Body's anti-HIV drug explained

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Humans have a built-in weapon against HIV, but until recently no one knew how to unlock its potential.

A study published online by the journal *Nature* reveals the atomic structure of this weapon – an enzyme known as APOBEC-3G – and suggests new directions for drug development.

APOBEC-3G is present in every human cell. It is capable of stopping HIV at the first step of replication, when the retrovirus transcribes its RNA into viral DNA.

The study's authors, led by Xiaojiang Chen of the University of Southern California, were able to show the atomic structure of the active portion of APOBEC-3G.

The discovery suggests how and where the enzyme binds to the viral DNA, mutating and destroying it.

"We understand how this enzyme can interact with DNA," said Chen, a professor of molecular and computational biology at USC. "This understanding provides a platform for designing anti-HIV drugs."

If APOBEC-3G works so well, why do people get AIDS? Because the HIV virus has evolved to encode the protein Vif, known as a "virulence factor," that blocks APOBEC-3G.

With APOBEC-3G out of the way, the RNA of the HIV virus can be

successfully transcribed to viral DNA, an essential step for infection and for producing many more HIV viruses.

Chen said his group's research offers important clues on where Vif binds to APOBEC-3G. The knowledge could be used to design drugs that would prevent Vif from binding and allow APOBEC-3G to do its job, Chen said.

That would unlock humans' innate ability to fight HIV.

"We were born with it, and it's there waiting," Chen said.

In addition to fighting HIV, APOBEC-3G can inhibit the Hepatitis B virus. Other members of the APOBEC family serve important roles in antibody maturation, fat metabolism and heart development.

Mapping the structure of APOBEC-3G at the atomic level is a goal that "has been sought after worldwide because of its significance," Chen said.

Source: University of Southern California