

# A more complex HIV family tree discovered

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Adding another component into an already complicated effort to identify weaknesses within HIV, a team of Los Alamos scientists discovered that HIV variation in the human population is driven by more than a person's immune response.

The common ancestry of HIV strains explains many of the viral mutational patterns that previously gave rise to a belief that the virus adapted in predictable ways within people with similar immune systems. While human immune responses do drive viral evolution, these recent findings show that the story is more complex, providing a more detailed, accurate picture of HIV's evolution and the need for a new path to the development of a viable vaccine.

In a paper published in the March 16 issue of *Science Magazine*, Los Alamos researchers Tanmoy Bhattacharya, Marcus Daniel, and Bette Korber — along with their colleagues — explain that the sequence of a virus is dictated not only by the way in which it mutates to escape detection by a host's immune system, but also by the common source and evolutionary track of the virus itself.

“In biology or any other system of evolving entities, when we try to find the relation between any characteristics and a mutational pattern — like a viral change and the immune system of the person it finds itself in — one should never forget that the organisms haven't arisen at random but are descended from a common ancestor,” said Bhattacharya.

Because viruses are similar due to common descent alone — i.e. HIV

transmitted among a group who shared needles or individuals infected via sexual transmission from each other -- Bhattacharya asserts that the common source, rather than just the similarities in the hosts' genetic structures, may account for many of the observed similarities among the viruses. He said population studies of this kind, in which scientists were investing, are probably not a good way to find all the parts of the virus visible to the immune system.

Conversely, the new research methodology, which accounts for such viral lineages, allows scientists to better understand how HIV adapts in the context of the human immune system. "The virus is changing in different people in different ways. This paper's main point is basic biology -- understanding the relationship between host and virus," said Korber.

"Also, it introduces new methodology for looking for correlations between viral mutations and a viral characteristic (like immune escape), taking into account a good model of the virus' evolutionary history," she said.

The researchers predict that this new discovery will have a major impact on vaccine design. "Since HIV escapes the immune system of the human host by mutation, and the virus finds multiple ways of escaping immune recognition, our findings have practical implications for defining relevant variants for inclusion in vaccine antigens," said Korber.

In addition, as the research presented shows that scientists cannot find all the regions of the virus (called epitopes) that are useful targets for the immune system without expensive patient by patient analysis -- and the virus finds multiple ways of evading the immune system -- a vaccine has to be versatile enough to address these complications. In a previous paper published on December 24, 2006 in *Nature Medicine*, Lab scientist

William Fischer, Korber, Bhattacharya, and team offer a vaccine model based on a mosaic of synthetic proteins that subsequently address these factors.

“We present ideas of how to deal with the situation of not knowing where the epitopes are and the virus having multiple escape paths,” said Bhattacharya.

Additionally, according to Korber and Bhattacharya, their findings are not limited to HIV and can be applied in researching other viruses like Hepatitis.

“The methods we developed are of generality and will be useful in studies whenever we want to know whether some property of the virus (like which person it was extracted from, when in the infection cycle it was found, etc.) is to be correlated with the genetic sequence data obtained for it,” said Bhattacharya. “It is this generality, and the basic biology, which actually makes the paper important.”

Source: Los Alamos National Laboratory

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