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New studies examine links between XMRV and human disease

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Xenotropic murine leukemia virus–related virus (XMRV) has been the subject of many studies since its discovery in 2006, but conflicting reports have created an unclear picture of XMRV's role in human disease. In three recent studies published in the November 15 issue of The *Journal of Infectious Diseases*, now available online, the evidence supports a possible link between XMRV and prostate cancer but not other links involving chronic fatigue syndrome, HIV infection, or hepatitis C virus (HCV) infection.

In one of the studies, led by Athe Tsibris, MD, investigators from Boston determined XMRV prevalence in a variety of North American clinic populations. The study included healthy subjects, participants with CFS, and participants with chronic immune activation or suppression. Study samples were obtained from adult patients presenting to outpatient clinics or from pre-existing samples at Brigham and Women's Hospital, Massachusetts General Hospital, and Dana-Farber Cancer Institute. Researchers did not detect XMRV in any of the 293 patients tested, and the investigators did not find an association between XMRV and patients with CFS, chronic immune suppression, or medical conditions associated with chronic immune activation.

Researchers were surprised that they did not detect XMRV in any of the study participants, despite the high prevalence previously reported. A previous study in the United States found evidence of XMRV DNA in 67 percent of subjects with chronic fatigue syndrome (CFS), compared to 3.7 percent of healthy controls. Subsequent studies in Europe,

however, were unable to demonstrate the presence of XMRV in CFS subjects or healthy controls.

"The findings suggest that in the population we tested, XMRV is not associated with chronic fatigue syndrome and suggests that differences in PCR technique from study to study do not explain the disparate results seen in XMRV studies of chronic fatigue syndrome," Dr. Tsibris said.

A second study, led by Eleanor Barnes, MD, aimed to detect XMRV in patients with HIV-1 or hepatitis C virus (HCV) infection in the United Kingdom and Switzerland. Because the route of transmission for XMRV has not been established, Dr. Barnes and the researchers tested individuals who were at high risk for contracting blood-borne or sexually transmitted infections. Investigators tested plasma and peripheral blood mononuclear cells to determine if these patients were at risk for XMRV infection.

Investigators did not find XMRV in any of the 230 patients with HIV or HCV infections. According to the researchers, "This study provides the first evidence that if XMRV is a human pathogen, it is not enriched in the blood of patients with HIV or HCV, and by implication it is unlikely to be spread though sexual or blood-borne routes in the UK and Western Europe." In light of these findings, Dr. Barnes noted that further studies are necessary to explore potential transmission routes and determine which members of the population may be at risk.

The possible association between XMRV and human prostate cancer has also been questioned by conflicting studies. Jason T. Kimata, PhD, and investigators from the Baylor College of Medicine looked for XMRV in 144 patients with prostate cancer from the southern United States. Researchers were able to detect XMRV in 22 percent of men with prostate cancer. XMRV was present in both normal and tumor tissue of men with prostate cancer. According to the authors, this suggests that the

virus may not specifically target cancer cells for infection and that infection may precede cancer. Dr. Kimata emphasized the need to "continue discussions about XMRV detection assay methodologies, so that discrepancies in the findings of different research groups can be addressed."

In an accompanying editorial, Frank Maldarelli, MD, PhD, and Mary Kearney, PhD, of the National Cancer Institute, pointed out that differences among various studies may be related to a variety of factors, including geography, patient selection, and detection techniques. They noted that these three new studies highlight the need for standardization of detection assays, prospective epidemiological surveys, and sharing of reagents and samples among investigators. Only when this is done in a rigorous fashion will it become clear what role XMRV or related viruses have in human disease.

More information: The three studies and the accompanying editorial are available online:

"Xenotropic Murine Leukemia Virus–Related Virus Prevalence in Patients with Chronic Fatigue Syndrome or Chronic Immunomodulatory Conditions" www.journals.uchicago.edu/doi/abs/10.1086/657168

"Failure to Detect Xenotropic Murine Leukemia Virus–Related Virus in Blood of Individuals at High Risk of Blood-Borne Viral Infections" www.journals.uchicago.edu/doi/abs/10.1086/657167

"Detection of Xenotropic Murine Leukemia Virus–Related Virus in Normal and Tumor Tissue of Patients from the Southern United States with Prostate Cancer Is Dependent on Specific Polymerase Chain Reaction Conditions" www.journals.uchicago.edu/doi/abs/10.1086/656146