MOUNT CARMEL COLLEGE

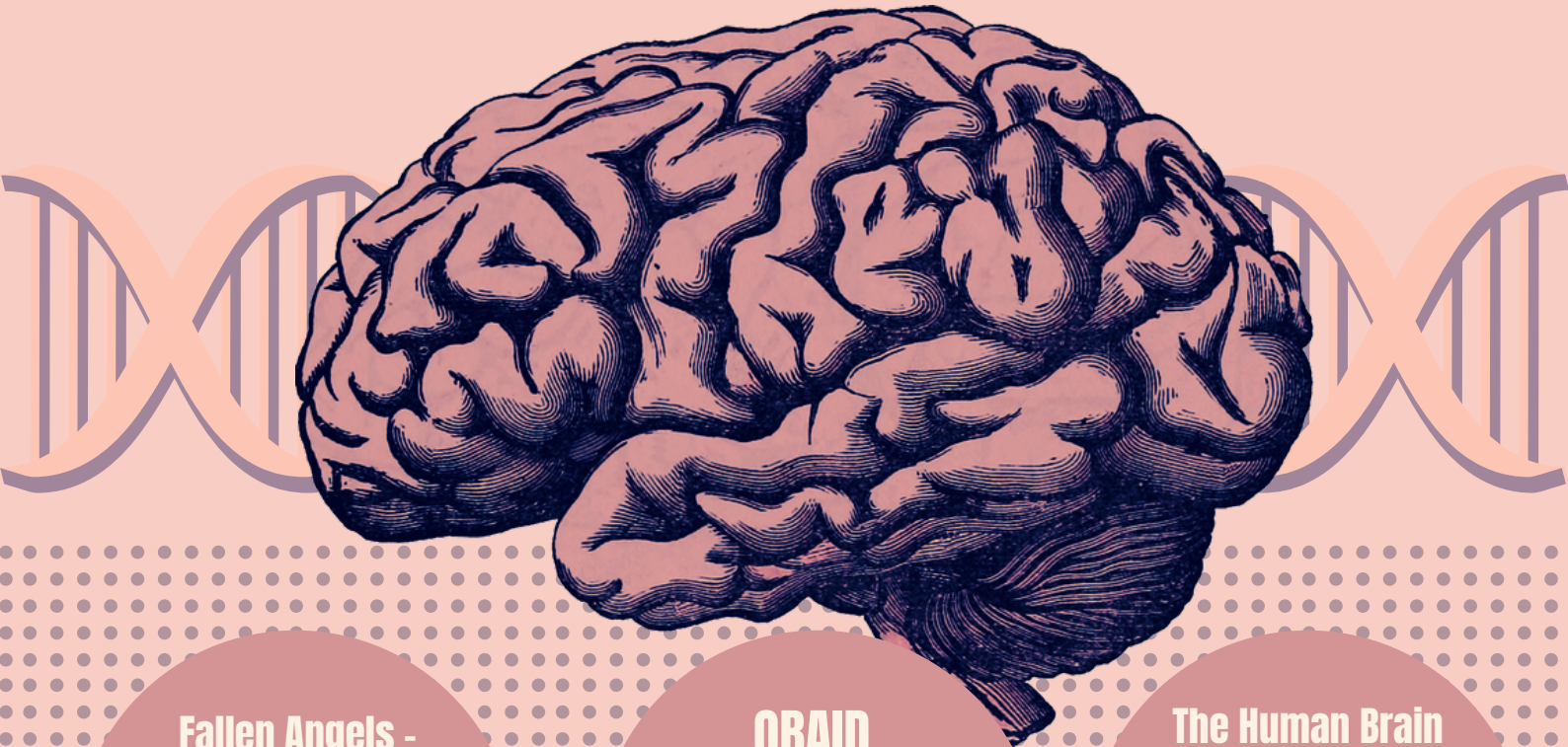
# BIOGENEIAC ASSOCIATION

# BIOGENESIS

## NOVEMBER 2021 ISSUE

FEATURE ARTICLE ON

# NEUROGENETICS



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# BIOGENESIS

THE OFFICIAL NEWSLETTER OF BIOGENEIAC ASSOCIATION
MOUNT CARMEL COLLEGE

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# RESEARCH ON PARKINSON'S DISEASE

JUHI SINGH | BTCZ 3RD YEAR

**Introduction**

Parkinson's disease is a nervous system disorder. Symptoms progresses over time, sometimes just a tremor in one hand. Tremors are very common, but the disease mostly causes stiffness or slowing of movement. In early stages of Parkinson's, your face may show little or no expression, arms may not swing while you walk, and your speech may become soft or slurred. Parkinson's disease symptoms worsen over time.

In Parkinson's disease certain nerve cells breakdown or die. Many of the symptoms are due to loss of neurons that produces a chemical messenger called dopamine. When the level of dopamine decreases it causes abnormal brain activity.

There is no specific text to diagnose Parkinson's disease. It is diagnosed based on your medical history, a review of signs and symptoms and a neurological physical examination. Doctors might suggest for a specific single-photon emission computerized tomography (SPECT) scan called **a dopamine transporter scan (DaTscan)**. Although this can help support the suspicion, it is your symptoms and neurological examination that will determine the correct diagnosis.

**Medication for Parkinson's**

Parkinson's cannot be cured, but medications can help to control your symptoms, often dramatically. The medications combat Parkinson's by helping nerve cells in the brain to make dopamine, mimicking the effects of dopamine, blocking an enzyme that breaks down dopamine in the brain and by reducing some symptoms of Parkinson's disease.

- **Levodopa:**

It is the main treatment for the slowness of movement, tremor and stiffness. Nerve cells uses levodopa to make dopamine, which replenishes the low amount found n the brain of person with Parkinson's disease.

- **Dopamine agonist:**

These drugs mimic the effect of dopamine in your brain. They are not as effective as levodopa in controlling slow muscle movement and muscle rigidity.

- **Catechol O-methyltransferase (COMT) inhibitors:**

These drugs block an enzyme that breaks down dopamine in the brain. They are taken with levodopa and slow your body's ability to get rid of levodopa.

Most patients with Parkinson's maintain a good quality of life with medications.

However, sometimes based on the severity of symptoms, surgical options are opted.

- **Deep Brain Stimulation (DBS):**

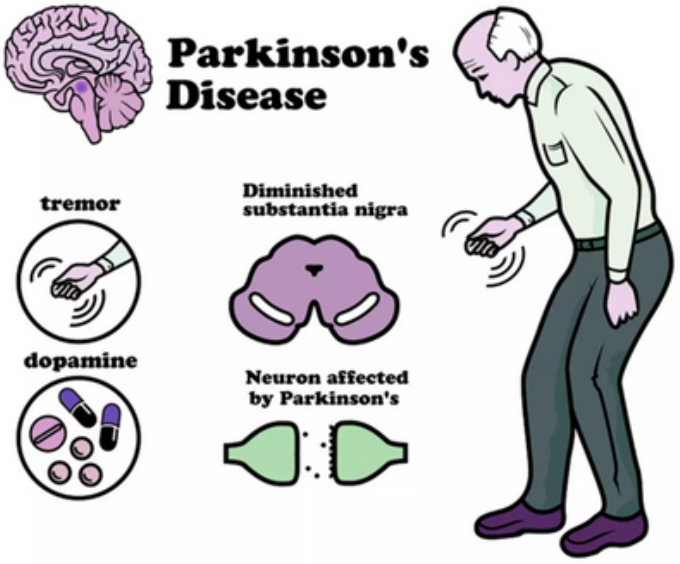
It involves implanting electrodes in the brain, which deliver electrical impulses that block or change the abnormal activity that causes the symptoms.

- **Pallidotomy:**

It involves destroying a small part of brain that controls movements (the globus pallidus).

- **Thalamotomy:**

Involves destroying a small part of the thalamus.



# REGENERATION OF NEURONS AFTER COMPLETE DEVELOPMENT - DOES IT HAPPEN? HOW AND WHY?

VINITIA PERSIS | BTCZ 1ST YEAR

## WHAT IS A NEURON?

Neurons are the fundamental units of the brain and nervous system. They are responsible for passing the received input from the external world, and send motor commands to our muscles and appropriate signals to the rest parts of the body.

A neuron has three main parts : dendrites, an axon and cell body. Neurons are classified into unipolar, bipolar and multipolar.

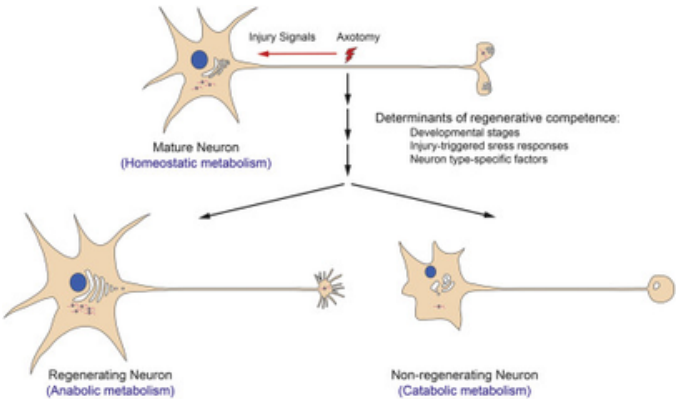
## NEURON REGENERATION CANNOT TAKE PLACE?

