



MEETING ABSTRACT

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Development of XMRV producing B Cell lines from lymphomas from patients with Chronic Fatigue Syndrome

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Previous studies have shown that CFS patients have an increased incidence of lympho-proliferative malignancy compared to the normal population [1]. While the incidence rate of non-Hodgkin's lymphoma in the United States is 0.02%, nearly 5% of the CFS patients developed the disease. Additionally, development of cancer coincides with an outgrowth of gamma delta T cells with specific clonal T-cell receptor gamma rearrangements. We hypothesized that infection with XMRV and/or other viruses can trigger a dysregulated immune response which favors the development of B-cell lymphoma.

In a study of 300 CFS patients, 13 developed lympho-proliferative disorders. Of those tested, 11/11 were positive for XMRV and 9/9 positive for clonal TCR gamma rearrangements. Spontaneous development of four B cells lines occurred during culture of cells from CFS patients. Three developed from B cells isolated from the peripheral blood (two of whom had B cell lymphoma) and one from a bone marrow biopsy. For all four lines, the B cells have a mature CD20+, CD23+ phenotype and produce infectious XMRV at a titer of $>10^6$ infectious units/ml. Virus production occurred despite extensive hypermutation of the proviruses in these cells by APOBEC3G. Therefore XMRV infection may accelerate the development of B cell malignancies by either indirect chronic stimulation of the immune system and/or by direct infection of the B-cell lineage. Since viral load in peripheral blood is low, these data suggest that B cells in tissues such as spleen and lymph nodes could be an in vivo reservoir for XMRV.

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