Of Mice and Men:
A Summary of the
First International XMRV Workshop

by K. Kimberly McCleary with Steven H. Kleinman, BSc, MD, and Suzanne D. Vernon, PhD

Following a brief welcome to participants and introduction of the first speaker, **Stuart LeGrice** of the National Cancer Institute (NCI) turned to **Francis Collins**, director of the National Institutes of Health (NIH), to officially open the First International XMRV Workshop. Dr. Collins' 10-minute address set the tone for the 15-hour meeting held Sept. 7-8, 2010, in the main auditorium of the Lister Hill Building on the NIH campus.

"Prostate cancer and chronic fatigue syndrome (CFS) are of enormous medical importance. Both are relatively common and the identification of a viral component has increased interest in both conditions. Over many years, CFS has been buffeted back and forth, leaving individuals with it wondering if they have been forgotten. So, this is a timely meeting, at a timely moment when science is at an interesting crossroads," Dr. Collins observed. He briefly recapped the discoveries leading up to the meeting, noting the conflicting data about the association of XMRV to both prostate cancer and CFS. Laying out questions that need to be answered, he underscored that differences between "X" (xenotropic) and "P" (polytropic) murine leukemia viruses (MLVs) might matter. As one of the steps being taken by NIH, he announced that **Anthony Fauci**, director of the National Institutes of Allergy and Infectious Diseases (NIAID), had tapped **Ian Lipkin** of Columbia University to conduct a multicenter study of the role of XMRV and PMLVs in CFS patients and matched controls with broad geographic distribution as a "critical next step." He reminded the 225 participants gathered that "association does not equal causation" and suggested the possibility that some underlying problem with the immune systems of patients with one or both of these conditions might make these viruses more easily detectable. He urged participants to maintain a healthy skepticism and to demand rigor of the studies. He defined the synergistic efforts that would be required by researchers working on prostate cancer and CFS and from different disciplines of science and medicine to uncover clearer answers. Concluding his remarks, he called the assembly a "brain trust" and reminded people that the suffering endured every day by patients with these conditions can only be overcome by strong science. Dr. Collins left shortly after delivering these opening remarks and returned the next day to participate in the sessions focused on prostate cancer and CFS.

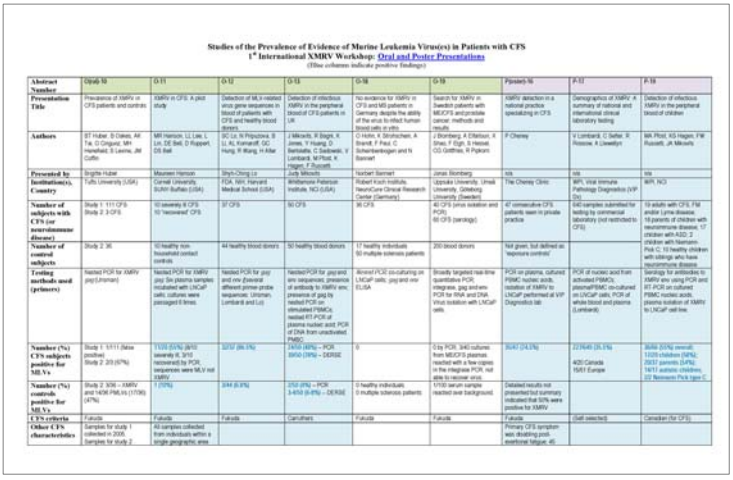

NIH Director Dr. Francis Collins

In the 10 plenary talks and 20 data presentations that followed, participants from 11 countries and 57 institutions heard new, but sometimes discordant, data about the structure and properties of these viruses of probable mouse origin, assay methods used to detect them, their prevalence in different populations (healthy and ill) and possible therapeutic and control measures. Twenty-three

posters supplemented the oral presentations, although the program did not include a summary or critical review of posters and the building's layout made it challenging to navigate people and posters during limited breaks. Written abstracts were provided for all data presentations, but not for the invited plenary lectures that led each of 6 distinct sessions. This summary is based on information gleaned from the presentations, the written abstracts, other publications by authors and follow-up correspondence that was occasionally required to clarify reported results. The time lag between the deadline for submitting abstracts and the meeting date contributed to some shifting of data, particularly related to the addition of evidence from **Shyh-Ching Lo** et al. as published in the *Proceedings of the National Academy of Sciences (PNAS)* on August 23, 2010, for the diversity of MLV sequences detected in human samples. A meeting synopsis has been published by in *NCI Cancer Bulletin* and the workshop's organizing committee is preparing a summary of the proceedings for publication in *Retrovirology,* an open access journal. The 2nd International XMRV Workshop is being planned for September 2011.