Neurons lack centrioles( which help in cell division) and because of this they are unable to perform mitosis and hence the division of cell does not take place.

## NEURON REGENERATION DOES TAKE PLACE!

In contrary to the above statement our neurons are able to regenerate, even in adults. This process of regeneration is called **neurogenesis**. The world is unaware about the process of neurogenesis but the recent finding by the scientists talk about the past and present in the history of biology. This process has been observed in the sub-ventricular region of the brain, where the nerve stem cells differentiate themselves into adult population of neurons.

The sub-granular area of hypothalamus region has also been known for the process of neurogenesis to take place. Experiments in the last third of the 20th century show how science in this sense has taken great steps forward.

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# RESEARCH ON HUNTINGTON'S DISEASE

PRIYANGIKA SINGH | BTCZ 2ND YEAR

**What is Huntington's disease?**

Huntington's disease (HD) is a neurodegenerative disease that is mostly inherited. It is a rare, inherited disease that causes the progressive breakdown (degeneration) of nerve cells in the brain. Huntington's disease has a broad impact on a person's functional abilities and usually results in movement, thinking (cognitive) and psychiatric disorders. Huntington's disease is inherited in an autosomal dominant fashion. The probability of each offspring inheriting an affected gene is 50%.

**What causes Huntington's disease?**

The defective gene identified in 1993 causes virtually all Huntington's disease. Huntington's disease is caused by an **autosomal dominantly inherited CAG trinucleotide repeat** expansion in the **huntingtin (HTT) gene** on chromosome 4. This results in the production of a **mutant huntingtin (mHTT) protein** with an abnormally long polyglutamine repeat. Those with greater than 39 CAG repeats are certain to develop the disease, whilst reduced penetrance is seen between 36 and 39 repeats. Anticipation can be seen when the gene is passed down the paternal line, such that a father with a CAG repeat length in the intermediate range may have a child with an expanded pathogenic repeat length. This is because sperm from males shows greater repeat variability and larger repeat sizes than somatic tissues.

**Research work on how to cure Huntington's disease:**

Research specialists in neurodegenerative are disease using gene editing to inactivate the mutated gene huntingtin.

CRISPR gene editing technology could achieve the same benefits through a single dose that permanently inactivates the defective gene with remarkable efficiency.

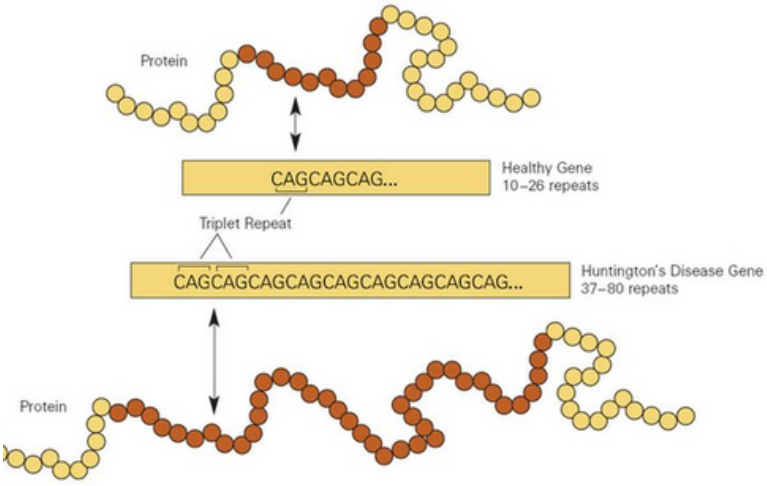
**How the CRISPR-Cas9 system works:**

The targeted DNA-snipping capabilities of CRISPR evolved in bacteria as a defense against viruses that transfer their genomic material into their microbial hosts. The system uses a short sequence of RNA known as a **guide RNA**, which can pair with a complementary DNA sequence.

Researchers have learnt how to target almost any genomic sequence by engineering an appropriate guide RNA. They couple it with an enzyme called Cas9, which can then cut both strands of a DNA sequence of interest at a specific site. Because the DNA-repair mechanism of cells is sloppy, it typically produces insertions or deletions that inactivate the affected gene.

One of the first decisions that would-be editors have to make is **whether to eliminate the gene that encodes huntingtin altogether, or to selectively target the repeat-laden mutated copy**. Scientists have obtained evidence from mouse studies that the depletion of huntingtin in

the brain might not be detrimental when it occurs in adulthood. They have subsequently demonstrated that a CRISPR–Cas9 approach that eliminates huntingtin can clear clumps of the protein from the brain. Most researchers are therefore erring on the side of caution by designing guide RNAs that recognize sequences found only in the mutated gene. This approach when showed that they could make edits with remarkable accuracy in cells that were collected from a person with Huntington's disease, by designing guide RNAs that recognize sequence variations found only on the chromosome that contains the mutated gene.




**Another concern is off-target editing**, in which genes other than the target are modified inadvertently — with potentially disastrous consequences. Software can be used to predict probable off-target edits and to help researchers pick distinctive guide RNAs with reasonable confidence.

But clinical researchers do need to consider the effects that CRISPR might have when used over the longer term. Unfortunately, most systems for getting the CRISPR machinery into the brain rely on its delivery by viral vector, which could lead to Cas9 being produced indefinitely.

**So how do we solve this?**

Scientists devised a promising alternative to CRISPR called **KamiCas9**, which includes a self-destruct button for Cas9. It uses **two guide RNAs** — one to target the gene encoding huntingtin, and another to target the gene encoding Cas9. This means that, after a brief flurry of activity by Cas9, production of the DNA-dicing enzyme is inactivated permanently, which dramatically reduces the risk of collateral damage. It was noted that several weeks after conventional CRISPR–Cas9 was applied to neural cells derived from people with Huntington's disease, low levels of off-target editing were detected — roughly 2% of modified cells received unwanted edits at a site that is particularly susceptible to off-target editing.

# The physically challenged regaining the ability to see, hear and speak with the help of neuroscience

ADITI SINGH | BTCZ 2ND YEAR

## INTRODUCTION

Neuroscience is the scientific study of the nervous system. It is a multidisciplinary science that combines Physiology, anatomy common molecule biology, developmental biology, psychology, computer science add mathematical modelling to understand the fundamental and emergent properties of neurons, glia an neural circuits. Scope of neuroscience has broadened overtime to include different approaches used to study the nervous system at different scales.

### Neuroscience in Hearing Aids

As technology advances, hearing aids continue to improve. Hearing aids are used to improve hearing by making sound audible to a person with hearing loss. The inability to make use of the amplified signal, especially in presence of competing noise, can vary across people.

Manufacturers can contribute to agent speech understanding in noisy environments, including device centered directional microphones, signal processing and gain and patient centered variables.

### Cortical neuroplasticity in hearing loss:

One of the most interesting aspects of the brain is it ability to adapt and change. The term **neuroplasticity** refers to changes in neural connections, pathways, our networks as a result of maturation and development, sensory deprivation, injury, disease, disco function, learning.

Neuroplasticity is a process which occurs at all levels of neural pathways and throughout the entire life span. Cortical development is dependent on stimulus driven learning. The absence of sensory input from board, as occurs in congenital deafness, effects normal growth and connectivity needed to form a functional sensory system resulting in deficits in oral language learning. Cochlear implant bypass cochlear damage by directly stimulating the auditory nerve and brain, making it possible to avoid many of the deleterious Effects of sensory deprivation. Congenitally deaf animals and children who received implants provide a platform to examine the characteristics of cortical plasticity in the auditory system.

# RECENT BREAKTHROUGH IN ALZHEIMER'S DISEASE

**RIA GURUNG | BTCB 1ST YEAR**

A neurodegenerative condition affecting parts of the brain associated with memory, thought, and language affected by various factors such as age, family history, diet, and environmental factors - "Alzheimer's Disease".

Lead study author Dr. John Mamo, Ph.D. — director of the Curtin Health Innovation Research Institute at Curtin University in Perth, Australia stated “To find new opportunities to prevent and treat Alzheimer’s, we need to understand what actually causes the disease, and presently that is not established.This study, shows that the exaggerated abundance in blood of potentially toxic fat- protein complexes can damage microscopic brain blood vessels called capillaries and, thereafter, leak into the brain, causing inflammation and brain cell death.”

He concluded by saying that by reducing the blood concentration of these toxic fat- protein complexes with changes in dietary behaviours or medications could possibly reduce the risk of Alzheimer's or atleast slow down its progress. The researchers have recently used two genetically modified mouse models part of the test group which would produce human amyloid beta in their liver that is believed to be the protein of the toxic fat- protein which may cause Alzheimer's disease. And on the other end the control group, without any genetic modifications. Tissues of mice of both groups were harvested including liver, duodenum to see the effect of human amyloid beta on the structure and function of these tissues.

