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Consortium of Researchers Discover Retroviral Link to Chronic Fatigue Syndrome

Scientists have discovered a potential retroviral link to chronic fatigue syndrome, known as CFS, a debilitating disease that affects millions of people in the United States. Researchers from the Whittemore Peterson Institute (WPI), located at the University of Nevada, Reno, the National Cancer Institute (NCI), part of the National Institutes of Health, and the Cleveland Clinic, report this finding online Oct. 8, 2009, issue of Science.

“We now have evidence that a retrovirus named XMRV is frequently present in the blood of patients with CFS. This discovery could be a major step in the discovery of vital treatment options for millions of patients,” said Judy Mikovits, Ph.D., director of research for WPI and leader of the team that discovered this association. Researchers cautioned however, that this finding shows there is an association between XMRV and CFS but does not prove that XMRV causes CFS.

The scientists provide a new hypothesis for a retrovirus link with CFS. The virus, XMRV, was first identified by Robert H. Silverman, Ph.D., professor in the Department of Cancer Biology at the Cleveland Clinic Lerner Research Institute, in men who had a specific immune system defect that reduced their ability to fight viral infections.

“The discovery of XMRV in two major diseases, prostate cancer and now chronic fatigue syndrome, is very exciting. If cause-and-effect is established, there would be a new opportunity for prevention and treatment of these diseases,” said Silverman, a co-author on the CFS paper.

Commonality of an immune system defect in patients with CFS and prostate cancer led researchers to look for the virus in their blood samples. In this study, WPI scientists identified XMRV in the blood of 68 of 101 (67 percent) CFS patients. In contrast, they found that eight of 218 healthy people (3.7 percent) contained XMRV DNA. The research team not only found that blood cells contained XMRV but also expressed XMRV proteins at high levels and produced infectious viral particles. A clinically validated test to detect XMRV antibodies in patients' plasma is currently under development.

These results were also supported by the observation of retrovirus particles in patient samples when examined using transmission electron microscopy. The data demonstrate the first direct isolation of infectious XMRV from humans.

"These compelling data allow the development of a hypothesis concerning a cause of this complex and misunderstood disease, since retroviruses are a known cause of neurodegenerative diseases and cancer in man," said Francis Ruscetti, Ph.D., Laboratory of Experimental Immunology, NCI.

Retroviruses like XMRV have also been shown to activate a number of other latent viruses. This could explain why so many different viruses, such as Epstein-Barr virus, which was causally linked to Burkitt's and other lymphomas in the 1970s, have been associated with CFS. It is important to note that retroviruses, like XMRV, are not airborne.

"The scientific evidence that a retrovirus is implicated in CFS opens a new world of possibilities for so many people," said Annette Whittemore, founder and president of WPI and mother of a CFS patient. "Scientists can now begin the important work of translating this discovery into medical care for individuals with XMRV related diseases."

Dan Peterson, M.D., medical director of WPI added, "Patients with CFS deal with a myriad of health issues as their quality of life declines. I'm excited about the possibility of providing patients, who are positive for XMRV, a definitive diagnosis, and hopefully very soon, a range of effective treatments options."

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Reference: Lombardi VC, Ruscetti FW, Gupta JD, Pfof MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, and Mikovits JA. Detection of

Infectious Retrovirus, XMRV, in Blood Cells of Patients with Chronic Fatigue Syndrome. Online October 8, 2009. *Science*.

The Whittemore Peterson Institute for Neuro Immune Disease exists to bring discovery, knowledge, and effective treatments to patients with illnesses that are caused by acquired dysregulation of both the immune system and the nervous system, often resulting in lifelong disease and disability.
www.wpinstitute.org.

The Lerner Research Institute is home to Cleveland Clinic's laboratory, translational and clinical research. Its mission: to promote human health by investigating in the laboratory and the clinic the causes of disease and discovering novel approaches to prevention and treatments; to train the next generation of biomedical researchers; and to foster productive collaborations with those providing clinical care. More than 1,200 people in 11 departments work in research programs focusing on cardiovascular, cancer, neurologic, musculoskeletal, allergic and immunologic, eye, metabolic, and infectious disease. The Institute also is an integral part of the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

The National Cancer Institute (NCI) leads the National Cancer Program and the NIH effort to dramatically reduce the burden of cancer and improve the lives of cancer patients and their families, through research into prevention and cancer biology, the development of new interventions, and the training and mentoring of new researchers. For more information about cancer, please visit the NCI Web site at <http://www.cancer.gov> or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).