Structural insights into a multidrug-resistant HIV-1 protease in complex with a protease inhibitor

Rishitha Kakarlapudi, Sirisha Kolli and Ravikiran S. Yedidi*

The Center for Advanced-Applied Biological Sciences & Entrepreneurship (TCABS-E), Visakhapatnam, Andhra Pradesh, India. 530002.

*Correspondence to RSY: tcabse.india@gmail.com

INTRODUCTION

HUMAN IMMUNODEFICIENCY VIRUS-1

HIV is a variation of virus that can be transmitted to African chimpanzees. Scientists suspect the simian immunodeficiency virus (SIV) jumped from chimps to humans when people consumed chimpanzee meat containing the virus.

Once inside the human population, the virus mutated into what we now know as HIV. This likely occurred as long ago as the 1920s.

HIV spread from person to person throughout Africa over the course of several decades. Eventually, the virus migrated to other parts of the world. Scientists first discovered HIV in a human blood sample in 1959.

It's thought that HIV has existed in the United States since the 1970s, but it didn't start to hit public consciousness until the 1980s.

HIV-1 is the most common type of Human Immunodeficiency Virus. It attacks your body's immune system. The virus destroys CD4 cells. These cells help your body fight infections. HIV-1 can severely damage your immune system and lead to Acquired Immune Deficiency Syndrome (AIDS).HIV infection is caused by the human immunodeficiency virus. You can get HIV from contact with infected blood, semen, or vaginal fluids. Most people get the virus by having unprotected sex with someone who has HIV. Another common way of getting it is by sharing drug needles with someone who is infected with HIV.

CAUSES OF HIV:

1. having vaginal or anal sex.
2. sharing needles or syringes for shooting drugs, piercings, tattoos, etc.
3. getting stuck with a needle that has HIV-infected blood on it.
4. getting HIV-infected blood, semen (cum), or vaginal fluids into open cuts or sores on your body.
5. by sharing tattoo equipment without sterilizing it between uses
6. during pregnancy, labor, or delivery from a pregnant person to their baby
7. during breastfeeding.

HIV DOES NOT TRANSFER THROUGH:

skin-to-skin contact,hugging, shaking hands, or kissing,sharing food etc.

HYPOTHESIS:

As HIV lowers the CD4 cell count, the immune system weakens. A typical adult's CD4 count is 500 to 1,500 per cubic millimeter. A person with a count below 200 is considered to have AIDS.

How quickly a case of HIV progresses through the chronic stage varies significantly from person to person. Without treatment, it can last up to a decade before advancing to AIDS. With treatment, it can last indefinitely.Also, treatment can typically help manage opportunistic infections.

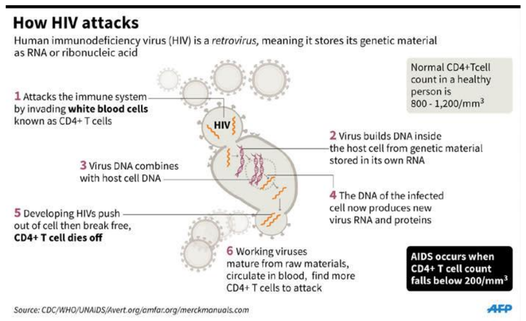
HIV and AIDS are related, but they're not the same thing. There is no cure for HIV,but can be controlled..to some extent.,

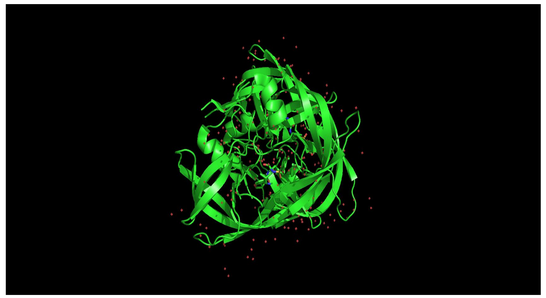
Many researches are being done to cure HIV.

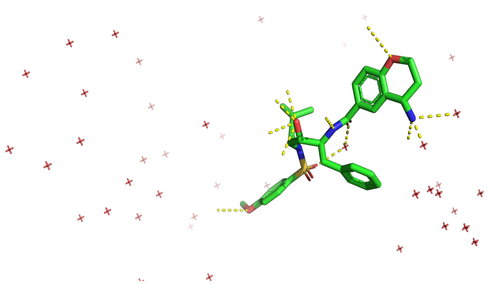
EXPERIMENTALS

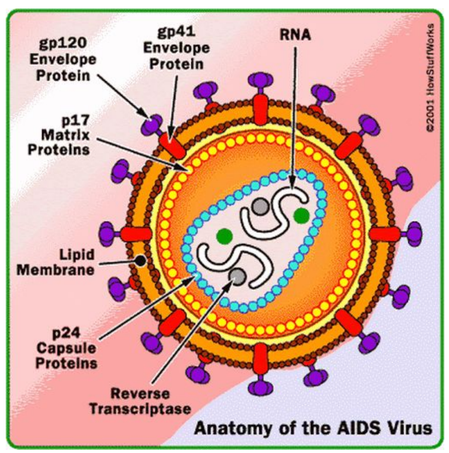
In order to understand the overall crystal structure of multidrug-resistant clinical isolate AO2 HIV-1 protease in complex with non-peptidic inhibitor, GRL079-3D dimensional analysis of the structure was done using computational biology tools.

Structure of GRL079 was downloaded from protein data bank(PDB ID:-4RVX).The analysis includes evaluation of the secondary structure(alpha helices and beta strands)followed by H-bonding analysis using PyMOL software.









RESULTS & DISCUSSION

There are 12 Hydrogen bonds in the drug molecule.The bond lengths are 3.4,2.9,2.7,2.7,2.0,3.1,3.3,3.3,3.1,2.7,2.7,3.5.(in Angstroms).
The average of all the bond lengths is 2.57(in Angstroms).
Strong bonds must have a bond length which is less than 3 Angstroms.Where as weak bonds have a bond length which is equal to 3 or more than 3 Angstroms.

So,by analysis we found that strong bonds =6.
weak bonds= 6.
There are alpha and beta helices.

ASSOCIATION OF H-BONDS:-

One end of Hydrogen bond should be attached with drug and other should be attached either with protein or water molecule which is the primary requirement .
4 H-bonds are in association with drug and water molecule.
The remaining 8 H-bonds are in association with drug and protein molecule.

SUMMARY:-

In general peptidic drugs have very poor pharmacological activity,poor oral bioavailability,rapidly excreted and susceptible to hydrolysis.
So,they will have short half lives in the bloodstream often requiring high doses to inhibit metabolism.
They also have side effects due to cross reactivity with endogenous proteases.

ADVANTAGE OF THIS DRUG:-

This drug is non peptidic,and it may have orthogonal resistance and diverse range of structural features make cross resistance less comparatively.

It helps patients to take doses of drug easily.And it will have less side effects.
This drug is valid .

REFERENCES

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