**Conclusion:**

The researchers found out that the human amyloid beta produced in the liver combines with the fat and when they travel to the brain affect the functioning of the capillaries present there. This inturn causes the protein- fat complexes to leak from the blood to flow into the brain causing inflammation and this was observed in both control and test groups. But was noticed much earlier in the test group. This research suggested that human amyloid beta might have a big role to play in the development of Alzheimer's disease.

# EPILEPSY AND LEIGH SYNDROME

SHIFA | BTCZ 3RD YEAR

Epilepsy, a disorder affecting the functioning of brain activity, leading to abnormalities, hence causing seizures or periods of unusual behavior, sensations and sometimes loss of awareness, is most commonly a a genetic disorder, but can also be developed due to brain injury, such as a trauma or stroke, while; Leigh syndrome is a disorder that causes psychomotor regression, ie; it is a mitochondrial cytopathy that presents as a neurodegenerative disease manifesting in the central nervous system. The main aim of the research done over at Yonsei University College of Medicine by the Departments of Pediatrics, and the Epilepsy Research Institute was to identify which of the 2 disorders was the dominant neurological clinical feature, and hence describe and analyze the data related to epilepsy in Leigh syndrome accompanied by a mitochondrial DNA mutation.

Leigh syndrome is genetically heterogeneous, occurring due to mutations in mitochondrial DNA and nuclear genes involved in the process of energy production in the mitochondria. mtDNA protein-coding genes are one of the few important genetic causes of mitochondrial disorders for Leigh syndrome, among whom novel heteroplasmic variant m.4142G>T (p.R279L) in MT-ND1 and a recurrent homoplasmic mutation m.10197G>A (p.A47T) in MT-ND3 were identified in 2 patients in this study.

As part of the research project, a sample of 125 individuals suspected of Leigh syndrome were chosen, and whole mitochondrial sequencing was carried out. Among them, 31 patients were genetically diagnosed with mtDNA-associated Leigh syndrome. Among them, there were seven patients who showed positive for the MT-ND3 mutation. The researchers reviewed various clinical findings, which included laboratory findings, brain images, electroencephalography (EEG) data, seizure types, semiology, seizure frequency, anti-epileptic drug use history, and current seizure status.

**Evaluation of Mitochondrial Disease and Leigh Syndrome** Diagnostic evaluations of patients with LS were performed, which involved laboratory assessments of serum lactate levels and neuroimaging. The severity of serum lactic acidosis was defined as normal, mild (≧2-fold:- normal reference value), moderate (≧3-fold:- normal reference value). Neuroimaging was done, ie; brain MRI, while MR spectroscopy was used to identify a lactate peak in degenerated lesions of the brain. DNA from all patients were assessed for mitochondrial DNA (mtDNA) mutations based on a molecular sequencing analysis.

**Epilepsy Related Analysis**

Factors related to epilepsy, including seizure semiology and the diagnostic evaluation tool developed by the International League Against Epilepsy (ILAE) (10) classification as well as EEG findings. Additional assessments of participant treatment responses were based on numbers of anti-epileptic drugs and seizure frequency.

**RESULT:**

14 out of 31 patients (56%) showed clinical seizures, with focal seizures being the most common type (6/14, 42.8%). Slow and disorganized background neural activity was also observed in all patients, while eight exhibited epileptic discharges on EEG. Mutations at base pairs 10,191 and 8,993 were found in a larger number of patients of Leigh syndrome with epilepsy. An increase in the prevalence of gastrointestinal symptoms (P = 0.042) was also observed, which might have been due to high energy demands associated with epilepsy. Diffuse cerebral atrophy was significantly increased (P = 0.042) and cortex signal abnormalities were also increased (P = 0.033) in the epilepsy group. The 7 patients with Leigh syndrome with MT-ND3 mutation showed nucleotide changes, and were divided into two groups: m.10191 T>C and m.10158 T>C. Six of the seven patients were found to have m.10191 T>C mutations. The median value of the mutant load was 82.5%, ranging from 57.9% to 93.6%. No particular reason/tendency was observed for the first symptom or seizure onset or mutant load. The six patients with an m.10191 T>C mutation were diagnosed with epilepsy, of whom, 3 were diagnosed with Lennox-Gastaut syndrome (LGS).

**CONCLUSION:** Patients with Leigh syndrome and mitochondrial DNA mutations were shown to have a high proportion of central nervous system comorbidities, though the frequency of epilepsy in the sample was not particularly high.

It is common for those with different mitochondrial disorders to present various types of seizure and EEG findings. Due to recent advancements in molecular genetic testing, there has been a rapid increase in the understanding of the genetics of Leigh syndrome, and hence several studies were conducted around the subject, most of which have suggested that Leigh syndrome with the MT-ND3 mutation is strongly associated with epilepsy. At the end of the research, a very strong association between epilepsy and the MT-ND3 mutation in Leigh syndrome, particularly the m.10191T> C mutation was defined. The possibility of an association between the epilepsy phenotype of the m.10191T>C mutation and LGS was noted.

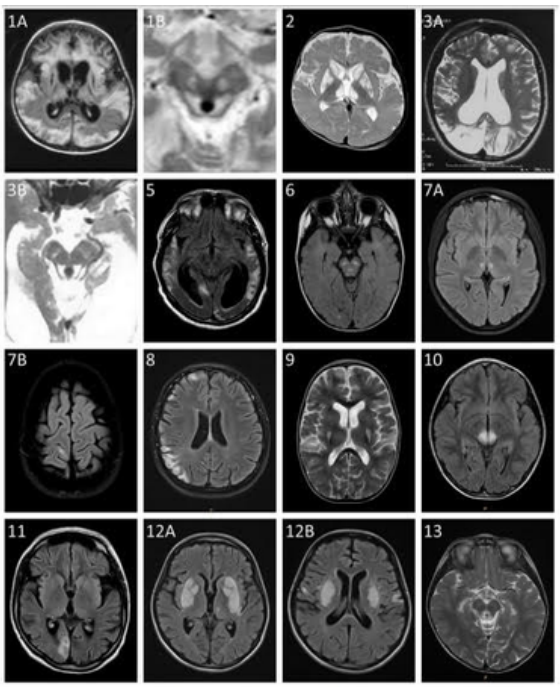



**Fig. 1** MRI of the brain in P1–P3 and P5–P12 with complex I deficiency. Signal changes in basal ganglia or brainstem characteristic for Leigh syndrome are present in patients P2, P6, P9, P10 and P13. Signal changes in the cortex and white matter of the hemispheres or cerebellum with stroke-like lesion are present in patients P5, P8, P11, and the combination of both changes are visible in patients P1, P3, P7 and P12. Moderate to severe periventricular atrophy was found in patients P1, P3 and P5.

# FALLEN ANGELS - WHEN PROTEINS GO ROGUE

SOPHIA EVANGELINE | 3RD YEAR BTCZ

**Prions** are misfolded pathogenic variants of the normal prion protein that transmit their misfolded shape onto the normal variants. **Accumulation of the rogue proteins (called amyloids) in brain tissue leads to fatal neurodegenerative diseases.** Prion diseases are characterized by long, pre-clinical incubation periods followed by rapidly progressing neurodegeneration and eventual death. Affected individuals die within a year or two after the initial onset of symptoms.

**Cellular prion protein (PrPC)** is coded by the **PRNP gene** located on chromosome 20 in humans. PrPCis a cell surface protein expressed in various organs and tissues with the highest expression levels in the nervous system. Misfolding and accumulation of **pathogenic cellular prion protein (PrPSc)** cause transmissible spongiform encephalopathies (TSEs) in mammals.

Propagation of pathogenic prions involves the reproduction of their structural conformation. PrPSc coerces PrPC to adopt the misfolded PrPSc conformation. The structure of PrPScis an extremely compact four-rung β-solenoid. The compact structure makes PrPSc highly resilient to degradation. While the pathological relevance of prion variants has been extensively studied, its mechanism of propagation remained highly debatable. Recently, researchers at Imperial College in collaboration with researchers at the University of Zurich made a striking breakthrough revealing the molecular events that cause a normal variant (PrPC) to to convert into a pathogenic variant (PrPSc).

The researchers used a mutant form of the human prion protein (T183A huPrP*) isolated from individuals with inherited TSEs as an observation model. Using nuclear magnetic resonance (NMR) spectroscopy and computational analysis, the research team determined theintermediate conformation of human prion protein (huPrP), denoted huPrP*, as the key driver that turns normal variants intoPrP mutant T183A.The intermediate conformation is aggressive and rapidly converts normal human PrP variants into pathogenic forms. The researchers also concluded that the molecular basis of T183A huPrP* enhances the promotion of amyloid formation in infected brain tissues.

