Development of drug molecules for targeting HIV with protease inhibitor

HIV is a major human health concern throughout the world. It is a virus that goes through many steps during its life cycle. Once HIV infects a human cell, the virus uses proteins and chemicals inside that cell to make more copies of it. Protease is a chemical, known as an enzyme that HIV needs in order to make new viruses. Protease inhibitors (PIs) block the protease enzyme. When protease is blocked, HIV makes copies of itself that can't infect new cells. Studies have shown that protease inhibitors can reduce the amount of virus in the blood.

When a person suffers from AIDS (Acquired Immunodeficiency Syndrome) also known as HIV (Human Immunodeficiency Virus) his body undergoes a condition in which his body's specific defence mechanisms stop functioning. This occurs due to the gradual loss of immune cell function. This happens because the cells of the body start allowing interference by other infectious agents, and the body to fight infection reduces. The HIV virus infects the white blood cells also known as macrophages, dendritic cells and T-helper cells.

There is no definitive cure for AIDS and therefore it is a serious public health problem especially in developing countries due to the high cost of current drugs where only a small percentage of infected people benefit from the available treatments. The therapeutic strategies include inhibitors directed at various stages in the life cycle of HIV.

Attempts for eradication of human immunodeficiency virus (HIV) resulted in discovery of powerful antiviral compounds. The highly active antiretroviral therapy (HAART) has showed significant improvements in the disease state therefore HAART is also called as Potent Antiretroviral Therapy (PART). Drugs help in control of viral replication but eradicating the same is being researched at.

The virus persists even after long periods of treatment due to the presence of cellular reservoirs. These contain latent viruses which are found to be capable of producing new infectious particles. Patients getting treatment stop mid-way due to the onset of side effects and viral resistance often develops, making one or more of the drugs ineffective. It is clear that HIV virus replicates itself in the human body, hence it is important that drugs are developed that can treat the virus at various stages.

Dr. Mala Rao and her research team at National Chemical Laboratory (NCL), Pune have isolated an extremophilic Bacillus sp., which produces an aspartic protease inhibitor (ATBI). ATBI has been characterized for its inhibition against recombinant HIV-1 protease, pepsin, and the protease from the fungus named Aspergillus saitoi. CSIR-NCL scientists also isolated and purified several other protease inhibitors from different natural sources. Currently, ATBI and the other purified inhibitors are being studied as a lead molecule for designing potent inhibitors.

The first biologically derived molecule that inhibits HIV-1 Protease has been isolated by the team at NCL led by Dr. Mala Rao. This enzyme is responsible for the multiplication of the AIDS causing virus. The molecules were isolated from a robust microbe that thrives in high temperatures and alkaline conditions in a hot spring at Vajreshwari, in Thane district. The effort is viewed as a new approach to isolation of rare bio-molecules.

Reference:

1. Chandravanu Dash and Mala Rao (2001), Interactions of a Novel Inhibitor from an Extremophilic *Bacillus* sp.with HIV-1 Protease, The Journal Of Biological Chemistry, Vol. 276, No. 4, Issue of January 26, pp. 2487–2493, 2001.
2. Dash, C, Ahmad, A, Nath, D and Rao M, (2008), Antimicrob. Agents Chemother, vol. 48, No. 7, pp. 2017
3. http://www.nclinnovations.org/technology.php

For further details contact Dr. Mala Rao at mb.rao@ncl.res.in or Dr. Absar Ahmed at a.ahmad@ncl.res.in