CFS Presentations

A total of nine (six oral and three poster) presentations offered data examining the prevalence of evidence of murine leukemia viruses in CFS cohorts. These reports are presented in a table format and summarized in this article. The study from **Dr. Lo** at the Food and Drug Administration (FDA) was the only presentation that repeated published data, aside from **Francis Ruscetti's** lecture on CFS in which he discussed the NCI's studies of XMRV in CFS, including the one reported in *Science*. Eight of the 9 studies reported on samples collected for the explicit purpose of testing for XMRV/MLVs, an advance from reliance on banked samples of convenience in earlier studies. Three of the 6 oral presentations found evidence of XMRV and MLV-related DNA in CFS (**Maureen Hanson** of Cornell University, **Lo** at FDA and **Judy Mikovits** of the Whittemore Peterson Institute); 2 did not (**Norbert Bannert** of Robert Koch Institute in Germany and **Jonas Blomberg** of Uppsala University in Sweden); and 1 concluded that positive results were due to contamination (**Brigitte Huber** of Tufts University).



Summary of CFS-related studies of prevalence of XMRV/MLVs

Of the 3 positive studies, all reported some diversity of sequences found, although Dr. Mikovits stated that the predominant variant detected by WPI was XMRV. Two of the three positive studies classified CFS patients using Fukuda criteria and the third used Carruthers (Canadian) criteria. The rates of positivity varied. Dr. Hanson's study tested samples obtained by **David S. Bell** from 20 CFS patients, 10 of whom reported having recovered but still demonstrated lower physical activity levels than the 10 healthy control subjects as measured by seven instruments employed by Dr. Bell. Of these 20 CFS patients, 11 (55%) were positive; 8 (80%) of the 10 patients currently meeting Fukuda criteria and 3

(30%) of the individuals who had recovered tested positive, compared to 1 (10%) of the 10 healthy controls. The *gag* sequences found by Dr. Hanson were more similar to those reported by Lo et al., than to the *gag* sequences for XMRV, although all are part of the same gammaretrovirus family. Her group is working to sequence the *env* sequence and the entire virus genome(s) now that they have external funding support from NIH. Thirty-two (86.5%) of the 37 patient samples tested by Dr. Lo, as published in the *PNAS*, were positive for MLV sequences. He responded to several questions about possible contamination and indicated that they had used sodium citrate tubes for sample collection in the 1990s and for the follow-up samples collected earlier this year. Dr. Mikovits reported on a cohort of 50 ME/CFS patients recruited from the London area; 24 (48%) of 50 were positive using PCR and 39 (78%) of 50 were positive using a DERSE cell assay described in another session by **Kyeong Lee** of NCI. Dr. Collins asked Dr. Mikovits about the rate of positives among healthy controls, to which she replied, "6-8% have antibodies with some indeterminant results and we're able to isolate virus from 11%." Following another question, she noted that the healthy blood donors used as controls were not matched by age or sex to the patients, but all came from the London area.

The two negative studies presented orally also used Fukuda criteria to select CFS patients and a variety of assay methods to detect XMRV and MLVs. The study presented by Dr. Bannert included patients with multiple sclerosis (MS) but did not find any evidence of virus in the 36 CFS patients, 50 MS patients or 17 healthy individuals. Dr. Bannert was able to demonstrate that the peripheral blood mononuclear cells (PBMCs) from CFS patients could be infected experimentally with XMRV. Dr. Blomberg reported some weakly positive results, but stated that they were ultimately unable to recover virus from any of the samples tested, which included 35 CFS patients, 15 fibromyalgia patients and 200 healthy controls. Additionally, he reported finding viral sequences in only 3 of 5 XMRV-positive samples received from the WPI. These 2 negative studies came closer to using the methods reported in *Science* than the four earlier negative attempts and the latest study from Hong et al. in China that all relied solely on polymerase chain reaction (PCR) assays.

Dr. Huber reported on two separate cohorts tested in her lab, the first of which included 111 patient samples collected by **Susan E. Levine**, only one of which was positive and was later determined to be a false positive result. In the second cohort, consisting of 3 CFS patients and 36 healthy controls, 2 (67%) of 3 patient samples were positive, but so were 17 (47%) of 36 control samples. Dr. Huber's laboratory conducted additional tests, including an assay for mouse intracisternal A-particles (IAP) that had been described the day before by **Oya Cingöz** of Tufts University, to look for minute traces of mouse DNA and RNA. Dr. Huber concluded that the results were likely due to contamination of a common lab reagent, but had not yet identified the particular contaminant. During the question and answer session that followed Dr. Huber's presentation, some participants suggested heparin in the tubes used to collect samples might be to blame for the results; however, the original report in *Science* from WPI also described the use of heparin tubes for sample collection in that study. Discussion did not address which suppliers' tubes were used in either study.