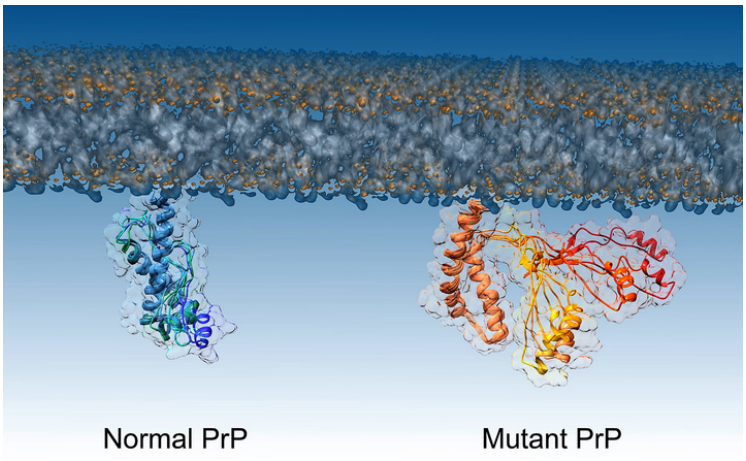
The unraveling of thesecret mechanism behind protein misfolding enabled the researchers to identify new approaches for a potential cure. They were able to produce a set of monoclonal antibodies, POM anti-PrPC antibodies. These anti-prion protein antibodies suppress the structural fluctuations that generate huPrP* from normal prion variants by inhibiting the structural misfoldingand locking huPrP in its native conformation. However, the blood-brain barrier (BBB)poses a problem because the antibodies are too big to pass through the BBB.Further research is required to refine the antibodies so that they can easily pass through the BBB.

Preclinical detection of prion infection was extremely difficult the last decade, highly sensitive assays: RT-QuIC (real-time quacking

-induced conversion) and sPMCA (serial protein misfolding cyclic amplification), were developed fordetecting prion infections. Both assays amplify minute amounts of the pathogenic proteins and the amplified proteins were identified by western blotting. A major disadvantage of these assays is that it requires invasive cerebrospinal fluid (CSF) samples. However, another recent study has shown that skin samples hold early signs of prion disease before the onset of symptoms. An international team of researchers used RT-QuIC and sPMCA to detect pathogenic prions in skin samples from infected rodents. Essentially, prions in the skin tissue are used as a biological marker for diagnosing and monitoring disease progression. Based on the research findings,currently availableassays can be improvisedto be minimally invasive for the detection of pathogenic prions in tissue samples.

In 2020, a US-based research group reported a possible antisense therapy for patients suffering from prions disease. Antisense therapy is a gene-silencingtechniqueto fight diseases using short complementary oligonucleotides that hybridize to a target mRNA,thus inhibiting the translation of harmful proteins. The researchers demonstrated that the use of antisense oligonucleotides lowered the levels of pathogenic prion amyloids and significantly increased the survival rate of the infected animals.

Despite its notoriety, PrPC has been highly conserved in vertebrates throughout evolution. Several research studies point to the essential functions of PrPC in neurobiological processes. Prion proteins mediate mechanisms of neuroprotection, aid in creating long-term memories, and promote cellular differentiation of neurons amongst several other functions. In conclusion, prion proteins are a necessary evil. Further research and advancement are required to combat the rogue side of prions. These novel research studies give us a better understanding of prion diseases and bring us a step closer to the development of effective therapeutics for such neurodegenerative diseases.



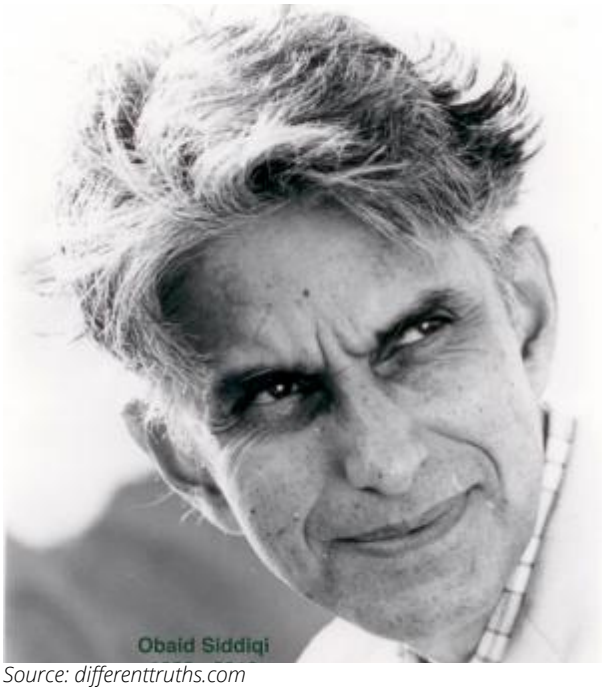

*Credits: www.imperial.ac.uk*

# OBAID SIDIQI

**ANANYA KALLIANPUR | BTCZ 3RD YEAR**

Obaid Siddiqi, formerly known as a leader in international neurogenetics and molecular biology until his untimely death in 2013' was born in 1932 in Uttar Pradesh. He received his early education at Aligarh Muslim University. He did his PhD from the university of Glasgow, where he worked with Guido Pontecorvo on microbial genetics. He carried out his post-doctoral work with Alan Garen at Cold spring Harbour Laboratory at the University of Pennsylvania. He was invited to set up the molecular biology and neurogenetics unit at the Tata Institute of Fundamental Research (TIFR) in Bombay in 1962. His pioneering spirit and contributions towards the field of behavioural neurogenetics used the genetics and neurobiology of Drosophila. Siddiqi was the gravitational force that brought together and attracted the best minds in science which was integral in the development and neuroscience and neurogenetics.

In the seventies, Siddiqi undertook a study on the genetic basis of behaviour, using Drosophila as the prime model. He joined forces with Seymour Benzer at Caltech and it was through his paramount work, that it was discovered that a mutant drosophila carrying the genes for temperature-sensitive paralytic and the generation and transmission of neural signal, actually exist. This work was a part of the foundation of the field of neurogenetics that we know today. This discovery led to a deep understanding of the mechanical basis of neuronal function and paved the way for modern behavioural genetics.



*Source: differenttruths.com*

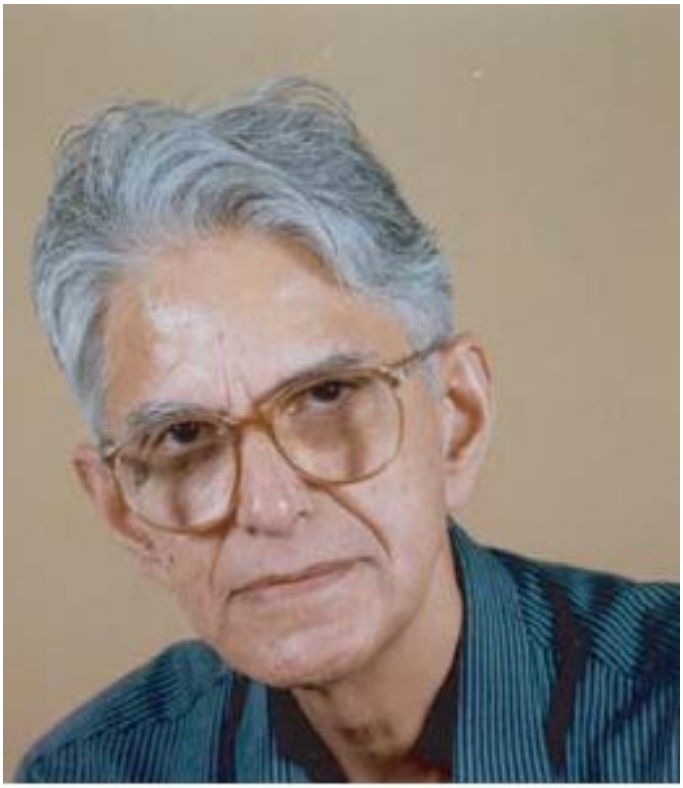
In the 90s at TIFR in Mumbai, Siddiqi and his pupil's work led to the revolutionary advances in understanding how taste and smell are detected and encoded in the brain by using Drosophila. He was active in this area of research and maintained an active lab as an Emeritus Professor at NCBS.

Siddiqi has made waves in the scientific community and have been equally recognised both nationally as well as internationally. He was elected as a member of the Royal society, London, the US national Academy of sciences, The World Academy of Sciences, Trieste, the Indian Academy of Sciences, Bangalore, National Academy of Science (Allahabad), and the Maharashtra Academy of Sciences.

He has been honoured with the Padma Bhushan, Bhatnagar Prize, INSA Golden Jubilee Medal, Birla Samarak Kosh National Award, Aryabhata Medal by INSA, and many more.

He was awarded visiting professorship privileges at colleges like Yale, MIT and innumerable universities in India. He was the Sherman Fairchild Distinguished Scholar at Caltech and was a lifelong member of the Clare Hall, Cambridge. Honorary Doctorates were conferred upon him by universities such as IIT Bombay, Jamia Millia Islamia, Banaras Hindu University.
His peers and all those who knew him, had great respect for him and his contributions to the fields of neurogenetics and molecular biology. In the words of former director of the NCBS, “There are a daring few who define new intellectual quests, and whose courage and leadership create a culture...today, we celebrate Obaid Siddiqi whose foresight, determination and quiet courage has transformed research in molecular biology in India at least twice and whose scientific successes span many fields of biology. While establishing institutional excellence and instilling an iconoclastic culture of independence and freethinking, these pioneering efforts have led to wide appreciation, both of the beauty and value of Obaid's science and his leadership in institution building, as models to emulate.”

