# HIV/AIDS Puzzle Cracked

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"Despite initially painstakingly slow progress and very many failed attempts, we did not give up and our effort was finally rewarded," said Peter Cherepanov of Imperial College London, who conducted the research with scientists from Harvard University.

The Imperial and Harvard scientists said that having the integrase structure means researchers can begin fully to understand how integrase inhibitor drugs work, how they might be improved, and how to stop HIV developing resistance to them.

When the human immunodeficiency virus (HIV) infects someone, it uses the integrase enzyme to paste a copy of its genetic information into their DNA, Cherepanov explained in the study published in the Nature journal on Sunday.

Some new drugs for HIV -- like Isentress from Merck & Co and elvitegravir, an experimental drug from Gilead Sciences -- work by blocking integrase, but scientists are not clear exactly how they work or how to improve them.

The only way to find out was to obtain high-quality crystals -- a project that had defeated scientists for many years.

"When we started out, we knew that the project was very difficult, and that many tricks had already been tried and given up by others long ago," said Cherepanov.

"Therefore, we went back to square one and started by looking for a better model of HIV integrase which could be more amenable for crystallization."

The researchers grew a crystal using a version of integrase borrowed from another retrovirus very similar to its HIV counterpart.

It took more than 40,000 trials for them to come up with one a crystal of sufficiently high quality to allow them to see the three-dimensional structure, they said.

They tested the Merck and Gilead drugs on the crystals, and were able to see for the first time how the medicines bind to, and block, integrase.

Almost 60 million people have been infected with HIV and 25 million people have died of HIV-related causes since the beginning of the AIDS epidemic. There is no cure and no vaccine, although drug cocktails can keep patients healthy.

United Nations data for 2008 show that 33.4 million people had HIV and 2 million people died of AIDS. The worst-affected region is sub-Saharan Africa, accounting for 67 percent of all people living with HIV.

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