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## Huntington's Disease

#### Source: TH

#### Why in News?

Recently, a study by researchers from the University of Szeged in Hungary published in *Scientific Reports* has uncovered new insights into <u>Huntington's disease</u> 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 <u>neurodegenerative disorder</u> 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.

The Vision

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