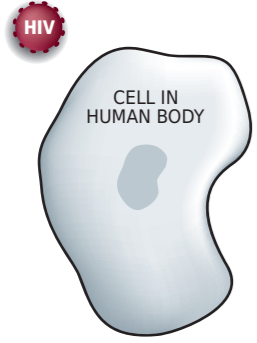
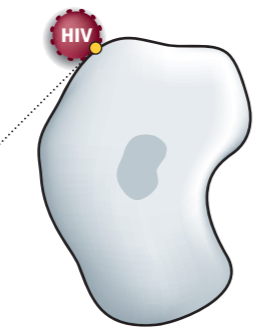


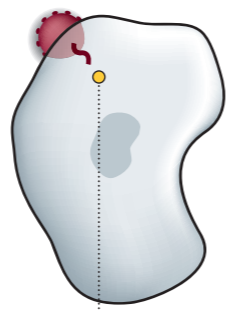
**Life cycle:
How HIV infects cells
and reproduces**



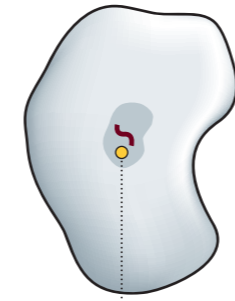
1. The HIV virus floats in the bloodstream along with thousands of other cells and microscopic organisms.



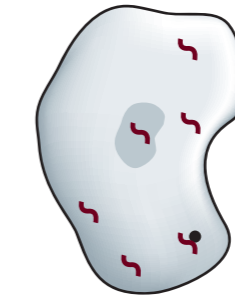
2. Receptors on the outside of the virus seek and attach to receptors on healthy cells, typically human immune cells.



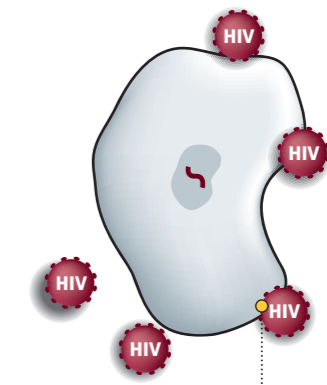
3. The virus then fuses into the cell, sending its genetic material toward the cell's nerve center, the nucleus. Along the way, an HIV enzyme, called reverse transcriptase, transcribes that genetic material into DNA.



4. Another enzyme, called integrase, takes this viral DNA and inserts it into the host cell's DNA. Once complete, this cell is permanently infected and begins creating more virus.



5. The host cell can remain dormant for months or years. Once activated it becomes an HIV factory.



6. An enzyme called protease triggers the final assembly of the virus. Once assembled, the virus breaks away, ready to infect another host.

**The four classes
of drugs that target
HIV's actions:**

Fusion / entry inhibitors
A new class of drugs seeks to disrupt the virus' docking mechanics, keeping the virus from connecting and fusing into a host cell.

Reverse transcriptase inhibitors
One of first treatments developed, it seeks to block the machinery that creates DNA. Without the DNA the virus cannot take over the host cell. Mutations have enabled the virus to overcome many of these drugs. The drug being developed by Eddy Arnold's team is this type; see below.

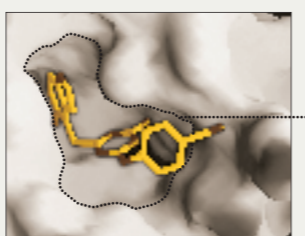
Integrase inhibitors
Theoretically, this class of drugs would disrupt the process of combining the HIV DNA and host DNA. So far this treatment has been difficult to develop.

Protease inhibitors
Disable the protease enzyme so the new virus does not mature and is noninfectious. Side effects and resistance have made these drugs increasingly unpopular.

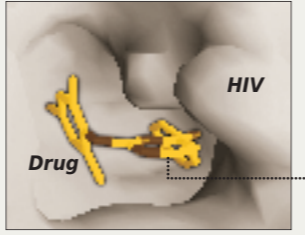
Resistance and the DAPY compounds

How resistance happens
Simply put, the virus, in its endless rounds of replication, constantly makes copies of itself that contain tiny mistakes in genetic code, producing offspring that are slightly different.
If the differences change the part of the virus a drug was targeting, the drug may no longer be effective and the virus is said to be a "resistant" strain.
As viral varieties targeted by drugs die off, mutant strains thrive, ultimately predominating.

How DAPY compounds avoid resistance
Early RT inhibitors were rigid. They jammed a "pocket" that is part of the machinery of RT. But new virus strains had a differently shaped pocket, and the inhibitors were rendered obsolete.
The DAPY compound is flexible and essentially "wiggles and jiggles" to jam the pocket on each strain of the virus. It is a master key made of silly putty, so far overcoming resistance that foiled earlier RT inhibitors.



Each panel shows a different HIV strain with a "pocket" whose shape is slightly different from the others.



Because of the DAPY compound's flexibility, it can effectively jam each variation.



Images provided by Kalyan Das, Rutgers University

ANDREW GARCIA PHILLIPS, THE STAR-LEDGER
SOURCE: Center for Advanced Biotechnology and Medicine, Rutgers University and UMDNJ