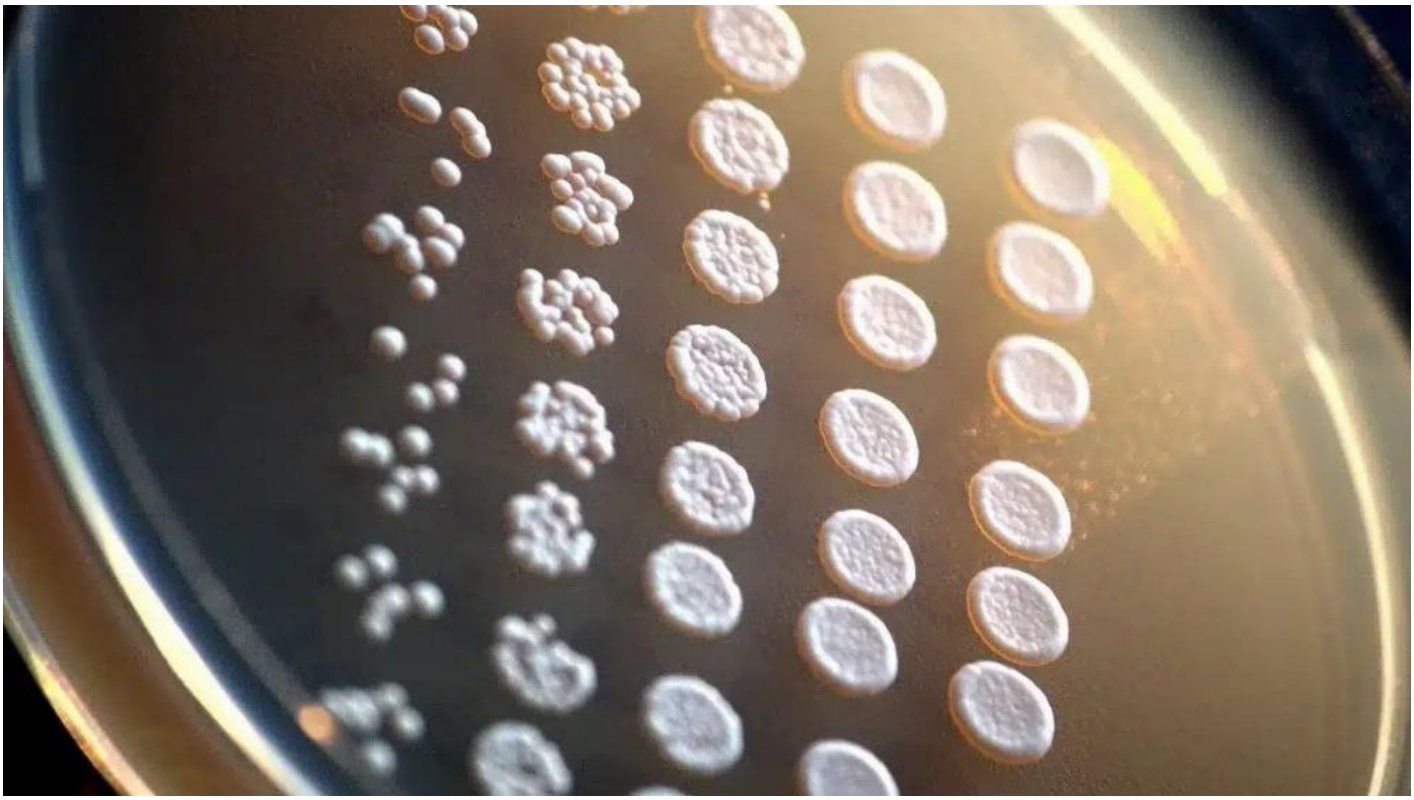
RNA Exosomopathies

May 11, 2025 • vajiramandravi.com



RNA Exosomopathies Latest News

Researchers at Emory University and the University of Texas Health Science Centre have shown that mutations causing brain defects in humans also produce similar effects in budding yeast (Saccharomyces cerevisiae), a simpler eukaryotic organism.

What was discovered?

- These mutations affect a **cellular complex called the RNA exosome**, which plays a critical role in **RNA processing, surveillance, and degradation**.
- This reveals the potential to use **yeast as a model organism** for studying **human neurological disorders** , particularly those related to **RNA exosome dysfunction**.

What are RNA Exosomopathies?

- **RNA exosomopathies** are disorders caused by **mutations in genes coding for RNA exosome components**.

- These disorders primarily lead to **brain maldevelopment**, affecting structures like the **pons** and **cerebellum**.
- A key example is **Pontocerebellar Hypoplasia Type 1 (PCH1)**, which results in **severe motor, cognitive, and developmental impairments** in infants.

Role of the RNA Exosome

- The **RNA exosome** is a **multi-protein complex** discovered in yeast in 1997.
- It is responsible for:
    - **Processing**, **surveillance**, and **degradation** of different types of **RNA molecules**.
    - Maturation of **ribosomal RNA (rRNA)** – essential for building **ribosomes**.
    - Elimination of faulty **messenger RNA (mRNA)** and regulation of **non-coding RNAs (ncRNA)**.

Experimental Findings (Study 1 – Journal *RNA*)

- Researchers **introduced human disease mutations** into corresponding yeast genes.
- Found **defects** in:
    - **RNA surveillance**
    - **Ribosome production**
    - **Protein synthesis**
- Each mutation had a **distinct molecular signature**, explaining the **varied clinical symptoms** in patients.

Creation of a Humanised Yeast Model (Study 2 – Journal *G3*)

- Scientists **replaced segments** of yeast RNA exosome with **human or mouse genes**.
- Of 9 core proteins, **6 were successfully replaced**, with **3 supporting normal yeast growth**.
- Introduced known **brain-defect mutations** into this model.
- Proved that mutations **directly impair RNA exosome function** and are not mediated through indirect processes.

Why Yeast?

- **Yeast is a simple eukaryote**, easy to genetically modify and culture.
- Offers a **cost-effective and fast** method for testing hypotheses and potential **drug interventions**.
- Using yeast models allows **rapid screening** of **RNA exosome mutations** and their **functional consequences**.

RNA Exosomopathies FAQs

Q1. What are RNA Exosomopathies?
Ans: RNA Exosomopathies are a group of genetic disorders caused by mutations in the RNA exosome complex, which regulates RNA degradation and processing in cells.

Q2. What are the common symptoms of RNA exosomopathies?

Ans: Symptoms vary but often include neurodevelopmental delays, skeletal abnormalities, and immune dysfunction, depending on the mutation.

Source: TH