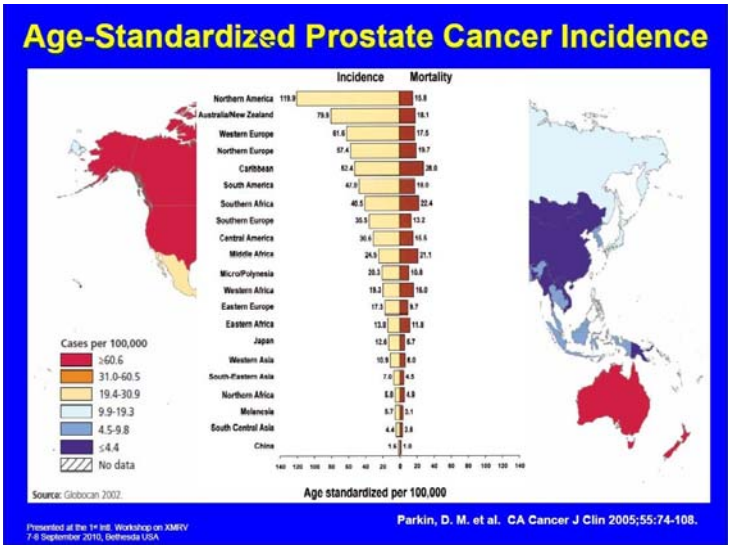
Three posters reporting positive findings were from investigators associated with the Whittemore Peterson Institute (WPI), using the WPI lab or its subsidiary, VIP Diagnostics, for testing.

Rates of positives ranged from 35.5% among 640 samples from individuals with a variety of conditions who paid to have their samples tested at VIP Diagnostics, to 74.5% in 47 consecutive patients seen by **Paul Cheney** at his private practice specializing in CFS. Two of the posters also reported results from other populations tested. Dr. Cheney reported that 50% of "exposure controls" were positive, while the WPI poster study authored by **Max Pfost** reported on a cohort of adults and children with a variety of neuroimmune diseases (including CFS, FM, Lyme, autism spectrum disorder and Neimann-Pick C) and healthy parents or siblings of those individuals. Overall, 55% of the 66 samples were positive for XMRV. While Pfost et al. suggest that the "significance of these findings is not clear," these results add another level of complexity to discerning the meaning of positive (and negative) data presented at the meeting and in the literature.

Another poster reporting results of XMRV testing, although not specifically oriented to prevalence, was from **David Strayer** at Hemispherx, manufacturer of the experimental drug Ampligen. Banked samples collected before a 40-week trial of Ampligen were tested for XMRV. Of the 208 Ampligen-treated CFS patients meeting Holmes, Fukuda and other severity criteria, 33.7% were positive for antibody to XMRV in testing conducted by WPI. Dr. Strayer reported that an analysis of data following 40 weeks of therapy indicated that Ampligen patients who were XMRV-antibody negative had lower (worse) activity of daily living (ADL) scores and lower overall activity levels than the Ampligen patients who tested positive for XMRV. A poster from **Isabel Silvestre** of WPI provided data that the drug boosts natural killer cell activity against XMRV in culture.

Prostate Cancer Studies

Although this summary is likely to reach readers more interested in the results of studies of CFS patients, it is worthwhile to include a few comparative notes about the studies of XMRV in prostate cancer. **Eric Klein** of the Cleveland Clinic provided an elegant overview lecture about prostate cancer, its epidemiology and its clinical presentation, for which there was no companion in the CFS section. Prostate cancer is the fifth most prevalent cancer in industrialized nations, with 782,600 new cases in 2007; it causes approximately 254,000 deaths each year. **Ila Singh** of the University of Utah gave an overview of disease pathogenesis, noting the difficulty of detecting XMRV because of its low copy number in cells and the small amount of virus found in tumor tissues. She also mentioned her study of 105 CFS patients and 200 healthy controls that is under way. There were four prostate cancer oral presentations and two posters. While all the CFS studies used blood as the test sample, studies of prostate cancer reflect more targets, including stromal and epithelial tumor cells, urine, prostatic secretions and blood.