He eventually became the founding director of the TIFR National Centre for Biological Sciences in Bangalore, where he continued to dedicate his life to research until his final days. It doesn’t come as a surprise that Obaid Siddiqi was one of the foremost researchers and decorated scientists. He was an exemplary mentor and inspired other scientists with his passion. Some of the scientists he mentored and worked with became subsequent Nobel laureates. He was a philosopher and a dreamer; we can respect his memory by delving into the world of science and building on the very strong foundation that he has left behind. He made India very proud.



UP NEXT

# NEWS BRIEFING

## The most exciting developments of the field in the month of November

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| ANIMAL BIOTECHNOLOGY |

| PLANT & AGRICULTURAL BIOTECHNOLOGY |

| INDUSTRIAL & ENVIRONMENTAL BIOTECHNOLOGY |

# Coronavirus Infection Found in Deer in US State of Iowa

Analysis has found that deer have contracted the virus from humans. Experts worry about a deep wild reservoir for the virus.

**RUPASHRI BALARAMAN | BTCZ 3RD YEAR**
02 NOV 2021
*Huck Institutes of Life Sciences, Penn (Pennsylvania) State University, USA.*

More than 80 percent white-tailed deer were sampled in different parts of the US state of Iowa between December 2020 and January 2021 by the Iowa Department of Natural Resources as a part of routine testing have tested positive for SARS-CoV-2. This finding implies that the white-tailed deer may be a reservoir for the virus to continually circulate and has raised concerns for the possible emergence of new strains of the virus that may affect humans.

*Credits: Greg Oberski/Wikipedia Commons. Found on: www.psu.edu*

This is also the first evidence that SARS-CoV-2 virus in another species of animal. They possess the threat of infecting other species and humans. But it is to be noted that this information is derived from observing the presence of the SARS-CoV-2 antibodies in the blood of the sampled deer, and doesn't prove the infection or the possibility of transmission as it could also be antibodies from an immunologically related organism. The viral lineages from the deer seemed to correspond to that in humans around the same time period of early 2021. This was the time when there was a notable peak in hunting of deer as well. So, this seems to suggest the occurrence of multiple spill-over events from humans to the deer.

The analysis was conducted by veterinary microbiologists at Penn State – Dr. Suresh Kuchupudi and Dr. Vivek Kapur. They examined the lymph nodes of samples of deer killed by vehicles on the road or hunters.

A shockingly high number of the samples from various locations across the state showed active infection.

The primary concern is if the virus becomes endemic within the deer population, it could mutate and evolve to become more virulent and infect people as a new strain that could overthrow our current vaccines.

But there is also no reason for immense alarm, as even if it so happened that a new strain of the coronavirus were to infect people, it can be tackled with a booster shot. A vaccine for infected deer also remains as a possibility, although the idea lacks practicality.

Several states in the US have now been warned to take precautions while hunting deer, and to properly dispose of the carcass and maintain above par sanitary measures.

This study raises the need for further research on the question of how other wild animals can carry the virus, and how their proximity to human life could have an effect on our chances of infection.

# RNA Molecule as a Prostate Tumor Suppressant

Long noncoding RNA regulates androgen receptor responsible for stimulating growth of the cancer

**MALEEHA AFAQ | BTCZ 2ND YEAR**
06 NOV 2021
*Washington University School of Medicine*

A new study from Washington University School of Medicine in St. Louis has identified an RNA molecule that suppresses prostate tumors. The scientists found that prostate cancers develop ways to shut down this RNA molecule to allow themselves to grow. According to the new research conducted in mice implanted with human prostate tumor samples restoring this so-called long noncoding RNA could be a new strategy to treat prostate cancer that has developed resistance to hormonal therapies. The key protein that drives prostate tumor growth, the androgen receptor, binds to testosterone and stimulates cancer growth. Studying the stretch of DNA that codes for the androgen receptor, the researchers discovered that a section of the DNA molecule next to the androgen receptor produced a molecule called a long noncoding RNA. They found that this long noncoding RNA plays a key role in regulating the androgen receptor and vice versa. Because of its position next to the androgen receptor in the genome, the researchers dubbed it NXTAR (next to androgen receptor).

The drug, called (R)-9b, was developed to attack a different aspect of prostate cancer biology, knocking down expression of the androgen receptor overall rather than just blocking its ability to bind to testosterone or reducing overall testosterone levels in the body, as currently approved drugs do.

But in this study, (R)-9b ended up serving as a tool to reveal the presence and role of NXTAR. Studying human prostate tumor samples implanted in mice, the researchers showed that restoring NXTAR expression caused the tumors to shrink. They also showed that they didn't need the entire long noncoding RNA to achieve this effect. One small, key section of the NXTAR molecule is sufficient for shutting down the androgen receptor.

# Zika virus-specific therapy protects the fetal mouse brain

A gene-silencing therapy protected against Zika virus transmission from pregnant mice to the mouse fetuses

**RUVIZA MUSKAN | BTCZ 2ND YEAR**

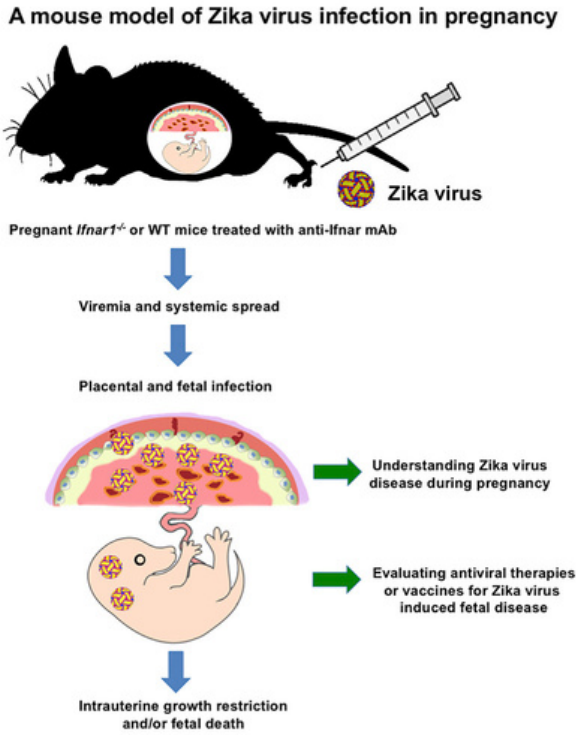
20 NOV 2021

*University of North Carolina, USA*

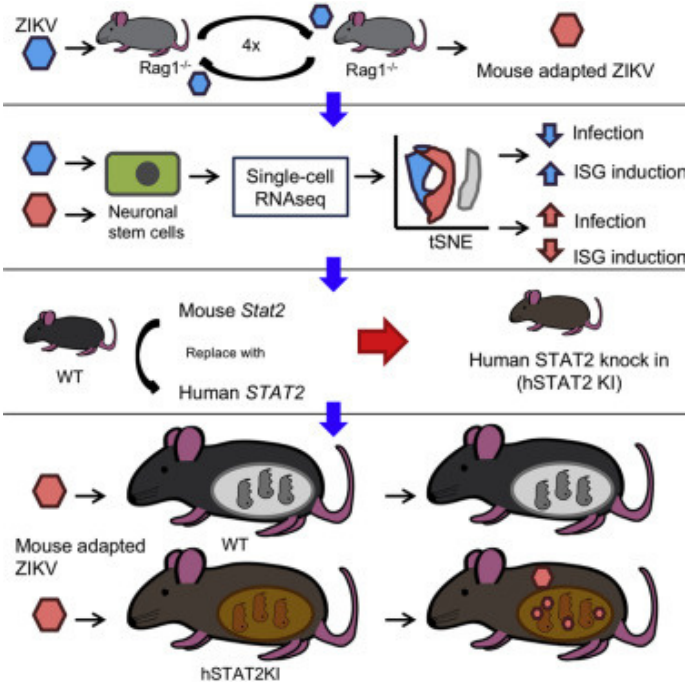
The Zika virus epidemic swept across the Asia-Pacific region in 2015-2017 and remains a global health threat to this day. The virus causes neurological and congenital conditions such as microcephaly, in which the baby's head is smaller than expected. It can cross the placenta and the blood-brain barrier, which a network of blood vessels and tissue that is made up of closely spaced cells.

In particular, gene silencing therapies using oligonucleotides have demonstrated unique advantages in clinical settings, but the delivery of nucleic acids into cells remains a major challenge. One potential solution is offered by **small extracellular vehicles or sEVs** - natural, biodegradable nanoparticles that are released from cells and are important mediators of cell-to-cell communication.

Senior study author Zhiwei Wu of Nanjing University says – "Our experiments indicated that targeted delivery via modified sEVs is a promising alternative to the traditional methods of delivery, especially for the treatment of brain viral infection. Increasing the yield and efficiency of producing sEVs and developing sEVs that target other tissues will broaden their application and will expand the effectiveness of this gene delivery technique." Currently, there is no Zika virus-specific therapy or vaccine available," Wu says.




