MedicalXpress

New Stanford list of HIV mutations vital to tracking AIDS epidemic

March 6 2009

In a collaborative study with the World Health Organization and seven other laboratories, researchers at the Stanford University School of Medicine have compiled a list of 93 common mutations of the AIDS virus associated with drug resistance that will be used to track future resistance trends throughout the world.

The researchers analyzed data from about 15,220 patients across the globe to develop an updated and accurate list of the most common, resistance-related mutations of the virus. The list will be published March 6 in the online journal *PLoS-One*.

"The epidemic is changing, especially as new drugs are being developed," said Robert Shafer, MD, associate professor of infectious diseases and geographic medicine at Stanford and the senior author of the paper. "To effectively track the spread of drug resistance, particularly transmitted drug resistance, you need a sensitive and specific list that's considered standard and is adopted by all the surveillance studies."

The list is important, he said, as it helps countries gauge the effectiveness of their HIV medication programs. But assembling such a list can be a challenge, particularly with a virus that has so many resistance-related variants. On the one hand, if the list is too liberally defined, then HIV drug funders and providers may believe resistance is more widespread than is actually the case.

"That will cause problems in countries. They may be concerned about whether their drugs will work," Shafer said.

On the other hand, if the list is too restrictive, there is a risk of underestimating the actual extent of resistance, he said.

"So there is a real challenge to using the right number of mutations," Shafer said.

In 2007, Shafer and his colleagues published a similar list of 80 HIV mutations that has since served as the basis for global AIDS surveillance work. However, with the scale-up of antiretroviral drug programs in the last two years and the introduction of new medications, resistance patterns have changed. So there was a need for a newly updated reference, he said.

The data used in the study was derived from a publicly available, searchable database that Shafer and his colleagues began at Stanford in 1998. Known as the Stanford HIV RT and Protease Sequence Database, it includes information on the two key proteins targeted by HIV drugs: reverse transcriptase and protease. More recently, the researchers have begun gathering resistance data on integrase inhibitors, the latest class of antiretroviral drugs to be introduced. However, this data was not included in the study, as these drugs are not yet in wide use, particularly in developing countries.

To compile the latest list, the researchers added data from other laboratories in Europe, Canada and the United States to include more than 15,000 sequences from untreated individuals, double the number available in 2007. To ensure geographic diversity, information was included for eight different subtypes of the virus, as these vary from one region of the world to another.

The researchers scoured the data to ensure they included only those mutations that were clearly recognized as causing or contributing to resistance. They excluded polymorphisms, or variants of the virus that can arise naturally, as well as drug-related mutations that occur rarely.

The result was that 16 new mutations were added to the 2007 list, while three were dropped. Shafer said it was reassuring to find minimal changes were needed.

"It shows the first list was quite good," he said.

Shafer's Stanford colleagues in the study are Mark Kiuchi, Tommy Liu, Soo-Yon Rhee and Jonathan Schapiro, MD. The research was funded by the National Institutes of Health.

More information: The Stanford database can be found at: http://hivdb.stanford.edu.

Source: Stanford University Medical Center