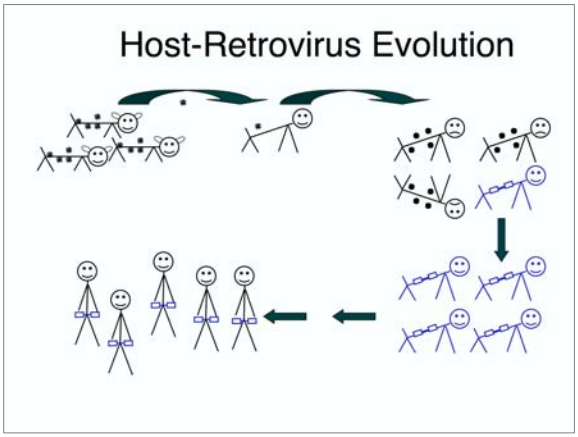
Dr. Klein gave an overview of prostate cancer, including the different rates of the disease around the world.

In general, the studies of prostate cancer involve more subjects than those of CFS, making them somewhat more statistically robust. However, the conflicting nature of findings is similar to CFS, with new data added to both the positive and negative studies of the prevalence of XMRV in prostate cancer. Of those reporting positive results, the rates of positivity were 2 (0.5%) of 355 tissue samples (**Nicole Fischer** of University Medical Center in Hamburg, Germany); 32 (22%) of 144 tissue samples (**Bryan Danielson** of Baylor University); 16 (6%) of 258 sera samples (**Natalia Makarova** of Emory University); and 31 (25%) of 120 urine samples (**Jaydip Das Gupta** of Cleveland Clinic). Studies reported by **Karen Sfanos** at Johns Hopkins University and **Yasuhiro Ikeda** at Mayo Clinic essentially found no association with XMRV. One study, presented by **John Petros** of Emory University, provided evidence of greater diversity among the strains of XMRV than had been reported previously. An interesting side note was the absence of registrants from organizations focused specifically on prostate cancer.

Virology, Host Responses, Assay Development, Epidemiology & Screening

The prostate cancer and CFS sections were held on the morning of Sept. 8, sandwiched between two sessions on Sept. 7 and two more on the afternoon of Sept. 8. The presentations made during these other four sessions provided important context and framework for the disease-specific data, and stimulated discussion throughout the entire meeting about how to interpret and/or resolve the different results reported.

John Coffin of Tufts University, widely considered one of the "founding fathers" of retrovirology, provided an overview of endogenous murine leukemia viruses and XMRV, tracing endogenous retroviruses back 30 million years to the relatively recent discovery of XMRV in 2006 and P-MLV (in human cells) in 2010. He stated his opinion that, "until the relationship of the two is further clarified, it is important to consider these two observations unrelated phenomena." He also clarified the current state of understanding of the results from Lo et al. The *PNAS* paper reported only fragments of PMLVs in the samples tested; until these fragments are fully sequenced, it is technically incorrect to refer to them as infectious viruses.



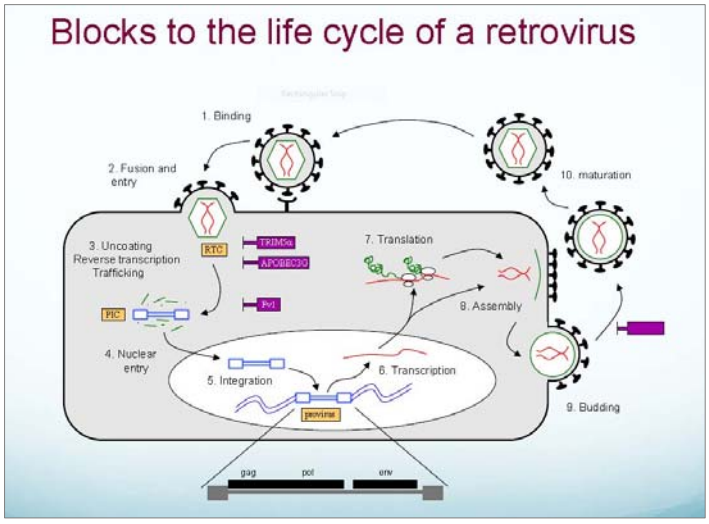
Dr. Coffin described possible transmission of MLVs from mice to humans.

One of Dr. Coffin's last slides showed a backyard swimming pool, illustrating the problem that lab contamination can cause for the sensitive assays being used to detect mouse viruses in these studies. Every mouse cell contains 100 proviruses. Exposure to even one mouse cell is like adding a single drop of human blood to the water in the swimming pool and drawing out one ml of water, but could be sufficient to taint results and yield falsely positive results. He offered this not as condemnation of any particular study or laboratory, but as a general caution in a field where samples, reagents, equipment and supplies might come in contact with mouse cells or mouse nucleic acid at any stage of the collection, storage, manufacturing and experimentation processes. His final caution of the lecture

was about the uncontrolled use of antiretroviral therapies at this stage of research. He reviewed the means by which antiretrovirals work in HIV therapy and stated that without a good assay to monitor viral load or the effect of drugs on the virus, it was premature to recommend clinical use of these medications. This topic drew more discussion during the final question and answer session. The consensus at the end of the dialogue was that only very small-scale, tightly controlled trials of antiviral medications would be acceptable until more is known.