Credits: https://www.cell.com/fulltext/S0092-8674(16)30556-6




Credits::https://www.sciencedirect.com/science/article/pii/S1931312818302002

In the new study, Wu and his team demonstrated for the first time that sEVs could deliver antiviral drugs to achieve targeted suppression of Zika virus infection in the fetal CNS and to control neurological damage. To home in on neurons, the researchers engineered sEVs that expressed rabies virus glycoprotein (RVG) on their surface. They then loaded them with Zika virus-specific small interfering RNA (siRNA) and injected them into pregnant mice. The RVG-modified sEVs crossed the placental barrier and blood-brain barrier, protecting against Zika virus transmission to the fetus. They concentrated in the fetal brain, where they suppressed infection and reduced inflammation and neurological damage, including microcephaly and defects in a brain region called the cerebellum. The findings echo another recent study showing that RVG-modified sEVs could cross the blood-brain barrier in mice to treat manifestations of Parkinson's disease. "Our therapeutic approach expanded the application of sEVs to treat viral infection of brains by intravenous injection," Wu says.

This work was supported by National Natural Science Foundation of China, the Major Research and Development Project, Nanjing University-Ningxia University Collaborative Project.

# First sprayable ds RNA biopesticide product

This RNA-based biopesticide targets proteosome subunit beta type 5 in Colorado potato beetle.

**NIKHILA MOHAN | BTCZ 2ND YEAR**

The Colorado potato beetle (CPB, leptinotarsa decemlineata) is a major potato pest in North America, Europe, and Asia. CPB causes damage to the entire plant if all foliage is consumed, insects start to feed on stem and exposed tubers. Feeding by this insect causes crop loss, with management costs reaching tens of millions of dollars annually. Many of the chemical pesticide classes control CPB. However, CPB has shown resistance to over 50 different compounds belonging to all major insecticide classes. Pesticides with new MoA(mode of action) are needed for control of CPB, especially those that have a low impact on the environment and beneficial insects. Thus, highly specific biopesticides for IPM of CPB, such as dsRNA, may be a viable alternative to synthetic chemistry.

Ledprona(ds PSMB5) is the active ingredient of a new biopesticide class based on RNAi that targets an essential gene for CPB. Ledprona is a 490bp dsRNA that has identical sequence complementarity to PSMB5 mRNA of CPB. PSMB5 encodes one of the key catalytic subunits of the proteasome beta molecular machine that catalyzes the degradation of proteins tagged by ubiquitin as part of ubiquitin -proteosome degradation pathway. Impairing this pathway is hypothesized to be lethal to CPB by accumulating protein molecules that are not degraded. CPB has a strong RNAi response to environment RNA as demonstrated by dsRNA targeting gene under a different experimental condition in laboratory and field. In this study, it was proved that consumption of leaf material treated with ledprona caused larval death overtime. Ledprona acted more slowly than chemical insecticides but reduced target protein levels and provided protection against defoliation similar to commercial standard, conferring a high percentage of pest mortality across a wide dsRNA dose range.

Credits: green light biosciences

# Illegal Cultivation Of Herbicide-Tolerant Bt Cotton Across India

Urges government to curb surge in illegal HtBt cotton

**TEJASWINI RAJASHEKAR & PRECILLA PAUL | BTCZ 3RD YEAR**

9 NOV 2021

The Federation of Seed Industry of India (FSII) and the National Seed Association of India (NSAI) have sought the government's immediate intervention to curb the surge in illegally cultivated Ht (herbicide tolerant) Bt (biotechnology) cotton.

The seed industry bodies said illegal cultivation of HtBt cotton poses a "serious threat to the environment, farmers, legitimate seed companies and the government revenue."

India currently allows Bt cotton, known as a pest-resistant cotton seed that combats bollworm, but the use of genetically modified HtBt cotton is prohibited.

The illegal cultivation of HtBt cotton doubled this year to around 7 million packets across India and was prevalent in major states like Maharashtra, Andhra Pradesh, Telangana, and Gujarat, the seed industry associations pointed out.

"It seems that the major seed production of this cotton is in Gujarat, and then the seed is moved to Maharashtra," they said.

Soon after the issue of farmers cultivating unapproved HtBt cotton hybrids illegally in many states was raised in Parliament in 2017, the Prime Minister's Office had appointed the Field Inspection and Scientific Evaluation Committee (FISEC) under the Department of Biotechnology.

Apart from confirming that HtBt cotton was being illegally grown across the country, the FISEC panel tested thousands of samples and concluded that nearly 15% of unapproved HtBt cotton was in Maharashtra, Andhra Pradesh, Telangana, and Gujarat.

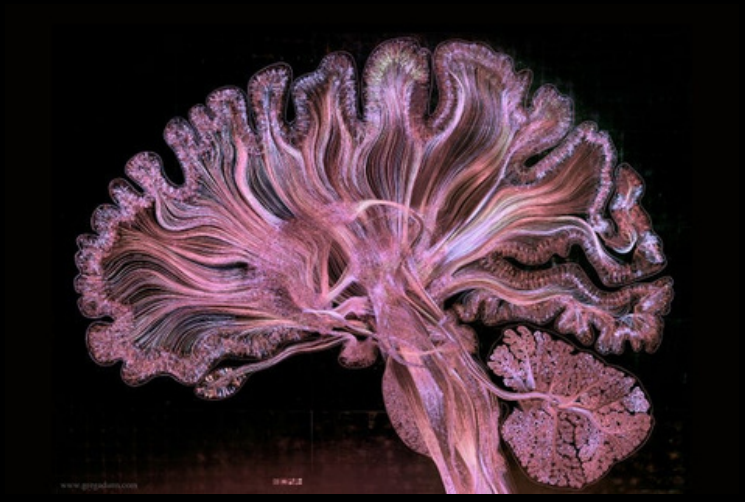
Pointing out that the area under cultivation of illegal HtBt cotton was increasing in India over the last few years, the chairman of FSII, M Ramasami, who is also the chairman of Rasi Seeds, said, "The packs show the presence of many technologies which could pose a very serious situation in the field. If it is not controlled immediately by the governments, it will spell disaster for the industry and farmers."

The NSAI said the spread of illegal seeds could contaminate legitimate seed production and put farmers in heavy losses.

“It will not only decimate small cotton seed companies but also threaten the entire legal cottonseed market in India. To make matters worse, the illegal seeds are sold using the brand name of prominent companies,” said NSAI president M Prabhakar Rao.

# GALLERY

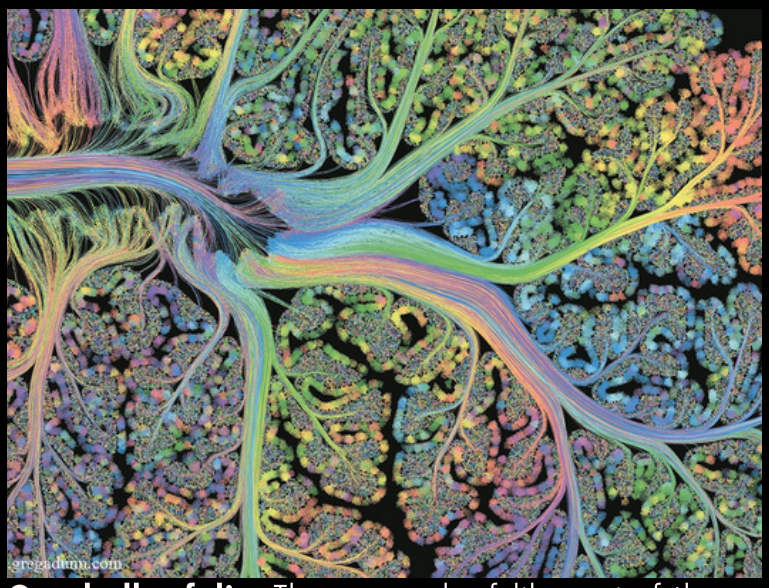
RUPASHRI BALARAMAN | 3RD YEAR BTCZ



**Self Reflected.** The entire micro-etching under violet and white light.

## THE HUMAN BRAIN IS A PIECE OF MARVELOUS ART

These images have been constructed by two scientists-turned-artists - Greg Dunn and Brian Edwards by using a technique called "micro-etching". They are on display at The Franklin Institute in Philadelphia.



