Increasing Efficacy of Gene Therapy

For Prelims: Gene Therapy, DNA, Alpha-1 Antitrypsin, Proteostasis

For Mains: Increasing Efficacy of Gene Therapy and its implications

Why in News?

Recently, a study titled **"Secretion of functional α1-antitrypsin is cell type dependent"** has been published, which shows that the Efficacy of **Gene Therapy** can be increased by changing protein regulation networks in the body, helping treat genetic diseases.

What is Gene Therapy?

- Gene therapy is a way to **treat genetic diseases by correcting the source of the error in a patient's** DNA (Deoxy-ribo Nucleic Acid)**.**
- Gene therapy techniques allow **doctors to treat a disorder by altering a person's genetic makeup** instead of using drugs or surgery.
- A harmless viral or bacterial vector is used to **carry a corrective gene into a patient's cells,** where the gene then directs the cell to produce the **proteins necessary to treat the disease.**
- Muscle cells are a common target because **gene therapies injected into the muscle are more accessible than introduction into the body by other routes.**
- But **muscle cells may not produce the desired protein** as efficiently as needed if the job the gene instructs it to do is very different from the one it specialises in.

What are the Findings?

- **Effectiveness of Gene Therapy:**
  - Developed a **strategy to use a harmless version of an adeno-associated virus as a vehicle to deliver AAT (Alpha-1 Antitrypsin) gene therapies** into the body via injection, allowing for sustained release of the protein over several years.
    - AAT is a condition in which **liver cells are unable to make adequate amounts of the protein AAT.**
    - It results in **a breakdown of lung tissue that can cause serious respiratory problems**, including the development of severe lung diseases such as chronic obstructive pulmonary disease (COPD) or emphysema.
  - Adding a molecule called **suberoylanilide hydroxamic acid, or SAHA**, helps muscle cells make AAT at a production level **more like that of liver cells.**
    - Proteostasis is the process that **regulates proteins within the cell in order to maintain the health** of both the cellular proteome and the organism itself.
    - Proteostasis involves a highly complex interconnection of pathways that influence the fate of a protein from synthesis to degradation.
  - Adding SAHA or similar proteostasis regulators to gene therapies can help increase the **effectiveness of these treatments** for many genetic diseases.
    - Patients are usually **treated by receiving AAT via infusion.** It requires patients

to either make regular trips to the hospital or keep expensive equipment at home for the rest of their lives.
    - Replacing the faulty gene that causes AAT shortage in the first place can be a boon for patients.
        - Current gene therapies inject the AAT-producing gene into muscle.
- **Implications:**
    - Increasing the protein production of muscle cells can potentially improve **vaccine immunity.**
    - Adding a protein homeostasis enhancer to the cell could optimize protein yield and increase the effectiveness of the drug.
        - Many drugs are derived from natural sources that rely heavily on a given cell's protein production capabilities.
        - But many of these drugs use cells that aren't specialized to make large amounts of protein.
    - Ways to improve the cellular machinery behind protein homeostasis can help **delay** aging **and open many new doors for treating a wide range of diseases.**

Source: DTE

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