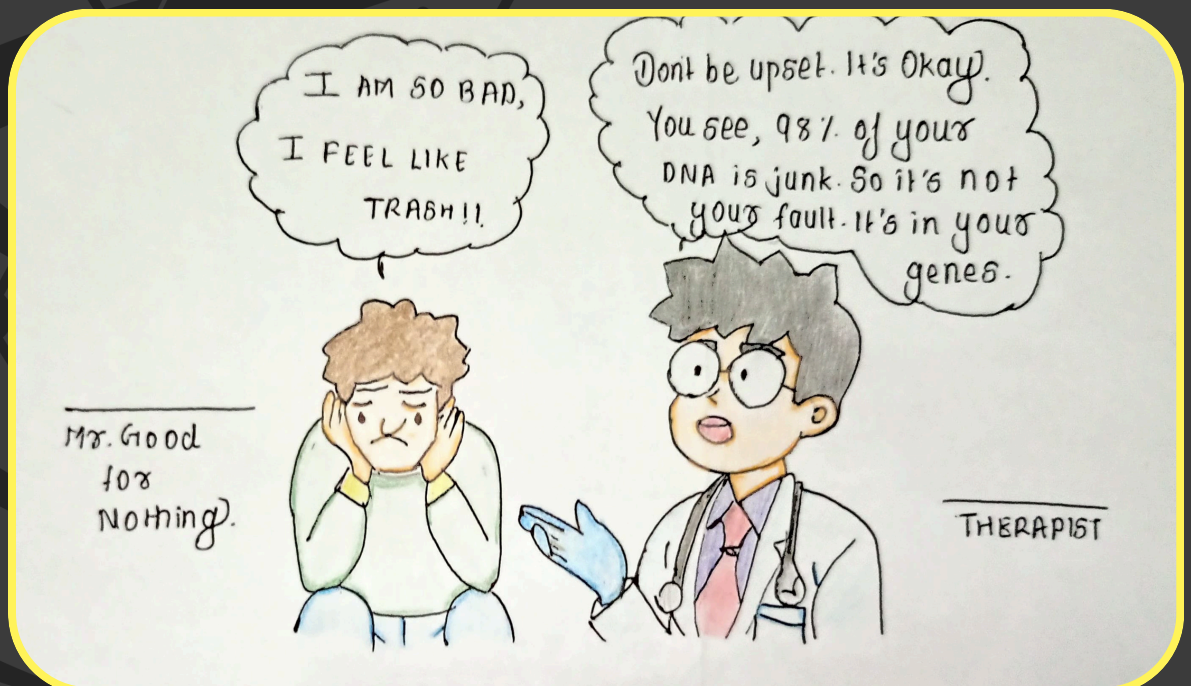
Scientists carry out whole genome sequencing by following these key steps:

- DNA shearing: Initially, scientists use molecular scissors to cut the DNA, which consists of millions of bases (A's, C's, T's, and G's), into fragments small enough for the sequencing machine to analyze.
- DNA barcoding: Next, scientists attach small DNA tags, similar to barcodes, to differentiate and track each piece of sheared DNA and its corresponding bacteria.
- DNA sequencing: The barcoded DNA from various bacteria is combined and inserted into a DNA sequencer. This device identifies the bases (A's, C's, T's, and G's) that form each bacterial sequence, using the barcodes to match the bases to the respective bacteria.
- Data analysis: Finally, scientists utilize computer tools to compare sequences from different bacteria, pinpoint variations, and determine relationships.



