ecDNA Challenging Genetics Principles

Source: TH

Why in News?

Recently, a study published in ***Nature*** has revealed that **extrachromosomal DNA (ecDNA)**, a previously overlooked component of **genetic material**, plays a significant role in **cancer progression and drug resistance**.

- These findings challenge the conventional understanding of genetics and open new avenues for understanding and treating cancer.

What is ecDNA and How It Challenges Conventional Genetic Principles?

- **About: ecDNA** is a type of **DNA** that **exists outside of chromosomes** in the nucleus of cells.
  - **DNA** stores **genetic information** crucial for an organism's growth, function, and reproduction. In eukaryotic cells, it is coiled into **chromosomes**.
  - Humans have **23 pairs of chromosomes**, with genes on them encoding proteins and determining traits.
- **Formation: ecDNA** forms when **portions of DNA break away from chromosomes** due to processes like **chromothripsis** (chromosomes are broken and rearranged) or **errors** in DNA replication, creating **circular structures** that exist independently within the nucleus.
- **Significance:** ecDNA is commonly **found** in **cancer cells**, where it can contain **multiple copies of oncogenes**, contributing to **tumor growth, genetic diversity**, and **drug resistance.**
- **Challenges to Conventional Law of Genetics:** The conventional principles of genetics are primarily based on **Mendelian inheritance** and the **chromosomal theory of inheritance**, which is challenged by **ecDNA in following ways:**
  - **Disruption of Random Gene Distribution:** Traditional genetics holds that genes are distributed randomly and independently during cell division. ecDNA **defies this principle by forming clusters of multiple genes** that are passed as intact packages, allowing cancer cells to inherit advantageous genetic combinations reliably.
  - **Facilitated Inheritance of Oncogenes:** ecDNA clusters often contain **oncogenes (genes promoting cancer growth)** and other regulatory elements that support tumor survival. This grouping ensures that **cancer cells can inherit and amplify beneficial traits** in a non-random, purpose-driven manner, enhancing their adaptability and resistance to treatments.
  - **Preservation of Favorable Genetic Combinations:** Chromosomes undergo crossing over and recombination during meiosis, leading to genetic diversity. In contrast, **ecDNA preserves specific advantageous** combinations without recombination, maintaining traits critical for tumor progression.

