Huntington's Disease

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Why in News?

Recently, a study by researchers from the University of Szeged in Hungary published in ***Scientific Reports*** has uncovered new insights into Huntington's disease **using fruit flies (Drosophila melanogaster)** as a model organism.

- This innovative approach has provided promising revelations about disease progression and potential therapeutic targets.

What is Huntington's Disease?

- **About:**
  - Huntington's disease is a severe **neurodegenerative disorder** affecting the central nervous system.
  - It is caused by a **mutation in the HTT gene**, producing a faulty **huntingtin (Htt) protein.**
    - Mutant Htt proteins are cleaved into toxic fragments, disrupting various cellular processes.
- **HTT Gene and Polyglutamine Tract:**
  - The HTT gene codes for the huntingtin protein crucial for nerve cell functioning.
    - Mutations in the HTT gene result in an expanded **polyglutamine tract** in the Htt protein, leading to misfolding and dysfunction.
    - The severity of Huntington's disease correlates with the length of the expanded polyglutamine tract.
  - Huntington's disease is **inherited in an autosomal dominant manner,** which means that a **person only needs to inherit one copy of the mutated gene** from either parent to develop the condition.
    - Each child of a parent with Huntington's disease has a 50% chance of inheriting the mutation.
- **Symptoms:**
  - Initial symptoms include forgetfulness, loss of balance, and clumsiness in daily tasks.
  - Symptoms worsen over time, affecting mood, and reasoning, and leading to uncontrollable movements. Patients face difficulties in speaking, swallowing, and walking as the disease advances.
  - Symptoms typically emerge **between ages 30-50.**
- **Treatment:**
  - There is **currently no cure for Huntington's disease,** and available treatments only alleviate symptoms.

What are the Key Highlights of the Study?

- Researchers engineered fruit flies to express the polyglutamine tract of a mutated human HTT gene in their nervous system.
- They used a gene called Gal4 from **baker's yeast(*Saccharomyces cerevisiae*)**, which activates

the expression of genes when bound to a DNA sequence called the upstream activating sequence (UAS).

- The Gal4/UAS system works in the fruit fly genome, allowing the expression of proteins specifically in neurons.
- Fruit flies with the mutated HTT gene displayed neuronal degeneration, impaired climbing ability, and lower viability and longevity.
- A **'control' group of fruit flies** with a normal range of glutamine units in the HTT protein **showed little to no effect.**
- The study found that expressing a **longer glutamine tract** produced symptoms resembling Huntington's disease in humans, while the **shorter tract did not.**
- Researchers found that overexpression of one gene (out of 32 investigated genes in flies) called **Yod1 gene** in flies effectively **eliminated disease-like effects** associated with Huntington's disease, including neurodegeneration and motor impairments.