Researchers identify two FDA approved drugs that may fight HIV

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Researchers at the University of Minnesota Academic Health Center have identified two drugs that, when combined, may serve as an effective treatment for HIV.

The two drugs, decitabine and gemcitabine - both FDA approved and currently used in pre-cancer and cancer therapy - were found to eliminate HIV infection in the mouse model by causing the virus to mutate itself to death - an outcome researchers dubbed "lethal mutagenesis."

This is a landmark finding in HIV research because it is the first time this novel approach has been used to attack the deadly virus without causing toxic side effects. Because decitabine and gemcitabine are already FDA approved, researchers believe that if their research is effective in large animal models, it will be much easier to expedite the development of the drugs for human use.

The study is a collaboration between molecular virologists Louis Mansky, Ph.D., and Christine Clouser, Ph.D., of the Institute for Molecular Virology and School of Dentistry, as well as medicinal chemist Steven Patterson, Ph.D., from the Center for Drug Design. The findings were recently published online in the Journal of Virology.

"The findings provide hope that such an approach will someday help the 33 million people worldwide who currently live with HIV," Mansky said.

Lethal mutagenesis

HIV mutates and evolves quickly. Rather than inhibiting virus growth and replication like current HIV drugs, this new drug combination forces the virus to do just the opposite - evolve beyond control, to the point of extinction.

"HIV's ability to mutate makes it difficult to target and treat," Mansky said. "We wanted to take advantage of this behavior by stimulating HIV's mutation rate, essentially using the virus as a weapon against itself."

Drug repositioning

One way to decrease cost and expedite the development of novel drugs is by the use of drug repositioning, the process of taking a drug that is used to treat one medical condition, and using it to treat a different illness.

By examining drugs that are already approved by the Food and Drug Administration, the researchers hope to expedite the development of this drug combination because the safety profiles of the two drugs are known.

U of M researchers found that the drug concentrations needed to eliminate HIV infection cause no measureable cell toxicity and were effective against HIV cultures at concentrations well below the current levels used for cancer treatment.

The path ahead

Gemcitabine and decitabine have been administered in pre-clinical trials with mice. Initial findings confirm that the drugs are an effective

antiviral therapy for HIV.

The researchers are now in the process of modifying the drugs to forms that can be absorbed by the human body when taken orally.

Provided by University of Minnesota