



May 9, 2011

While WPI researchers continue to review the data presented by Dr. Singh, we believe that it is important to correct and clarify information regarding this study. Several individuals were consented to participate in this study as positive controls to enable Dr. Singh to develop assays to detect multiple variants of XMRV. Of these, only three were from the original **Lombardi et al.** cohort, two of whom were among those positive for a XMRV. A XMRV was isolated from one of those patient's PBMCs, cloned and fully sequenced (GenBank® accession number GQ 497343 as identified in the NIH genetic sequence database). Sequence data demonstrates that this virus is clearly distinct from XMRV (vp62) and 22Rv1. A budding virus particle from that sample was pictured in an electron micrograph in **Lombardi et al.** Virus from that patient sample was also transmitted both from the PBMCs and plasma to an uninfected indicator cell line, LNCaP. Finally, these results were supported by a separate lab using serological methods as reported by **Lombardi et al.**

Twelve additional samples from individuals not included in the **Lombardi et al.** study were independently collected by a third party and sent directly to Dr. Singh's lab. Some of these subjects were positive for highly related sequences, including the polytropic and modified polytropic sequences identified by **Lo et al.**, as determined by the WPI prior to the publication of the Singh study. Many of those subjects were also positive for ENV antibodies to a XMRV (vp62 and other XMRV family members), indicating that these patients had an immune response to a XMRV.

In addition, WPI investigators and others have provided evidence of sequence diversity between a XMRV (vp62), other similar XMRVs detected by WPI (designated internally with a number corresponding to a clinical isolate), a XMRV (p variant), and other related human gamma retroviruses. Therefore, we believe that it is vitally important that investigators interested in furthering the understanding of blood borne XMRV as a human pathogen use a proven positive clinical isolate as the control when developing tests to detect this newly discovered human retrovirus.

WPI and the U.S. clinical laboratory performing XMRV tests pursuant to a license agreement with WPI have extensive controls in place to prevent and detect contamination. Approximately three thousand tests have been performed on patient samples to date using clinically validated tests; about one third have been found to be positive. Multiple sequences from these three thousand samples have been submitted to GenBank® and are awaiting publication. It is critical, in light of these findings, that all treatment decisions are left to physicians and their patients, including the use of antiretrovirals.

While WPI researchers acknowledge that there is still much to be learned about the lifecycle and *in vivo* reservoirs of this family of human gamma retroviruses, we remain confident in the results reported in **Science** by **Lombardi et al.** Most importantly, we are committed to human gamma retroviral research in neuro-immune disease and will continue to offer our help to the medical and scientific community when requested.