New natural mechanisms have been identified that prevent the common marmoset from becoming infected with HIV

Researchers at the Severo Ochoa Centre for Molecular Biology (jointly run by the UAM and CSIC), and the Dana-Farber Cancer Institute of Boston (USA) have demonstrated the existence of new mechanisms that prevent HIV infection in monkeys in Latin America. The study, published in the journal Scientific Reports, could help in the development of new drugs to fight the virus.

A team with Spanish participants has demonstrated the existence of at least two new factors that block infection by HIV-1 in certain monkeys on the American continent, specifically the common marmoset. The work, published in the journal Scientific Reports, identifies that these blocks act at an early stage of the virus’s replication, soon after its entry into the cell.

“Although we still don’t know the identity of the cellular proteins responsible for these blocks, our study gives some clues as to how and where these factors act,” says Beatriz Pacheco, the CSIC researcher who led the research.
According to this work, the first block, called Lv5, acts at a very early stage of the replication cycle: following the entry of the virus into the cell, there is a process of reverse transcription in which the virus genome is copied from an RNA molecule to DNA, and is subsequently integrated into the cell genome, where it can help to form new viruses. Thus Lv5 intervenes by preventing this reverse transcription process.

The second factor, Lv4, acts by blocking the integration of proviral DNA into the cellular genome. In addition, the researchers observed that the viral capsid plays an important role in this block, and identified some mutants capable of countering the action of Lv4.

“Many of the current antiretroviral drugs act by inhibiting the reverse transcription process, or the integration of the virus into the viral genome. Our results are interesting because they are a natural antiretroviral mechanism that is present in some species,” explains Beatriz Pacheco.
Natural resistance

Other studies have identified that there are some people infected with HIV who, even without antiretroviral treatment, do not develop AIDS and are capable of maintaining a viral load at extremely low or even undetectable levels. They are the so-called long-term non-progressors and elite controllers.

The reasons for this intrinsic resistance to the virus appear to be varied and in some cases are still unknown. However, sometimes it appears due to factors intrinsic to the innate immune system of these individuals.

A study of the factors responsible for natural resistance in some primates against HIV or the simian immunodeficiency virus (SIV), as well as the capacity of some people to control HIV infection, could open up the way to the development of new therapies that allow the virus to be eliminated in infected patients, or to prevent new infections.

Resistance in American monkeys

The current pandemic of infection by HIV has its origins in the zoonotic transmission of very similar viruses, called simian immunodeficiency viruses (SIV), which infect many monkeys and great apes on the African continent. In its natural host, SIV rarely cause illness, due to a long process of viral-host coevolution. However, when one of these viruses jumps from one species to another, it may sometimes lead to illness. This was what happened with the HIV that infects human beings.

Type 1 HIV, which is responsible for the vast majority of infections, is only capable of infecting humans and chimpanzees (and also probably gorillas). This limited tropism is due to the presence of factors that block the replication of the virus in a species-specific manner.

These barriers may be factors that the virus needs at some point in its cycle to replicate in the cells of the infected individual, but that exhibit differences between species preventing the virus from making use of them. Another barrier may be the existence of factors called restriction factors that act in a dominant way, preventing the replication of the virus in some species. These restriction factors form part of the innate immunity system.
The team responsible for the present work, made up of scientists from the Severo Ochoa Centre for Molecular Biology, a centre run jointly by Universidad Autónoma de Madrid (UAM) and the Higher Council for Scientific Research (CSIC), and the Dana-Faber Cancer Institute of Boston, USA, is working to study the reason for natural resistance to HIV-1 infection in the common marmoset (*Callithrix jacchus*).

To date, no virus similar to HIV or its cousin SIV has been identified that infects monkeys on the American continent naturally. In addition, the common marmosets are apparently resistant to infection by HIV and SIV. “Our research project is focused on identifying and characterising the cellular proteins responsible for this resistance. We have managed to observe that in the lymphocytes of these monkeys, the HIV target cells, there are many blocks to the replication of HIV-1,” says Beatriz Pacheco.

**Bibliographical Reference:**

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