Science Retracts Original Report Linking CFS to XMRV

In its Dec. 23, 2011 issue, Science issued a full retraction of the 2009 paper by Lombardi et al. that first linked CFS to XMRV.

“Science is fully retracting the report “detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome.” Multiple laboratories, including those of the original authors, have failed to reliably detect xenotropic murine leukemia virus–related virus (XMRV) or other murine leukemia virus (MLV)–related viruses in chronic fatigue syndrome (CFS) patients. In addition, there is evidence of poor quality control in a number of specific experiments in the Report. Figure 1, table S1, and fig. S2 have been retracted by the authors. In response to concerns expressed about Fig. 2C, the authors acknowledged to Science that they omitted important information from the legend of this figure panel. Specifically, they failed to indicate that the CFS patient–derived peripheral blood mononuclear cells (PBMCs) shown in Fig. 2C had been treated with azacytidine as well as phytohemagglutinin and interleukin-2. This was in contrast to the CFS samples shown in Figs. 2A and 2B, which had not been treated with azacytidine.

“Given all of these issues, Science has lost confidence in the Report and the validity of its conclusions. We note that the majority of the authors have agreed in principle to retract the Report but they have been unable to agree on the wording of their statement. It is Science’s opinion that a retraction signed by all the authors is unlikely to be forthcoming. We are therefore editorially retracting the Report. We regret the time and resources that the scientific community has devoted to unsuccessful attempts to replicate these results.

Bruce Alberts, Editor-in-Chief, Science
Retraction for “Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors,”


The authors wish to note the following: “Although our published findings were reproducible in our laboratory and while there has been no evidence of contamination using sensitive mouse mitochondrial DNA or IAP assays or in testing coded panels, we have the following concerns:

1. The original chronic fatigue syndrome (CFS) patient samples were of insufficient volume to distribute to other laboratories for independent confirmation.

2. Only one (1) of many laboratories has found a similar association between polytropic murine leukemia viruses (pMLV) and CFS and a careful study of 100 CFS patients (2), as well as a coded panel recently constructed by the National Heart, Lung, and Blood Institute (NHLBI) (3), have found no evidence for either xenotropic murine leukemia virus-related virus (XMRV) or pMLVs in CFS patient samples.

3. Our attempts, through collaborations, to demonstrate antibody in affected patients, to isolate the virus by culture, or to show integration sites in the human genome have failed to support the initial findings.

4. While recall of eight patients from the original cohort 15 y later showed pMLV gag sequences in seven, the copy number was very low and phylogenetic analysis showed these sequences were not direct descendents of the original dominant strains (4). Still later samples from four of these patients tested negative in the NHLBI panel. While this result could be explained by viral clearance over time, it fails to support a sustained retroviral infection in human cells.

Although a more definitive, National Institute of Allergy and Infectious Diseases (NIAID)–sponsored, coded panel of samples from 150 well-characterized and geographically diverse CFS patients and controls is being assembled for further study, in consideration of the aggregate data from our own laboratory and that of others, it is our current view that the association of murine gamma retroviruses with CFS has not withstood the test of time or of independent verification and that this association is now tenuous. Therefore, we retract the conclusions in our article.”

Shyh-Ching Lo, Natalia Pripuzova, Bingjie Li, Anthony L. Komaroff, Guo-Chiuan Hung, Richard Wang & Harvey J. Alter


He said that all the scientists and doctors involved in the NIH study — including Alter, and other co-authors of the retracted PNAS and Science papers — “are committed to completing this study because none of us believes that the issue of retroviral infection in CFS/ME is resolved.”

A Message from CII Director W. Ian Lipkin Regarding the XMRV/MLV CFS/ME Study

December 28, 2011

Dear Colleagues and Friends in the CFS/ME Community:

This letter is written to clarify the status of the XMRV/MLV CFS/ME study I am coordinating at the request of the National Institutes of Health. Although frequently described as the “Lipkin Study,” it is in fact the Alter, Bateman, Klimas, Komaroff, Levine, Lo, Mikovits, Montoya, Peterson, Ruscetti, and Switzer study, designed by these 11 investigators to bring their best methods for case ascertainment and characterization and state-of-the-art molecular and serological diagnostic tools to address the question of whether a retrovirus is associated with disease. My role in conjunction with Mady Hornig and Bruce Levin at Columbia University is to ensure that the study represents an appropriately powered, definitive, representative sample of CFS/ME patients across the United States; to receive and distribute samples; and to assess results obtained in individual laboratories for consistency and evidence for or against an association between retroviral signal and disease. I use the term “signal” because any finding related to a retrovirus, whether infectious or noninfectious, genetic material, protein, or antibody, may provide insights into disease or allow development of diagnostic tests even if a causative relationship is not established. My condition on accepting this charge from the NIH and the clinical and laboratory investigators is that each participant agree to unconditionally accept group criteria for defining cases to be used in this study. Laboratory investigators were also required to unequivocally endorse their results at the conclusion of the study. Several months were required to develop clinical criteria for case and control definition and to complete approvals for human subject protection. We encountered additional delays when Dr. Mikovits could no longer pursue her work at the WPI. At that juncture, some parties suggested that the work proceed at WPI without her.

However, in my judgment, the value of this study rests in its inclusion of the original investigators who reported the XMRV/MLV findings. Thus, I was grateful when we found a way to fully engage Dr. Mikovits. At the time of this writing we have collected and distributed for laboratory analysis samples from 123 CFS/ME patients and 88 matched control subjects. We intend to complete collection and analysis of samples from 150 patients and 150 controls in early 2012.

There is criticism in some quarters that this study is unnecessary given results obtained by other investigators with other samples. However, the participating clinical and laboratory investigators and our team at Columbia do not agree. We are fully committed to completing the work rapidly and rigorously. For those who continue to express concerns that this study is an inappropriate use of resources in a challenging fiscal environment, please be assured that more than 85% of the funding associated with this initiative is invested in patient recruitment and characterization and sample collection, archiving, and distribution. Thus, irrespective of study outcome there will be unprecedented opportunity to explore hypotheses other than that disease is due to XMRV or MLV infection.

Sincerely yours,

W. Ian Lipkin, MD, Director, Center for Infection and Immunity