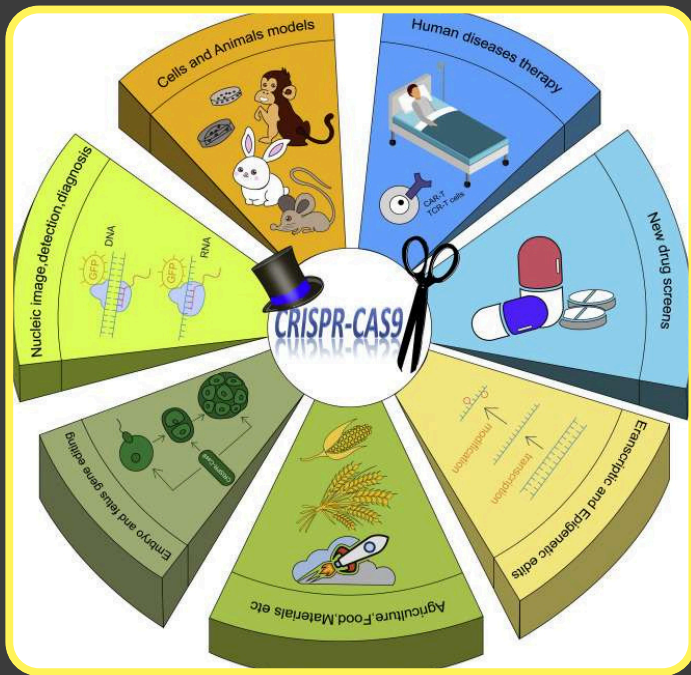
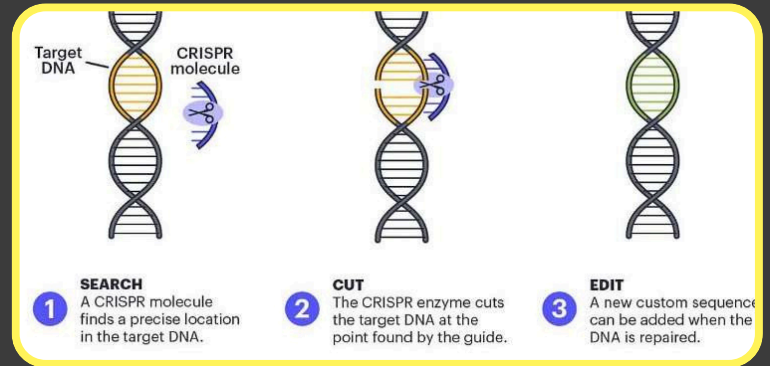
TALE-O-MERS

2.0



CRISPR-Cas9

Within the intricate web of molecular biology, few breakthroughs have intrigued and inspired scientists as deeply as the CRISPR-Cas9 gene editing tool. This groundbreaking technology has not only reshaped the limits of genetic manipulation but has also opened doors to a realm of possibilities across various scientific fields. Delving into CRISPR leads us through a terrain defined by remarkable progress, versatile applications, and important ethical dilemmas.



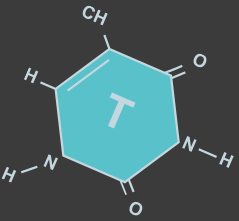
The versatility and precision of CRISPR-Cas9 have unlocked a wide range of applications across various fields of science and medicine. In biomedical research, CRISPR has become an indispensable tool for studying gene function, disease mechanisms, and therapeutic targets. By introducing targeted genetic modifications into cell lines and model organisms, researchers can elucidate the role of specific genes in health and disease. CRISPR-mediated knockout and knock-in experiments enable the creation of disease models for a wide range of genetic disorders, providing valuable insights into their pathogenesis and potential therapeutic strategies.

Ethical Considerations

One of the most pressing ethical issues is the potential for off-target effects and unintended consequences of CRISPR-mediated genome editing. Despite efforts to improve targeting specificity, CRISPR still has the potential to introduce unintended mutations at off-target sites, raising concerns about the safety and reliability of the technology.

Another ethical dilemma posed by CRISPR is the prospect of germline editing, where heritable genetic modifications are made to embryos or gametes. While germline editing holds the promise of eradicating genetic diseases and hereditary disorders, it also raises profound ethical questions about the implications for future generations, the potential for unintended consequences, and the specter of designer babies.

