

## DETECTION OF INFECTIOUS XENOTROPIC MURINE LEUKEMIA VIRUS-RELATED VIRUS (XMRV) IN BLOOD CELLS FROM PATIENTS WITH CHRONIC FATIGUE SYNDROME

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Chronic fatigue syndrome (CFS) is a debilitating disease manifested by inflammatory sequelae including innate immune activation and low natural killer cell numbers and function. The recent discovery of the human gammaretrovirus xenotropic murine leukemia virus-related virus (XMRV) in men with familial prostate cancer suggested to us that XMRV might also be present in CFS patients because both diseases are associated with dysfunction of the antiviral enzyme RNase L. To investigate the prevalence of XMRV infection in CFS, we screened nucleic acids from banked samples by nested PCR for XMRV *gag* sequences. We identified XMRV nucleic acids in the peripheral blood mononuclear cells (PBMC) of 68/101 (67%) of CFS patients, compared with 12/320 (3.75%) regional, healthy controls. Using a monoclonal antibody to the envelope glycoprotein of SFFV, which is highly related to XMRV, as well as goat antiserum to MuLV *gag* proteins, we could detect XMRV expression by Western blot analysis in the activated PBMCs from CFS patients but not normal donors. XMRV protein expression could also be detected in purified, activated T and B lymphocytes from CFS patients. The XMRV detected was infectious because it could be transmitted from activated primary PBMC as well as from purified B and T cell cultures and plasma derived from CFS patients to uninfected primary lymphocytes and indicator cell lines. Data will be presented to show XMRV can infect cells of the innate immune system. The association of XMRV with CFS was further supported by the presence of circulating antibody to the XMRV envelope protein in patient plasma and by the detection of type C retrovirus particles in patient PBMCs. Phylogenetic analysis revealed that XMRV isolates from CFS and prostate cancer patients form a distinct branch and are highly related. Preliminary data will be presented showing that blood cells from patients with other neuroimmune diseases are also productively infected with XMRV. Taken together, these data demonstrate the first direct isolation of infectious XMRV from humans and implicate a role for productive XMRV infection in the pathogenesis of CFS and other neuroimmune diseases.