GNB1 Encephalopathy- a genetic brain disease

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In news– Researchers from India, Israel, US trying to develop drug to treat rare disease 'GNB1 Encephalopathy'.

About GNB1 Encephalopathy-

- With less than 100 documented cases worldwide, **GNB1 Encephalopathy is a kind of brain disease or neurological disorder which affects individuals in the foetus stage.**
- Delayed physical and mental development, intellectual disabilities, frequent epileptic seizures, are among the early **symptoms of the disease** and since genome sequencing is an expensive exercise, not many parents opt for it early on.
- Researchers at the Indian Institute of Technology (IIT), Madras, Tel Aviv University and Columbia University are studying a rare genetic brain disease called "GNB1 Encephalopathy" and trying to develop a drug to treat it effectively.
- According to a former PhD scholar at IIT Madras, a single nucleotide mutation in the GNB1 gene that makes one of the G-proteins, the **"Gβ1 protein," causes this disease.**
- This mutation affects the patient since they are a foetus. C**hildren born with GNB1 mutation experience mental and physical developmental delay, epilepsy (abnormal brain activity), movement problems.**
- Every cell in the human body has a wide variety of signalling molecules and pathways that help in communicating with other cells and within itself. The major signalling mechanism used by cells is **'G-Protein Coupled Receptor' (GPCR) signalling.**

- **GPCR is a receptor that receives a signal** (e.g. a hormone, light, neurotransmitter) from the outside of the cell and transduces it to the inside of the cell.
- GPCR is present in the cell membrane and has a G-protein (αβγ) attached to it from inside the cell.
- **G-proteins are the immediate downstream molecules** that relay the signal received by the GPCR.
- These G-proteins are present in every cell, and any malfunction will cause disease.
- **Mutations in GNB1 gene cause the neurological disorder (GNB1 Encephalopathy) characterised by general developmental delay,** epileptiform activity in the electroencephalogram (EEG) and seizures of several types, muscle hypotonia or hypertonia, and additional variable symptoms, are seen in the patients.
- As the developmental issues start at the fetal stage, gene therapy is the most plausible option to alleviate the effects of the mutation. However, the development of this complicated procedure will take many years and great investment of funds.
- On the other hand, epilepsy can be treated using specific drugs to increase the patient's quality of life.
- To treat epilepsy, specific targets have to be identified.
- Most epilepsies are caused due to altered ion channel function. Ion channels are proteins that underlie the electrical activity of neurons and heart cells.
- It is also possible that a combination of already existing drugs help in a customised treatment line for the rare disease.

- **The research was supported by Indo-Israel Binational grant offered by Israel Science Foundation (ISF) and India's University Grants Commission (UGC).**
- The researchers pointed out that whole genome sequencing, the elucidation of the full genetic analysis

of the baby, can be very helpful in early diagnosis of the disease.

- They have found that a **potassium channel called G-protein gated Inwardly Rectifying K+ (GIRK) channel (present in brain, heart and endocrine glands) function is affected significantly.**