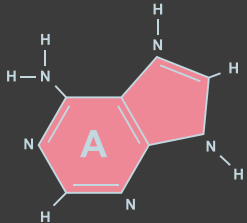
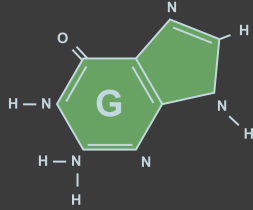
TALE-O-MERS 3.0



*DNAia

*Adenine

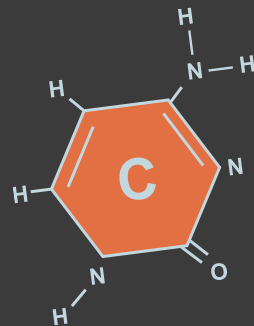
Adenine has 2 wives - Thymine from DNAia and Uracil who lives in RNA Kingdom. He shows some love and affinity to both without annoying any and is living quite happily since a long time. He is handling 2 at a time... you can try to at least handle one!



Long ago DNA was single and in love with Helicase. But their family opposed their intercaste marriage and made DNA marry another single DNA.



Since then, Helicase has made it his resolve to separate both of them whenever he sees them together.



It's Game time!!!

Riddles Recombined!

1. I'm a master regulator, I run the show,
control the expression of certain genes.
I'm essential to progress and development,
who am I, combining the two?

2. I'm , the molecular wizard and master of
twists.
I exist expertly in the realm of DNA.
I release tension and unwind my spiral,
but in the replica I work and struggle.

What am I?

3. In the code of life, I chanted the spell of
silence.
Subtle changes have taken place where
once everything was fine.
I bring diversity, but sometimes conflict.
I shape life within my genome.

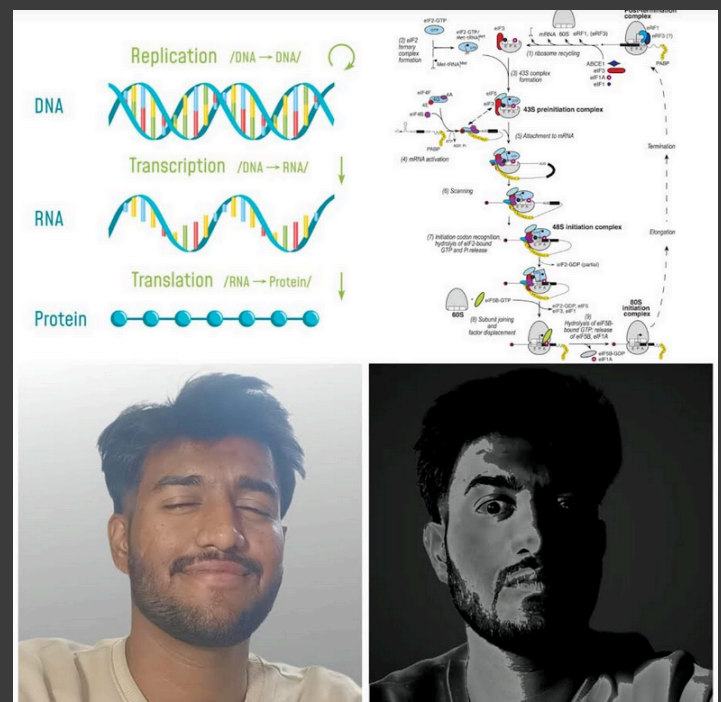
What am I?

4. I hide it in plain sight, in my genetic
script.
Non-code, but important, just out of
sight.
Edited out, but I'm doing my part
invisibly.
In the DNA story, I am the connection
between.

What am I?

5. I'm a string of life, woven in sets,
Within the core, my nearness
announces.
X or Y, a hereditary direct.

What am I?



