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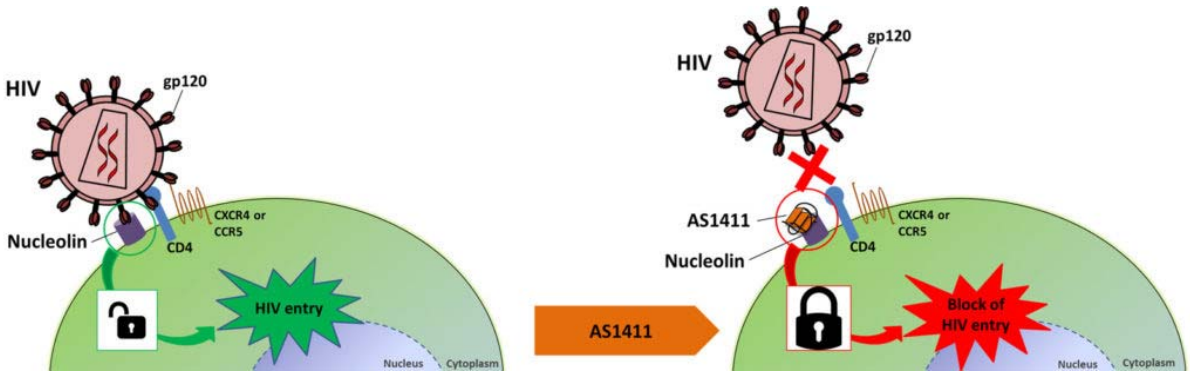
Locking out HIV from human cells: a new powerful approach

Picture your home, the safest place in the world. And now imagine a criminal that wants to enter and become you home landlord. And imagine that the criminal has the key. What would you do to protect your home? Probably you would block the lock as soon as possible. No lock means no unwanted entry.

We can compare HIV, the virus that has afflicted human health worldwide since the 80's, to a criminal that wants to enter your cells, your home in the above example, and destroy them. HIV has the key to our cells. How can we block HIV entry? We recently found an answer.



Inhibition of HIV-1 entry by AS1411. AS1411 is able to block HIV-1 infection by binding to the cell surface Nucleolin and interfere with HIV-1 cell attachment

HIV has a special key to recognize and infect human cells, a viral protein called gp120. This key is able to recognize and bind the locks, cellular proteins located at the external surface of the cell: when this binding occurs the "lock" opens and the virus enters.

The lock we have focused on is a cellular protein called Nucleolin. We were able to find a specific blocker of Nucleolin, named AS1411.

The lock: Nucleolin is a cellular protein that is present in all our cells playing several essential roles. One of the most interesting roles related to HIV infection occurs when Nucleolin is located on the outer membrane of the cell. Here Nucleolin can be recognized by a specific viral protein, the HIV gp120, favouring the first recognition between the virus and the cell.

The blocker: AS1411 is a small piece of synthetic DNA that is able to adopt a very peculiar shape that perfectly fits on Nucleolin. One of the major advantages of AS1411 is that it has already been tested in patients as an antitumor drug: it displayed no antitumor activity but it has been shown to be extremely well tolerated by patients. This evidence makes AS1411 an excellent drug candidate.

Combining the above information, we tested our idea: if AS1411 binds to Nucleolin and masks it, gp120 the key of the virus, would no more be able to contact the lock. And so, HIV would not be

able to enter into the human cells. Our results indeed proved that this small fragment of DNA is able to completely block the viral infection with no side effect for the cell. AS1411 is active against different viral strains of HIV and in different types of infected cells, including cells from a human donor. We also confirmed that Nucleolin is indeed the target of AS1411. Thus, we propose AS1411 as an effective, safe and inexpensive antiviral agent with a new mechanism of action against HIV. The fact that AS1411 has been already tested in humans makes it available for priority testing against HIV patients.

This discovery is very exciting since new therapies against HIV are extremely needed because the virus tends to become resistant to all other available drugs during the therapy.

And HIV is as yet a worldwide health and socio-economical emergence as evinced by the following data: 78 million people have been infected by HIV since the beginning of the pandemic in the 80's; 36.7 million people were seropositive worldwide in 2015: of these, 2.6 millions were children. Less than 50% of seropositive people have access to current antiretroviral therapy. New infections were estimated to increase by 8% per year in 2012 in Europe; 2 million new infections worldwide occur per year. 1.2 million HIV-related deaths were reported in 2014.

Imagine a world without HIV and AIDS….we have made a step forward to make it real.

Rosalba Perrone *and* ***Sara N. Richter***
Department of Molecular Medicine, University of Padua, Padua, Italy

Publication

The G-quadruplex-forming aptamer AS1411 potently inhibits HIV-1 attachment to the host cell.
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