mRNA Vaccines to Fight COVID

Why in news?

Recently, 2023 Prize in Physiology or Medicine was awarded to Katalin Karikó and Drew Weissman for their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19.

Nobel Prize in Medicine 2023
• In human cells, genetic information encoded in DNA is transferred to messenger RNA (mRNA), which is used as a template for protein production. • In 1980s, researchers were able to produce mRNA "in vitro", which was highly unstable and triggered the immune system, leading to inflammatory responses in the body. • Kariko and Weissman found out that *mRNA with chemically modified bases did not lead to inflammatory reactions*, and it significantly increased protein production. • Their work helped in understanding how mRNA interacts with our immune system thereby contributing to the unprecedented rate of vaccine development during the pandemic.

What are mRNA vaccines?

- **Messenger RNA (mRNA)** – It is a type of vaccine that uses a copy of mRNA to produce an immune response. mRNA is a molecule that encodes a sequence that can be made into a protein.
- mRNA vaccine attempts to activate the immune system to produce antibodies that help counter an infection from a live virus.
- **Spike protein**- mRNA vaccines *only introduce a piece of the genetic material* that corresponds to a viral protein.
- This is usually a protein found on the membrane of the virus called *spike protein.*
- Therefore, the mRNA vaccine *does not expose individuals to the virus itself.*
- **Foreign protein**- The vaccine delivers molecules of antigen-encoding mRNA into immune cells, which use the designed mRNA as a blueprint to build foreign protein that would normally be produced by a pathogen or by a cancer cell.
- The vaccines inject cells with instructions to generate a protein that is normally found on the surface of SARS-CoV-2, the virus that causes COVID-19.
- **Immune response**- The protein molecules stimulate an adaptive immune response that teaches the body to identify and destroy the corresponding pathogen or cancer cells.

Advantages	Disadvantages

They are easy to design, speed and lower cost of production. They only need the genetic code and is possible to update vaccines to emerging variants and use them for a variety of diseases.	They may require ultra-cold storage before distribution. They need to be frozen from -90 degree Celsius to -50 degree Celsius.
They induce both cellular and humoral immunity.	They may cause adverse reactions in people susceptible to an autoimmune response.
They do not interact with the genomic DNA.	They may have unknown long term effects.

How mRNA vaccine is different from traditional vaccines?

- **Working-** Traditional vaccines work by giving a person either viral proteins or an inactivated or weakened version of a virus that triggers an immune response.
- Viral vector vaccines like Covishield, carry DNA wrapped in another virus, but mRNA are only a sheet of instructions to make spike proteins wrapped in a lipid (or a fat molecule) to keep it stable.
- **Impact on DNA-** There is no risk of an mRNA vaccine changing DNA because mRNA does not have the ability to alter DNA.
- **Rapid development-** While traditional vaccines can take years, creating an mRNA-based vaccine that targets a newly discovered virus can be accomplished in a short period of time (days to weeks).
- Creating an mRNA vaccine primarily requires knowledge of the viral genetic code. This greatly speeds up vaccine development.

What is the significance of mRNA vaccines?

- **Flu vaccines**- As influenza kills up to 6,50,000 people globally each year, mRNA technology offers the potential of a universal influenza vaccine.
- **Inducing broad immunity -** The mRNA vaccines are based on a specific part of the influenza protein, called hemagglutinin, teaching the cells to recall it and therefore inducing broad immunity across many influenza strains.
- **Cancer treatment-** mRNA is used to mimic “neoantigens” (short bits of tumour proteins on the surface of the tumour cells) identified from an individual patient’s tumour cells.
- Once delivered to the patient’s immune system, their body should produce powerful killer cells called cytotoxic T cells, eliciting a strong anti-tumour immune response.
- **CAR-T therapy**- With mRNA technology, the time consuming and most expensive steps are could be eliminated by delivering the CAR gene directly to T cells in the bloodstream.

  Chimeric antigen receptor T cells (CAR-T) therapy is a form of cancer immunotherapy currently in use around the world to treat certain forms of leukaemia. It uses immune cells called T cells that are genetically altered in a lab to help them locate and destroy cancer cells more effectively.

- **Genetic disease**- mRNA technology is also transforming our response to some genetic diseases such as hereditary angioedema, ATTR amyloidosis, etc.

What lies ahead?

- mRNA is short-lived in cells and protein is only made for a short time. Increasing the lifespan of mRNA in cells would reduce the amount of dosage.

References

1. The Hindu- Beyond COVID vaccines
2. The Hindu- Use of mRNA research to fight COVID