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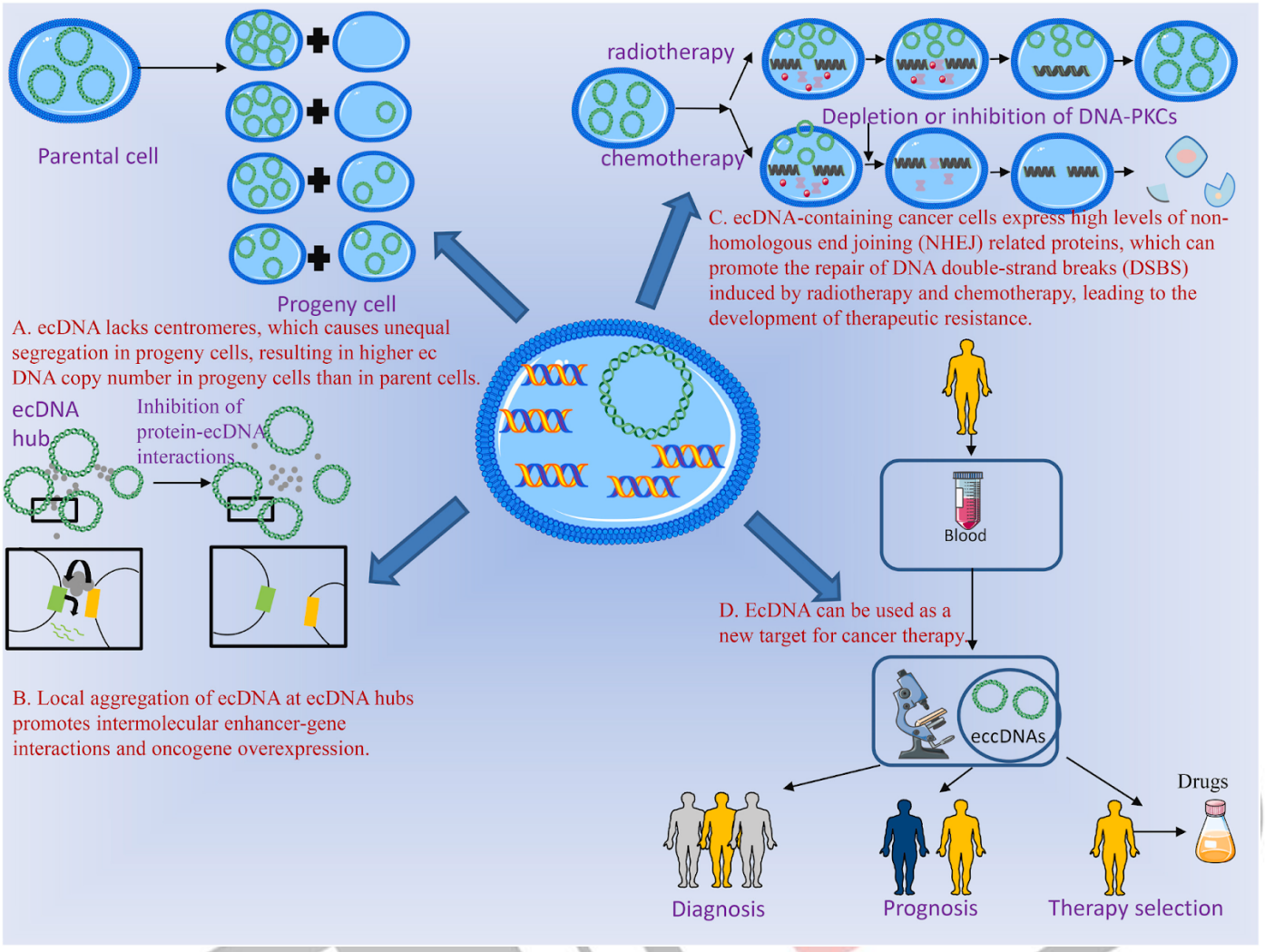

How ecDNA Contributes to Cancer and Drug Resistance?

- ecDNA can carry **multiple copies of oncogenes**, leading to **increased expression of cancer-promoting genes** and **tumor growth.**
    - It can take **regulatory elements (enhancers)** from other parts of the **genome**, causing **abnormal gene activity** that promotes cancer.
- The **non-Mendelian inheritance of ecDNA** creates **genetic diversity within tumors**, complicating targeted treatments.
- ecDNA can **increase the number of genes that help cancer cells pump out drugs** or **change their targets,** making it harder for chemotherapy to work.
    - It allows **cancer cells to quickly develop new mutations**, helping the **tumor resist treatment** and adapt to drugs.

Mendel's Laws of Genetics on Inheritance of Traits

- **Law of Dominance:** Dominant traits always express if present; recessive traits appear only when both gene copies are recessive.
- **Law of Segregation:** Each parent passes one gene copy to offspring during gamete formation.
- **Law of Independent Assortment:** Genes for different traits are inherited independently, unless located close on the same chromosome.

UPSC Civil Services Examination Previous Year Question (PYQ)

Prelim:

Q. Consider the following statements:

1. Genetic changes can be introduced in the cells that produce eggs or sperms of a prospective parent.
2. A person's genome can be edited before birth at the early embryonic stage.
3. Human induced pluripotent stem cells can be injected into the embryo of a pig.

Which of the statements given above is/are correct?

(a) 1 only
(b) 2 and 3 only
(c) 2 only
(d) 1, 2 and 3

Ans: (d)