Patients, patience, and the publication process

The publication of the article "Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors," by Shyh-Ching Lo, Natalia Pripuzova, Bingjie Li, Anthony L. Komaroff, Guo-Chiuan Hung, Richard Wang, and Harvey Alter, raises important issues regarding the release of research results to the public and the need for close collaboration with the authors and funding agencies when there is a direct link to public health.

The paper by Lo et al. (1) shows that MLV-related viral sequences were detected in the blood of chronic fatigue syndrome patients and were present in some blood donors. Although the paper had undergone peer review and was accepted for publication in PNAS on May 27, on June 4, the authors contacted PNAS and requested a delay of publication while conflicting results from another government-funded study by Switzer et al. (2) that was submitted to *Retrovirology* were considered. Switzer et al. (2) did not find XMRV or other MLV-related virus sequences or associated antibodies in their chronic fatigue syndrome patient population or in healthy controls. The *Retrovirology* paper published online July 1.

In light of the conflicting findings, on June 18, PNAS provided Lo et al. with additional comments including a recommendation that direct evidence of viral gene integration into the host genome be provided. The authors submitted a revision on July 22 that was evaluated by the PNAS editors. The final version of the article, which is published in this issue of PNAS, was received on July 30. The following comment was added to the paper, "The ultimate proof of low-grade infection by MLV-related viruses in humans may rely on demonstrating the integration of the viral genes into the human genome (3). The identification of provirus integration sites will take more time and effort to investigate, given that we estimate only one virus gene copy in every 400–4,000 nucleated peripheral blood mononuclear cells. Previous work with XMRV indicates that integration sites are quite variable (4) and that the same may be true for the polytropic mouse endogenous retroviruses, which are predominant in this study."

As a publisher, when authors or their funding agencies request additional time to ensure that work is ready for public release, particularly when there are public health implications, we strive to work closely with them to promptly address their concerns. Although PNAS was urged not to delay the paper by Lo et al., our greatest concern has been the documentation and validity of the evidence in light of the possible public health implications of this work. We trust that the revisions to the paper have resulted in a stronger article.

Randy Schekman, *Editor-in-Chief*

1. Lo S-C, et al. (2010) Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors. *Proc Natl Acad Sci USA*,10.1073/pnas.1006901107.
2. Switzer WM, et al. (2010) Absence of evidence of xenotropic murine leukemia virus-related virus infection in persons with chronic fatigue syndrome and healthy controls in the United States. *Retrovirology* 7:57.
3. Voisset C, Weiss RA, Griffiths DJ (2008) Human RNA "rumor" viruses: the search for novel human retroviruses in chronic disease. *Microbiol Mol Biol Rev* 72:157–196.
4. Kim S, et al. (2008) Integration site preference of xenotropic murine leukemia virus-related virus, a new human retrovirus associated with prostate cancer. *J Virol* 82:9964–9977.