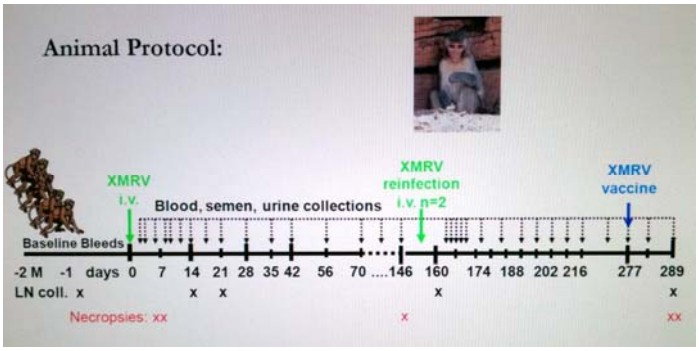
Robert Silverman of the Cleveland Clinic, senior author among the first group to publish evidence of XMRV in human prostate tumor tissues, discussed the basic biology of XMRV and animal models during the first session. His presentation previewed others' data on host restriction factors and stimulation of XMRV by hormones (in particular androgen and glucocorticoid). Consistent with his group's review article published in June 2010 *Nature Reviews Urology,* Dr. Silverman suggested that immune activation might awaken XMRV from latency. The final invited lecture of the first session was given by **Ellen Sparger** of University of California-Davis who began with a disclaimer that she does not study XMRV, but was asked to relate her experience in vaccine development for the control of feline leukemia virus (FeLV), first isolated in 1964. FeLV is a retrovirus passed by infected cats through saliva and nasal secretions. Young cats are especially susceptible to the disease it causes that can be fatal if not effectively controlled by the immune system. However, 60-80% of adult cats exposed to the virus do not get sick. Four types of vaccines help control FeLV and associated morbidity. She outlined several issues that needed to be resolved in the study of XMRV before vaccine development was likely to be successful: mode(s) of transmission (including source and risk groups); pathogenesis in the host (including sites of entry and modes of replication in acute and chronic infection); genetic determinants and other host regulatory factors; stages of infection; and types of infection.

Kate Bishop of the National Institute of Medical Research (U.K.) described a group of proteins shown to inhibit retroviruses by interrupting the replication cycle: APOBEC, TRIM-5 alpha, Friend virus 1 (*Fv1*) and tetherin. XMRV appears to be sensitive to mouse $FV1^n$ and $FV1^b$ and human APOBEC 3G and APOBEC 3B, but not TRIM-5 alpha. While there is limited understanding of exactly how the human factors behave in cells confronted with XMRV, Dr. Bishop suggested that XMRV might replicate most efficiently in cells that do not express these proteins.



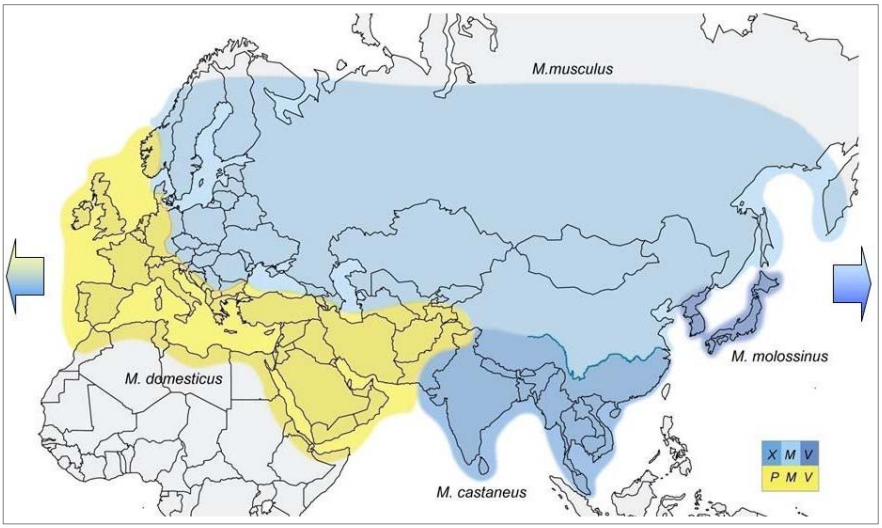
Dr. Bishop described how host restriction factors interrupt the virus replication cycle.