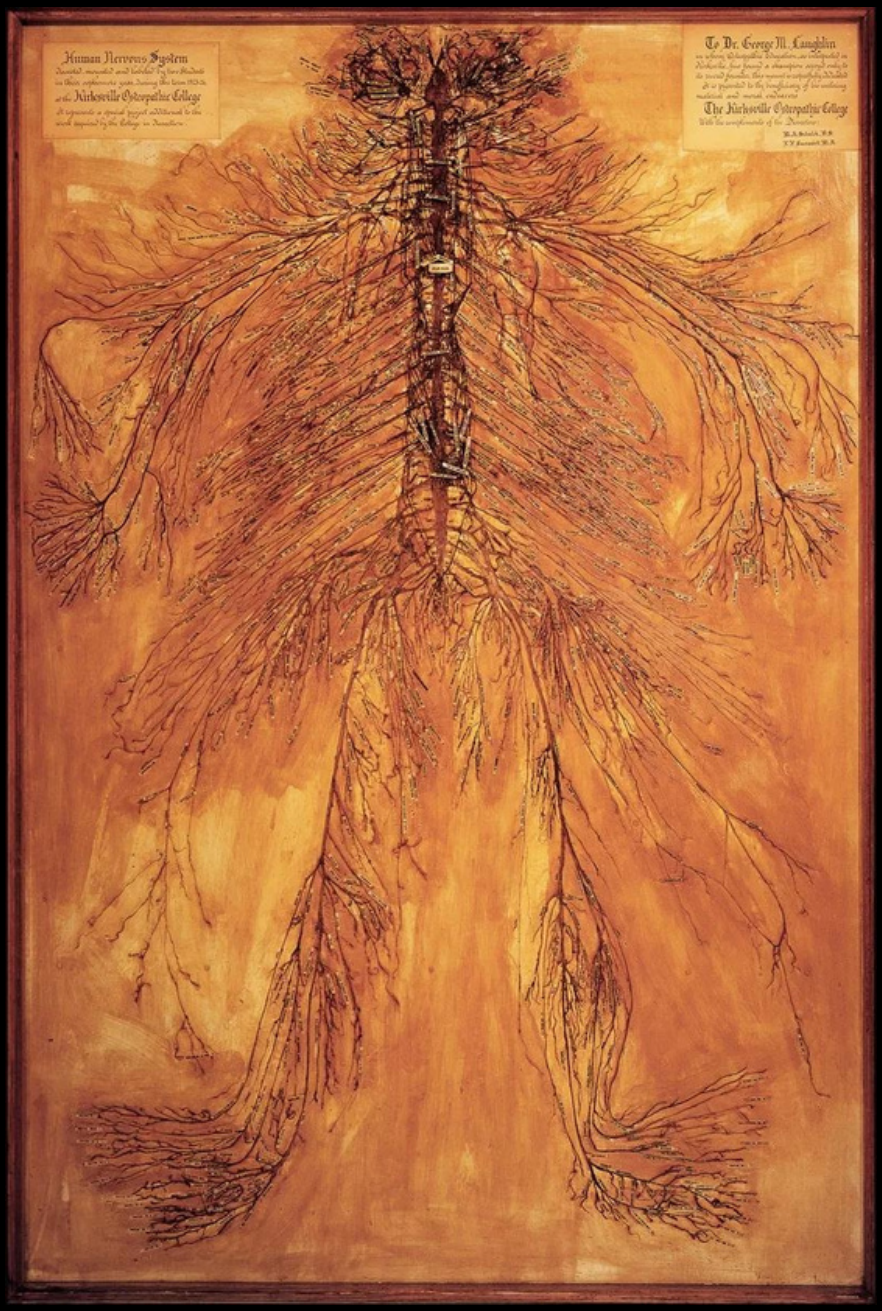

**Cerebellar folia.** The narrow leaf-like gyri of the cerebellar cortex.

Titled “Self Reflected,” the piece maps beautiful illustrations of neurons and axons. LEDs scan across the surface and reflect off the varying depths and angles of the gold leaf grooves of the micro-etchings to make each neurological pathway shimmer like it is truly alive with electrical firings.

*Images Credit: Greg Dunn, Brian Edwards, and Will Drinker*

# GALLERY

RUPASHRI BALARAMAN | 3RD YEAR BTCZ




**In-tact dissected nervous system.** M.A. Schalck and L.P. Ramsdell — spent 1,500 hours of their lives completing the painstaking dissection.

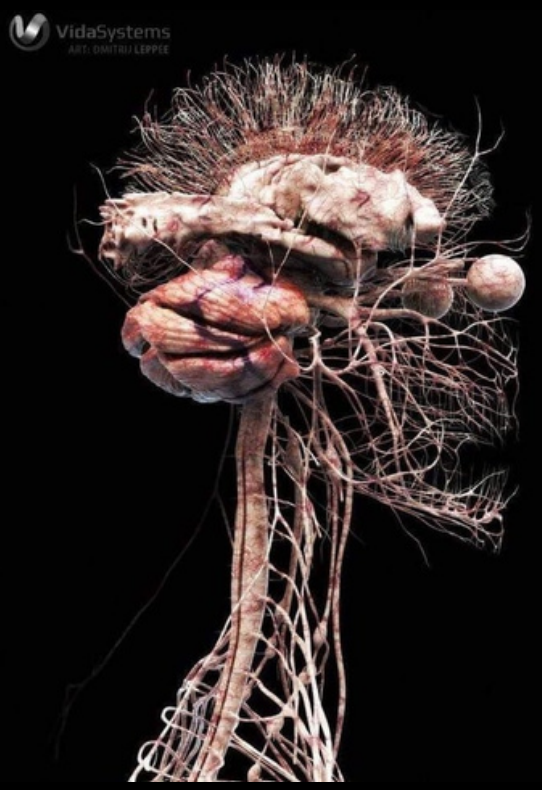
## THE DISSECTED HUMAN NERVOUS SYSTEM

In the fall of 1925, two medical students in Kirksville, Missouri, received a cadaver and a challenge, which was to dissect the body's nervous system, beginning at the base of the brain and working downward, leaving the system in one continuous piece. And they did it, leaving behind this work of wonder, displayed now at The Museum of Osteopathic Medicine at A.T. Still University (ATSU) in Kirksville.

*Image Credit: Museum of Osteopathic Medicine*

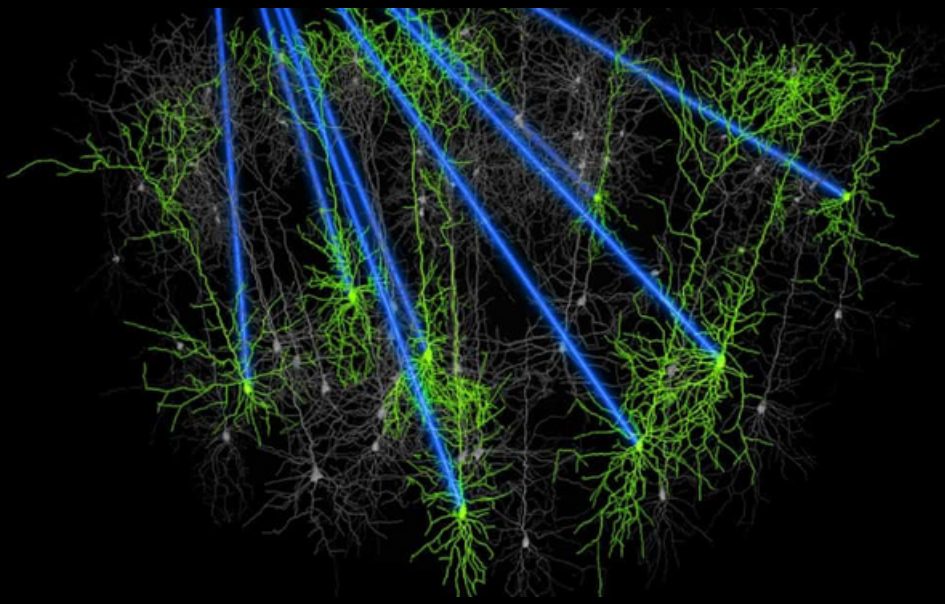
# GALLERY

VISMITHA S | 3RD YEAR BTCZ




3D model of the human nervous system
*Image Credit: Dmitru Lepee*


Stylized three-quarter view of the human brain and it's internal structures in isolation.
*Image Credit: Science Picture Co*



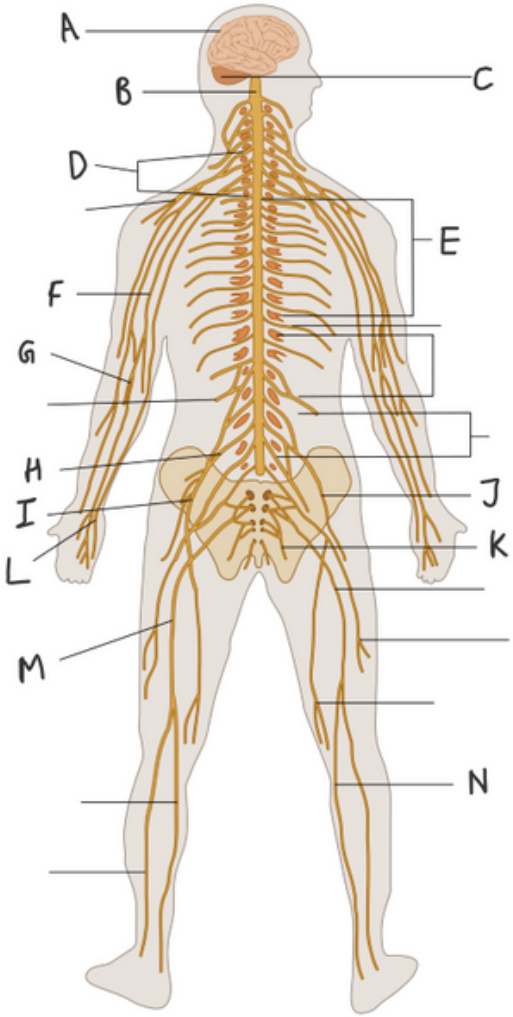
Holographic targeting of laser beams to individual neurons in the mouse barrel cortex.

