Cancer Cells' Resistance to Chemotherapy

For Prelims: Chemotherapy, **Cancer,** National Cancer Awareness Day,

For Mains: Government Initiatives related to Cancer, Scientific Innovations & Discoveries

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Why in News?

Recently, a new study, published in *Cell Reports* carried out by researchers at the Netherlands Cancer Institute made a breakthrough in understanding why **certain cancer cells resist a drug called anti-cancer drug (chemotherapeutic agents) Taxol.**

- Their research has the potential to improve cancer treatment by finding ways to overcome this resistance, bringing hope to patients facing this formidable adversary.

What are the Key Highlights of the Study?

- **Challenges of Chemotherapy:**
  - Chemotherapy is a fundamental cancer treatment but poses significant challenges.
  - It involves the **targeting of rapidly dividing cancer cells**, often leading to programmed cell death or apoptosis.
    - However, this mechanism also affects non-cancerous cells. Any tissue with a significant number of normal cells that are also dividing, such as cells in the digestive tract, the bone marrow, and hair follicles are also affected by **chemotherapeutic agents** and **suffer apoptosis.**
    - This cell death underlies the **unpleasant side-effects of chemotherapy**, such as painful **inflammation of the oral cavity and the gut, and nausea,** diarrhoea**,** anaemia**, and hair loss.**
  - Striking a balance between effective cancer cell destruction and manageable side effects is a challenge faced by oncologists.
- **Antibody-Drug Conjugates (ADCs):**
  - Researchers have developed ADCs as a more targeted approach for certain cancer types.
  - ADCs involve attaching drugs to antibodies designed to **recognize proteins predominantly found in cancer cells.**
    - This targeted delivery helps direct chemotherapy directly to cancer cells while sparing healthy ones, reducing collateral damage.
- **Chemotherapy Resistance:**
  - Some **cancer cells can evade the effects of chemotherapy,** which may lead to a **higher risk of cancer relapse.**
    - The study focuses on understanding resistance to Taxol, a commonly used chemotherapeutic agent.
  - **The Role of the ABCB1 Gene:**
    - Resistance to Taxol is closely linked to the **location of the ABCB1 gene** within the

cell's nucleus.
- Sensitive cells exhibit different ABCB1 gene locations compared to resistant cells.
  - In resistant cells, the **gene has detached from the nuclear envelope(membrane) and shifted deeper into the nucleus.**
  - This relocation results in a remarkable 100-fold increase in RNA corresponding to the ABCB1 gene.

- **P-gp Efflux Pump:**
  - The increased RNA levels lead to the production of the **P-gp efflux pump**, which plays a **pivotal role in chemotherapy resistance.**
    - The P-gp pump effectively removes **Taxol and other toxic compounds from the cell**, preventing their accumulation at levels necessary to **arrest cell division and trigger apoptosis.** This allows **cancer cells to persist.**

- **Identifying Lamin B Receptor (LBR):**
  - Researchers sought to understand what anchors the ABCB1 gene to the nuclear envelope in sensitive cells.
    - The study identified the **Lamin B Receptor (LBR) as a crucial protein** influencing the **ABCB1 gene's location and activation.**
  - When LBR is absent, **cells can activate the ABCB1 gene** when exposed to Taxol. However, deleting the gene responsible for making LBR doesn't immediately increase ABCB1 expression; it requires exposure to Taxol. This indicates the involvement of additional factors in silencing ABCB1.

- **Variability in Cancer Cell Responses:**
  - The study highlights variations in how different types of cancer cells respond to the absence of LBR.
    - Some, like lung cancer cells, expressed high levels of ABCB1 RNA.
    - Depleting LBR in lung cancer cells didn't significantly increase Taxol resistance.
    - Breast cancer cells, on the other hand, showed an increased Taxol-resistant fraction after LBR depletion, unlike head and neck cancer cells.
  - This variability in responses of different cancer cells depends on LBR to varying degrees to tether genes to the nuclear envelope.

Chemotherapy

- It is a type of **cancer treatment** that uses powerful anti-cancer drugs to kill **fast-growing cells in the body.** Cancer cells **grow and multiply much more quickly than most cells** in the body.
- Chemotherapy can be used alone or in combination with other therapies, such as surgery, radiation, or hormone therapy.

Cancer

- It is a complex and broad term used to **describe a group of diseases characterised by the uncontrolled growth and spread of abnormal cells in the body.**
  - These abnormal cells, **known as** cancer cells, have the ability to invade and destroy healthy tissues and organs.
- In a healthy body**, cells grow, divide, and die in a regulated manner,** allowing for the normal functioning of tissues and organs.
  - However, in the case of cancer, certain genetic mutations or **abnormalities disrupt this normal cell cycle,** causing cells to divide and grow uncontrollably.
  - These cells can form a mass of tissue called a **tumour.**

What are the Government Initiatives Related to Cancer Treatment?

- **National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke.**
- **National Cancer Grid.**

- **National Cancer Awareness Day.**
- **HPV Vaccine.**

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