Two animal models for XMRV were presented by **Yasuhiro Ikeda** of the Mayo Clinic and **François Villinger** of Emory University. Dr. Ikeda showed data from a mouse model of XMRV using a strain of laboratory mice called *Mus pahari* or Gairdner's Shrewmouse. When injected with XMRV, his team was able to detect virus in the blood and tissues in the spleen and brain, although the mice did not exhibit clinical or behavioral symptoms of illness before they were sacrificed eight weeks after infection. Dr. Villinger's team studied five *rhesus* macaques, expanding on data presented at the March 2010 Conference on Retroviruses and Opportunistic Infections (CROI) and published in *Retrovirology*. He reported that following intravenous inoculation with XMRV, the sites of infection in the acute stage were the pancreas, testes and prostate and that during the chronic phase, infection shifted to the lung, spleen and seminal vesicle in the male animals and the gut, spleen, cervix and vagina of the female animal. Brain tissue examined was mostly negative, with just one cell positive for XMRV searching by fluorescence in situ hybridization (FISH). They had not looked at thymus, breast tissue or spinal cord samples and could not make any statements about the transmissibility of the infection from one animal to another. While it was possible to detect XMRV in the PBMCs of the animals within two weeks of inoculation, the antibody response was weak and short-lived. He stated that there was no sign of depletion of cell subsets, but indicated that there was some evidence of the spread of virus in spite of low levels of virus release. These animals did not display evidence of a clinical syndrome. The group is repeating its experiments in another group of animals and hopes to extend its observations.



Basic protocol for the study of XMRV in *rhesus* macaques

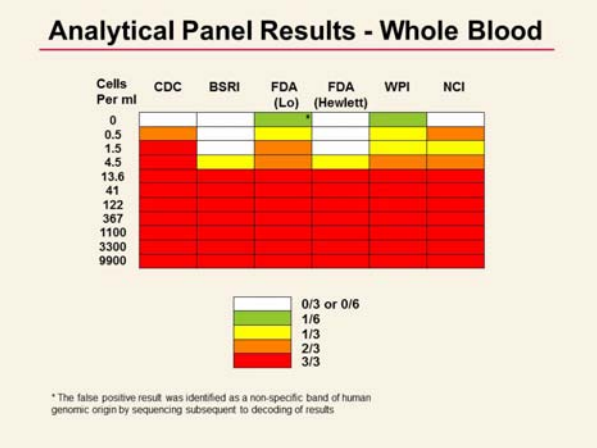
Xenotropic and polytropic murine leukemia viruses gain entry into hosts' cells through a receptor on the cellular envelope called XPR1. **Christine Kozak** of NIAID described her long-term study of the co-evolution of XPR1 and X- and P-MLVs in mice and other mammals. She showed maps of the geographic origins of various mouse species and the presence of retroviral sequences found in different species of mice. She reported that species of wild mice her team studied and some common species of laboratory mice were susceptible to XMRV – a direct contradiction to the term "xenotropic" coined to differentiate murine leukemia viruses that could not infect mouse



Dr. Kozak presented data about mouse species origins and their relationship to gammaretrovirus genes.

species. In the map on the previous page, blue color blocks indicate the general ranges of wild mice that carry chromosomally integrated copies of xenotropic gammaretrovirus envelope genes. Yellow is the range of the species that carries polytropic *env* genes. The arrows indicate that these mice travelled with man to the Americas. The mice with PMVs carry a permissive XPR1 receptor, but all three species carrying XMVs have receptor variants that can restrict virus entry. Dr. Kozak agreed with Dr. Ikeda that based on its origins and characteristics, *Mus pahari* was a good choice for a mouse model of XMRV.

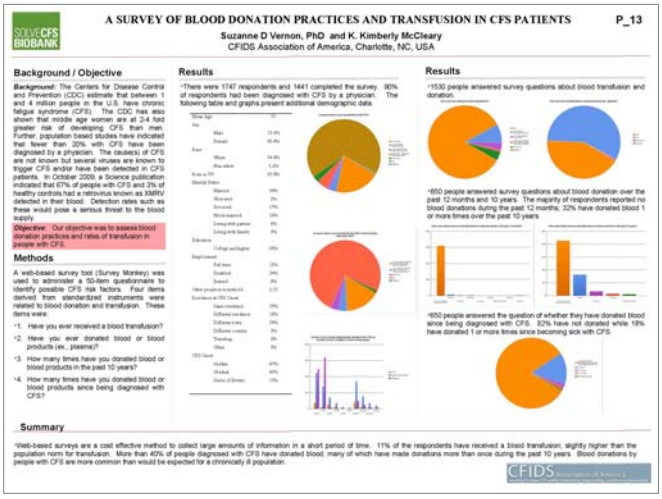
Research studies published in the literature and presented at the workshop employed several different assays including: PCR (nested and real-time) and FISH for direct detection of the viral sequences; serologic assays for detection of circulating antibodies against XMRV using flow cytometry, Western blot and chemiluminescent immunoassays (CLIAs) and enzyme-linked immunoassay (EIA) techniques; immunohistochemical assays for direct detection of viral proteins; and cell culture assays for detection of infectious virus. A session dedicated to assay development provided details about specific tests being developed by groups at NCI, Abbott Diagnostics/Cleveland Clinic/Emory University and NCI/University of Pittsburgh/Tufts University for the varied purposes of screening, clinical testing and large-scale epidemiologic studies. The sensitivity (correctly identifying all the positives) and specificity (correctly identifying all the negatives) of testing methods was described using different groups' experimental viral strains, most of which were laboratory clones of XMRV from prostate-derived cell lines. The need for panels of validated positive samples reflecting the diversity of sequences now detected in humans was identified as being critical to making progress in assay development.



