HIV Drugs Also Target Prostate Cancer and Chronic Fatigue Virus

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Four antiretrovirals (ARVs), notably Merck's integrase inhibitor Isentress (raltegravir), can inhibit a virus linked to prostate cancer and chronic fatigue syndrome, according to a press release from Emory University in Atlanta highlighting a paper published online earlier this month by the journal PLoS ONE.

Discovered in 2006, xenotropic murine leukemia virus (XMRV) has been detected in some prostate cancer patients' tumor biopsies. However, its precise role in driving prostate cancer is unclear. In addition, a research team at the Whittemore Peterson Institute in Nevada has suggested that XMRV is the causative agent of chronic fatigue syndrome in a majority of patients. However, other laboratories have yet to confirm these results.

"Not all studies that have looked for XMRV have been able to detect [the virus] in prostate cancers or in samples from chronic fatigue syndrome," says Ila Singh, MD, PhD, associate professor of pathology at the University of Utah School of Medicine and a study collaborator.

Singh led another recently published study demonstrating the presence of XMRV in 27 percent of prostate cancers examined, with the virus more likely to be found in the most-aggressive tumors. XMRV may promote cancer by integrating into the host cell DNA and warping the cell's ability to regulate its own genes.

Although both XMRV and HIV are retroviruses, there is little similarity between HIV and XMRV at the protein level. Yet there are only a few retroviruses known to infect humans—human T-lymphotropic viruses 1 and 2, HIV and now XMRV—with similar traits and treatment approaches.

Singh and Raymond Schinazi, PhD, DSc, professor of pediatrics and chemistry at Emory's Center for AIDS Research and the Atlanta VAMC, and their colleagues teamed up to test 45 approved and experimental ARVs and other antiviral compounds against XMRV in cell culture.

The most potent drug against XMRV was Isentress, originally approved in 2007 for treatment-experienced patients.

Besides raltegravir, three other compounds—another integrase inhibitor in addition to zidovudine (found in Retrovir, Combivir and Trizivir) and tenofovir (found in Viread, Truvada and Atripla), two

reverse transcriptase inhibitors—also inhibit XMRV replication. These ARVs, the Emory and University of Utah researchers suggest, could be used together in combination therapy, much like they're used to treat HIV.

None of the protease inhibitors stopped XMRV in test tube studies.

"Our study showed that these drugs inhibited XMRV at lower concentrations when two of them were used together, suggesting that highly potent 'cocktail' therapies might inhibit the virus from replicating and spreading," Schinazi said. "This combination of therapies might also have the added benefit of delaying or even preventing the virus from mutating into forms that are drug-resistant."

"We will need to see the results of clinical trials before these [HIV] drugs can be used in a clinical setting," Singh said.

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