HIV Capsid as a Drug Target

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Why in News?

A recent study has confirmed that the HIV capsid remains an effective drug target even when resistance develops, reaffirming the potential of drug lenacapavir and opens door for a new generation of HIV drugs.

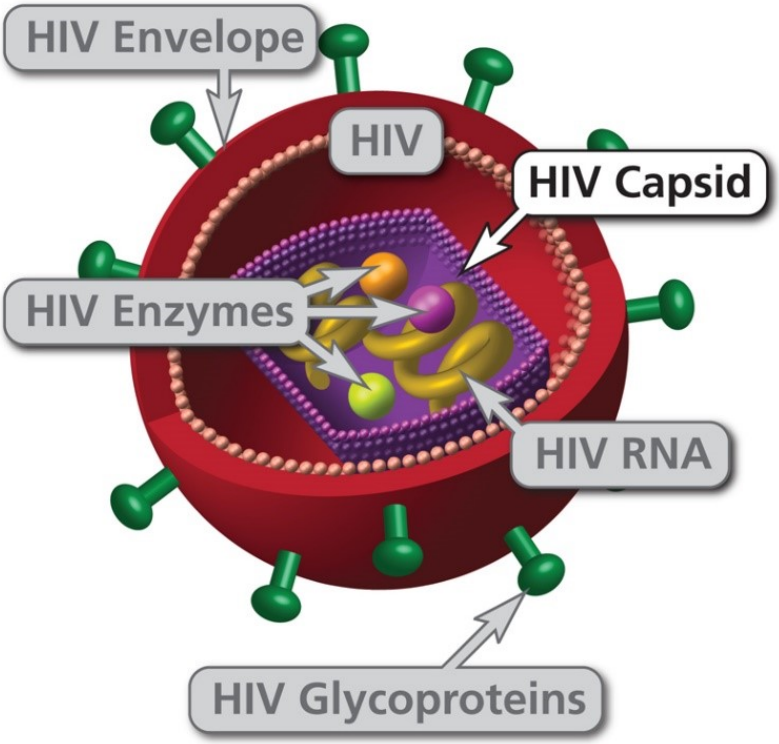
- **HIV –** HIV (Human Immunodeficiency Virus) is ***a type of RNA virus.***

  Viruses contain either DNA or RNA as genetic material, where DNA viruses are more stable and replicate in the nucleus, while RNA viruses mutate rapidly and evolve quickly.

- HIV attacks the body's immune system. Without treatment, it *can lead to AIDS* (acquired immunodeficiency syndrome).
- Once people get HIV, they have it for life. But proper medical care can control the virus.

  A mutation is a permanent change in the genetic material of a cell or microorganism.

- **HIV Mutation –** HIV mutates rapidly while converting its RNA into DNA, creating many variants.
- Some viral parts are vital for survival and cannot change much, such as the HIV capsid protein.
- **HIV Capsid –** The capsid is a ***protective protein shell surrounding the viral RNA.***



Key Findings

- **First HIV Drug –** In 1987, the first HIV drug, *zidovudine*, targeted the enzyme reverse transcriptase.
  - **Resistance –** The drug slowed the virus, but the virus soon became resistant.
- **Target "Must-Keep" Regions –** Researchers focus on essential viral components that cannot mutate without stopping the virus from functioning, effectively closing the window for resistance.
- **Combination Therapy –** This led to the development of combination antiretroviral therapy targeting multiple viral proteins such as reverse transcriptase, protease, and integrase.
- **1999 study –** Found that the capsid forms a unique 3D shape necessary for the virus to survive.
- **Mutation Defect –** Drug-resistant HIV viruses had mutations in specific capsid positions in order to escape the drug, which damaged their own capsid.
- **Efficacy –** Most changes in the capsid protein stop the virus from infecting cells.
- **Lenacapavir –** Initially faced poor water solubility, which is usually a problem for medicines to circulate effectively in the body.
- **Advantage –** This low solubility later became an advantage, allowing it to form a slow-release reservoir under the skin and work for six months with a single injection.

Lenacapavir is the world's first capsid-based HIV inhibitor approved in 2025 by the U.S. Food and Drug Administration.

- **Lenacapavir Effect –** Patients treated with lenacapavir showed small mutations in the virus's capsid protein that diminished the drug's effect.
- **Monotherapy Resistance –** Resistance mainly developed when lenacapavir was used alone. When used with other active HIV drugs (combination therapy), the virus remained well controlled.
- **High Efficacy –** Showed 100% effectiveness in preventing HIV infection in high-risk individuals.
- **Result –** Lenacapavir in combination therapy made the virus weaker, and the resistant viruses ***multiplied at only 20–30% of their normal rate.***
- But it is *not a cure, and is considered close to an HIV vaccine* in preventive potential.

Reference

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