*Photograph: Lloyd Russell/Häusser Lab/UCL*

# Getting On My Nerves!

**RUPASHRI BALARAMAN | 3RD YEAR BTCZ**

Below is an un-labelled diagram of the human nervous system. Try to guess the names of as many parts and names of nerves marked with capital letters as you can! Look closely at the place where the nerve is located to take a guess at its name. You can look at the hints below the image to get the starting letter of the name.




Hints:

[A] - begins with 'B'
[B] - begins with 'S'
[C] - begins with 'C'
[D] - begins with 'B'
[E] - begins with 'I'
[F] - begins with 'R'
[G] - begins with 'M'
[H] - begins with 'G'
[I] - begins with 'O'
[J] - begins with 'F'
[K] - begins with 'P'
[L] - begins with 'U'
[M] - begins with 'P'
[N] - begins with 'T'

(answers on pg 28 of this publication)

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***GALLERY***

*The Human Brain is a Piece of Marvelous Art*

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*3D Model of the Human Nervous System*

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*Stylised View of the Human Brain*

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*Holographic laser targeting of nerve impulses*

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*Getting on my nerves! (credit for image)*

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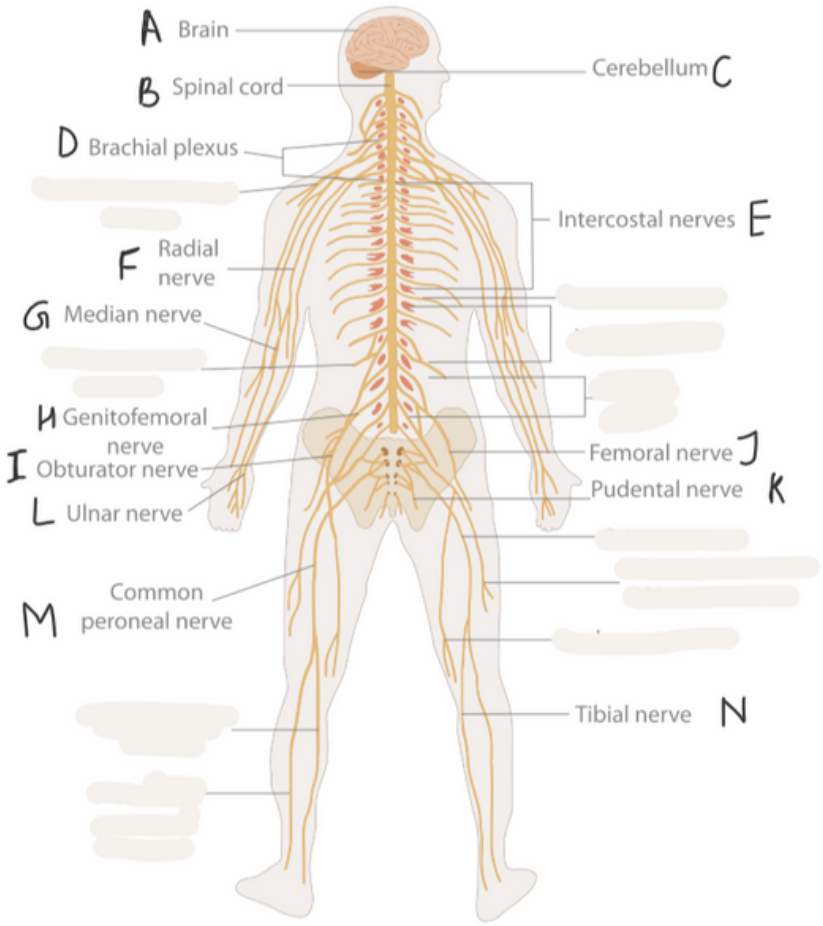
# ANSWERS - 'GETTING ON MY NERVES!'

**A Brain:** The brain is the organ that serves as the center of the nervous system.
**B Spinal Cord:** is a column of nerve tissue that runs from the base of the skull down the center of the back. Together with the brain, it forms the central nervous system (CNS).
**C Cerebellum:** is the part of the brain that controls many motor movements of the body and our balance.
**D Brachial plexus:** nerves connecting the spinal cord to the shoulders for movement of the hands
**E Intercostal nerves:** the nerves that supply the thoracic wall, pleura and peritoneum of the lungs
**F Radial nerve:** it arises from the brachial nerves and supplies the muscle movement of the triceps of the forearms
**G Median nerve:** supplies the front of the forearm. also called "laborer's nerve" as its responsible for coarse movements of our front arms.
**H Gentifemoral nerve:** nerve that receives sensory impulses from the genitalia and legs
**I Obturator nerve:** innervates the thigh muscles, and the hip and knee joints. Arises from the lumbar parts of the spinal cord
**J Femoral nerve:** the main nerve for the front of the thighs and responsible for how we straighten our legs
**K Pudental nerve:** nerve that supplies the external genitalia and the anal sphincters
**L Ulnar nerve:** supplies the muscles of the wrist and the little finger
**M Peroneal nerve:** supplies movement and sensation to the lower leg, knees and toes
**N Tibial nerve:** innervates muscles of the lower leg and the foot



MOUNT CARMEL COLLEGE

# BIOGENEIAC ASSOCIATION

# ...BIOGENESIS...

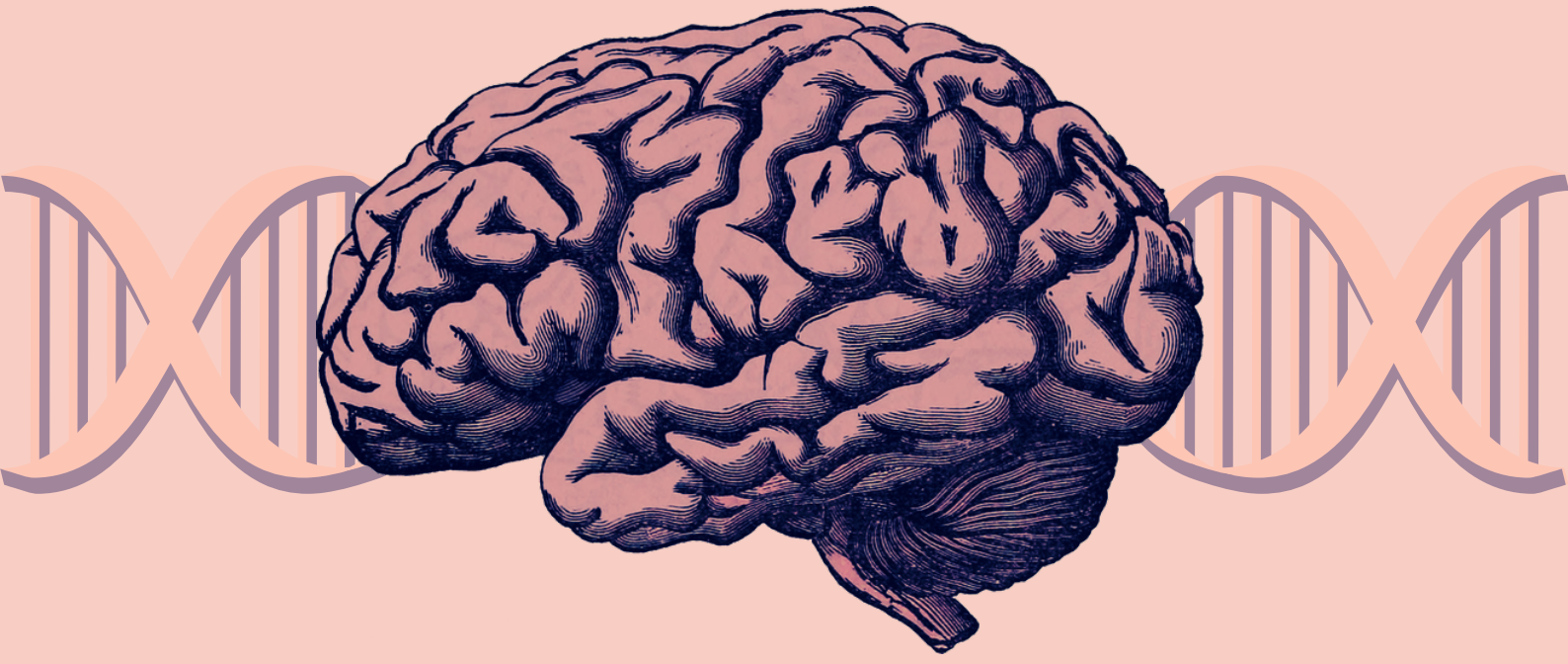
## NOVEMBER 2021 ISSUE

FEATURE ARTICLE ON

# NEUROGENETICS

THANKYOU FOR READING!

Stay tuned for more.



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