Results of the Blood XMRV Scientific Research Working Group's tests of a panel of samples by 6 laboratories.

The final presentation given was a report on the study being led by the National Heart, Lung and Blood Institute (NHLBI) through a collaboration established as the Blood XMRV Scientific Research Working Group. A four-phase study has so far compared the performance of XMRV assays using an analytical panel of samples, showing that investigators at NCI, CDC, FDA (two groups), WPI and Blood Systems Research Institute (BSRI) have similarly effective means of detecting XMRV RNA in blood and plasma. These results were reported at the July 26, 2010, meeting of the FDA's Blood Products Advisory Committee. Just days before the XMRV workshop, the laboratories participating in the study shared results of phase II and phase III experiments; however, there was sufficient ambiguity about the interpretation of results that the group determined it would be better not to report them until after additional experiments are completed. **Graham Simmons** of BSRI indicated that additional tests are being conducted to discern how sample collection and processing might affect assay results and how well assays performed against panels containing validated pedigreed XMRV-negative samples and samples from XMRV-positive patients supplied by WPI.

Two posters focused on blood safety issues, one from the CFIDS Association and other from WPI and Cerus Corporation. **Suzanne Vernon** of the CFIDS Association of America reported results of an online survey of CFS patients about risk factors that included four questions about blood donation and transfusion history. Blood donation was more common than expected for a chronically ill population. Forty-two percent (42%) reported having donated blood at some time, and 115 of 640 respondents who were blood donors had donated since becoming ill with CFS. About 8% reported having had a blood transfusion before becoming ill, similar to the figure for the U.S. as a whole. WPI's **Judy Mikovits** reported that Intercept, a pathogen inactivation technology by Cerus Corp., was shown to be effective against XMRV in a laboratory study of platelets and red blood cells contaminated with a natural isolate of XMRV from a CFS patient. Intercept is not approved for use in the U.S., but the manufacturer is holding discussions with FDA about conducting clinical trials.


A SURVEY OF BLOOD DONATION PRACTICES AND TRANSFUSION IN CFS PATIENTS P_13

Suzanne D Vernon, PhD and K. Kimberly McCleary

CFIDS Association of America, Charlotte, NC, USA

Background / Objective

Methods

Results

Summary

This poster by Suzanne Vernon and Kim McCleary is representative of the format used to display data.

Q&A Session

A one-hour question and answer session with a panel led by **Jonathan Stoye** of the U.K.'s National Institute of Medical Research was webcast live to the public and archived for later viewing. Joining Dr. Stoye on the panel were **Donald Blair** of NCI's extramural division, **Jerry Holmberg** of the Department of Health and Human Services, **John Coffin** and **Judy Mikovits.** Before taking questions from participants, Dr. Stoye reminded everyone that this was a scientific session and not a political one, a reference to a pointed question posed in the earlier session about the lack of governmental pursuit of XMRV research prior to publication of the paper from WPI. This had been the only tense moment in a meeting where those with differing perspectives and discordant data addressed one another with collegial respect. As **Stuart LeGrice** said during his introductory remarks at the beginning of the meeting, "This isn't the frenzy some in the media have portrayed. We're just doing what we're trained as scientists to do." But by the end of second day, with many puzzled by the conflicting data and complex array of information that didn't present any obvious solutions, frustration was more palpable. Cameras located around the bowl-shaped auditorium were reminders that there was a larger audience watching too.

