

Comprehensive study finds no link between XMRV retrovirus and chronic fatigue syndrome

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New findings from University of Utah School of Medicine researchers show that the retrovirus called XMRV is not present in the blood of patients who have chronic fatigue syndrome (CFS). These findings contradict a widely reported 2009 *Science* study that linked CFS to XMRV.

The study, performed by a team of U of U researchers led by Ila R Singh, M.D., Ph.D., associate professor of pathology, was published May 4, 2011, in the [*Journal of Virology*](#) online, and is the most comprehensive to date regarding the purported link between chronic fatigue syndrome and XMRV.

The 2009 study linking CFS and XMRV led some CFS patients to take antiretroviral agents in hope of alleviating the symptoms of chronic fatigue syndrome, a debilitating condition of unknown cause. But in light of her new findings, Singh believes the off-label use of antiretrovirals by CFS patients is not appropriate and potentially dangerous.

"Our investigation found no trace of XMRV in any of the blood samples taken from patients we obtained ourselves, or from patients previously tested in the 2009 *Science* study," Singh said. "Because of our findings, we believe chronic fatigue syndrome patients should reconsider the merit of taking antiretroviral agents to alleviate their symptoms."

CFS is a devastating disorder characterized by overwhelming fatigue that is not improved by bed rest and may be exacerbated by physical or mental activity, according to the U.S. [Centers for Disease Control and Prevention](#). It affects millions of people in the United States and worldwide. XMRV (xenotropic murine leukemia virus-related virus), which was first described in 2006, is a [retrovirus](#). Other retroviruses are known to cause AIDS in humans, and many kinds of cancer in animals.

In 2009, a researcher at the Whittemore Peterson Institute in Reno, Nev., Judy A. Mikovits, Ph.D., published a study that found XMRV in the blood of 68 percent of CFS patients she sampled. That study, which engendered much controversy, was followed by another one performed by National Institutes of Health and the U.S. Food and Drug Administration researchers that also detected DNA sequences related to XMRV in CFS patients. Since then, however, several other studies in Europe and China found no trace of the retrovirus in CFS samples.

Singh and her colleagues in the U of U departments of anesthesiology and pathology, and ARUP Laboratories analyzed blood samples from 100 CFS patients and 200 healthy controls from the greater Salt Lake City area using molecular, serological, and viral growth assays, including assays used by researchers who previously found XMRV or XMRV-related viruses in CFS patients. CFS patients for the study were provided by the Fatigue Consultation Clinic, headed by Lucinda Bateman, M.D., in Salt Lake City.

In addition, Singh also analyzed samples from individuals from the 2009 study linking XMRV and CFS. Those samples were obtained by a third-party phlebotomy service that collected blood in home visits, de-identified the samples, and sent them to the Singh lab. Thus, the samples were not opened in any other research lab where XMRV might be present, minimizing chances of contamination. All samples were analyzed in a blinded manner.

Singh's study is more comprehensive and differs from other studies in a number of significant ways:

- It comprises a larger set of patients who fall under well-recognized criteria for CFS
- Patients and controls were from the same geographical area, which was not true for either of the previous studies that showed a correlation between XMRV and CFS
- They analyzed blood samples using multiple, well-defined, sensitive and specific methods, including methods used in the original study
- Unlike many other studies, Singh and her colleagues used blinded methods to evaluate samples
- Singh's study tested blood samples obtained from individuals tested in the original 2009 study

XMRV is closely related to many mouse retroviruses, and contamination of blood samples or testing reagents with mouse DNA could result in a false-positive test for XMRV. Singh and her colleagues found that some of the positives obtained in other CFS-XMRV studies could be due to the presence of mouse DNA in a reagent used in testing; other positives could be attributed to carry-over of XMRV from positive controls to other samples.

In her own study, Singh initially obtained false positives for XMRV in blood samples. But she determined those false readings were related to robotic equipment that previously had been used for extraction of DNA from XMRV-infected tissue culture cells. Several months later, this

equipment led to new samples getting contaminated. When the robotic equipment was abandoned, no more false positives were detected in either CFS patients or healthy patients. "It's easy to see how sample extraction and tissue culture processes might be vulnerable to contamination," Singh said.

Although she found no evidence for XMRV or any related virus in either her study samples or those tested at the Whittemore Peterson Institute, Singh says there is much data to encourage further research into whether other infectious agents are associated with CFS.

"These research efforts must continue," she says. "[Chronic fatigue syndrome](#) is a devastating disease for which a cure needs to be found."

Provided by University of Utah Health Sciences

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