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Tale-o-mers 1.0, 2.0 & 3.0

By: *Anushka Agarwal, Prayukt Kalme, Harshwardhan Shetgar*



COMIC: The twisted tale of RNA Maturation

By: *Samarth Patrike, Fritzi Isaac, Samar Doleeb, Mayuri Raut, Janhavi Giri, Samruddhi Gour & Mithilesh Kale*



Cellular Scrabble

By: *Siddhesh Shinde, Riya Marsale, Priti Giri*



Riddles Recombined

By: *Parth pawale, Aryan Paste, Priyansh Wadhwa, Tushar Shep*



UNVEILING THE DARK LEGACY

By: *Sakshi Dutande, Shruti Wantaram, Aditi Khandate*

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SYMPHONY OF SCHIZOPHRENIA

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Telomere: Key to ageing

By: *Vaidehi Mhatre, Aarti Jadhav, Ayush Dongare, Aromal Pillai*

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DECODING ONCOLOGY

By: *Yashvi Shah & Mandar Tijare*

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NAVIGATING THE DEPTHS THROUGH MOLECULAR ODYSSEY

By: *Yogita Sawant, Sneha Gavali, Diya Sharma, Srushti Balkawade and Mayuri Salunke, Awadhoot Ogale, Shreekanth Patil, Prasad Sonawane*

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NOBEL PRIZE FOR MRNA VACCINE

By: *Khushi Khasliwal, Yukta Nachane, Arpita Swami*

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Wound repair and regeneration: Mechanisms, Signaling and Translation

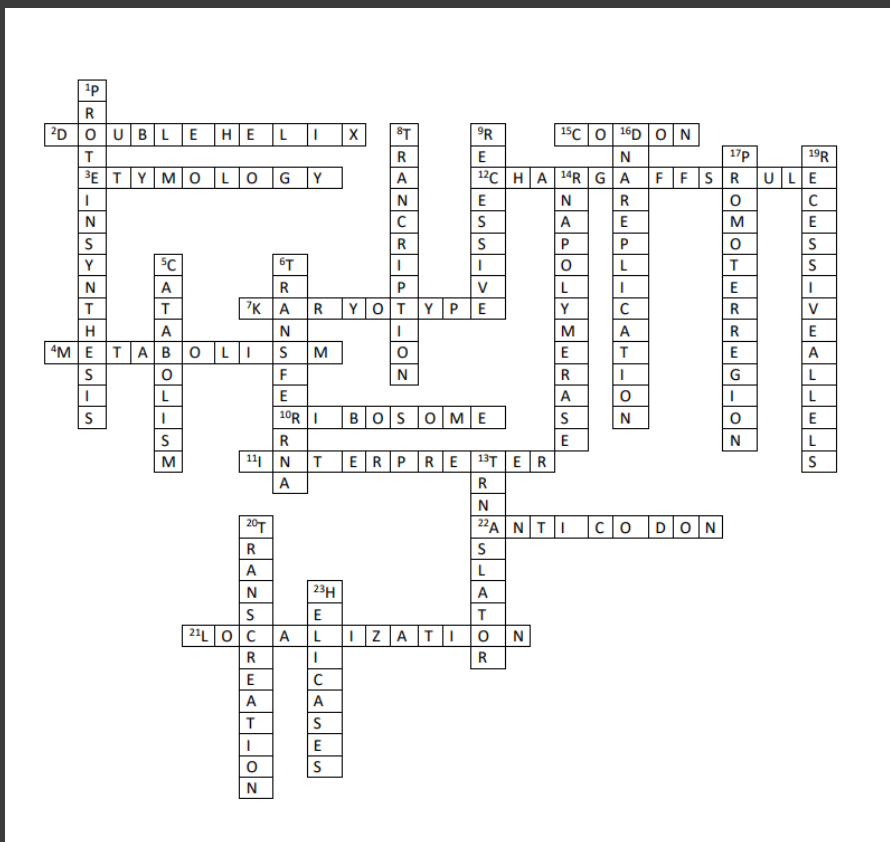
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Biographia

Answers :
Scrabble



Answers :
Riddles Recombined:
1. Transcription Factor 2. Topoisomerase 3. Mutation 4. Introns 5. Chromosome