Don Blair, Jerry Holmberg, John Coffin, Judy Mikovits and Jonathan Stoye during the webcast Q&A session

Questions about what to call the different sequences that had been reported and how to prove they were transmissible were met with long answers that can be summarized as, "We need more research and classical virology before we'll know." The blood safety study was offered as a near-term indicator of how different sample collection and processing protocols might be contributing to discordant results. It was also cited as an effort by several labs to test samples from the same patients collected under standardized conditions, although some pushed for expanded efforts to do this outside the context of blood safety to resolve discrepancies between the groups. There was consensus that greater collaboration and coordination was needed, and an offer to arrange the sharing of XMRV-positive samples was tendered by **Judy Mikovits** and accepted by **Myra McClure**, one of the authors of the first paper that found no evidence of XMRV in CFS samples. There was also consensus that stand-alone PCR was not sufficient for detection of the virus in clinical samples. Several questioners noted the vast differences between groups, in that some found high rates of positive cases in CFS cohorts while others found zero, suggesting that differences in case definition alone would be more likely to yield a range of positive rates rather than such extremes. Host genetics, background influences and restriction factors were offered as unknowns that still needed to be sorted out, in addition to technical differences in sample handling and assay methods. The need for funding to support this research was another point of strong consensus, with even intramural NIH researchers noting that the work done so far had largely been carved from other budgets and would need to be sustained by larger, dedicated sums. **Don Blair** noted that the number of research applications on XMRV was still small, in spite of the capacity crowd attending the workshop. Some questioners sought to understand the connection between prostate cancer and CFS, beyond the first link suggested by similar defects in the RNaseL antiviral pathway. Immune defects that suppress the immune system to allow viral infection or presentation of latent viruses were suggested, while others stated it might be more advantageous not to consider prostate cancer and CFS together since different mechanisms might be at work. The idea that XMRV might be a passenger virus and that the immunosuppressive state associated with disease might result in the viral infection (rather than the virus possibly causing disease) received some attention. Participants named lessons learned from other retroviruses like gibbon ape

What's Next?

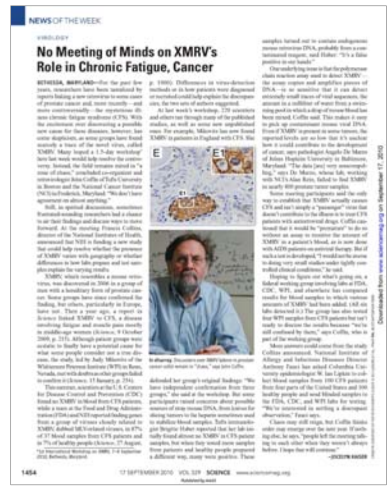
Refinement and reporting of data from the Blood XMRV Scientific Research Working Group's Phase II and Phase III studies that will help optimize sample collection and processing for detection of XMRV/MLVs.

Details of the study supported by NIAID in which "microbe hunter" Ian Lipkin of Columbia University will test samples collected from CFS patients in distinct geographic areas for MLVs.

Meeting of the DHHS CFS Advisory Committee featuring a "science day" on Oct. 12 prior to its formal two-day session on Oct. 13-14.

New publications from groups attending the workshop and others.

retrovirus (prevalent but not disease causing) and HTLV-1 (one agent causing two distinct diseases). At a few different points, including the discussion of XMRV as a possible passenger virus, the discussion shifted to using clinical trials of antiretroviral agents as a means to learn about the virus itself, as well as to treat individuals who had tested positive. This was by far the most contentious point of the meeting, with great caution expressed about the off-label use of HIV drugs, while others stated that controlled trials of agents shown to have some utility against XMRV could be instructive. In the end, there was some agreement that a small study of patients identified as XMRV-positive by standardized tests, with close monitoring using a quantifiable assay for viral load could be conducted when appropriate methods were available to follow the individuals receiving therapy. Questions about issues deemed by the panel chair to be political (rather than scientific) were deferred, including a repeated question about why CDC selected the subjects it did for its study and why it used a lab that had reported negative results in prostate cancer for confirmation of its own negative results. Regardless of the chair's direction, this conversation would have likely been a short one owing to the fact that nearly half of the 200+ meeting participants were federal employees.


NEWS OF THE WEEK

VIROLOGY

No Meeting of Minds on XMRV's Role in Chronic Fatigue, Cancer

***Science* magazine reported on the XMRV Workshop.**

The first XMRV workshop was brought to a close without definitive answers to questions about the origins of MLVs in humans, disease associations, testing, therapeutic approaches or preventive measures. Dr. Coffin's repeated characterization of the state of current knowledge being a "zone of chaos" was quoted in *Science* magazine's meeting report. There were no easy answers offered, and the discrepant data presented so far in CFS and prostate cancer are unlikely to be resolved by one simple explanation. However, there was considerable optimism among speakers and panelists about the accelerating pace of progress and that accord on key issues is likely less than a year away. While that timetable is little comfort to people whose lives have been derailed by any of the conditions linked to this family of retroviruses, this meeting demonstrated that XMRV has rallied scientific interest unmatched in the history of CFS.

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