

Comparison of Published Studies of XMRV and Sequences of Other Murine Leukemia Viruses in Patients with CFS (ME/CFS) (updated as of May 4, 2011)

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Article Title	Detection of an infectious retrovirus, XMRV, in blood cells of patients with CFS ¹	Failure to detect the novel retrovirus XMRV in CFS ²	Absence of XMRV in UK patients with CFS ³	Prevalence of XMRV in patients with CFS in the Netherlands: retrospective analysis of samples from an established cohort ⁴	Absence of evidence of XMRV infection in persons with CFS and healthy controls in the United States ⁵	Detection of MLV-related virus gene sequences in blood of patients with CFS and healthy blood donors ⁶	Failure to detect XMRV in Chinese patients with CFS ⁷	XMRV prevalence in patients with CFS or chronic immunomodulatory conditions ⁸	No evidence for XMRV in German CFS and MS patients with fatigue despite the ability of the virus to infect human blood cells <i>in vitro</i> ⁹	Serologic and PCR testing of persons with CFS in the U.S. shows no association with xenotropic or polytropic murine leukemia virus-related viruses. ¹⁰	Investigation into the presence of and serological response to XMRV in CFS patients ¹¹	Analysis of CSF from chronic fatigue patients for multiple human ubiquitous viruses and XMRV ¹²	Absence of XMRV and other MLV-related viruses in patients with CFS ¹³
Journal (ISI Impact Factor, a journal rating system)	<i>Science</i> (29.78)	<i>Public Library of Science ONE</i> (PLOS ONE, 4.351)	<i>Retrovirology</i> (4.11)	<i>British Medical Journal</i> (12.827)	<i>Retrovirology</i> (4.11)	<i>Proceedings of the National Academy of Sciences</i> (9.432)	<i>Virology Journal</i> (2.44)	<i>Journal of Infectious Diseases</i> (5.543)	<i>PLoS ONE</i> (4.351)	<i>Retrovirology</i> (4.11)	<i>PLOS ONE</i> (4.351)	<i>Annals of Neurology</i> (9.317)	<i>Journal of Virology</i> (5.15)
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Institution(s), Country	Whittemore Peterson Institute, National Cancer Institute, Cleveland Clinic, USA	Imperial College, United Kingdom	Medical Research Council, United Kingdom	Radboud University, Nijmegen Medical Center, the Netherlands	U.S. Centers for Disease Control & Prevention, Robert Koch-Institute, Blood Systems Research Institute	Food and Drug Administration, National Institutes of Health, Harvard Medical School	Chinese Academy of Medical Sciences, Beijing Hospital, Peking Union Medical College Hospital	Brigham and Women's Hospital, Mass. General Hospital, Harvard Medical School, Mass. Inst. of Technology, Harvard University, Cambridge, and Dana-Farber Cancer Institute	Centre for Biological Security, Robert Koch-Institute, Institute for Medical Immunology, and NeuroCure Clinical Research Center, Germany	Cooperative Diagnostics, U.S. Centers for Disease Control & Prevention	Imperial College, University of Geneva, King's College London	University of Medicine and Dentistry of NJ, Ibis BioSciences, Inc., and Albert Einstein School of Medicine	University of Utah, Fatigue Consultation Clinic, ARUP Laboratories
Number of CFS subjects	101	186	142 (PCR, serology)	32	51	37	65	32	39	45	130	43	100 (FCC) 14 (selected by WPI)
Number of control subjects	218	None	157 (PCR) 395 (serology)	43	53 healthy controls, 121 blood donors, 26 sera samples from HTLV- and HIV-infected individuals	44	65 healthy blood donors and 20 controls with hep-B, hep-C, HIV-1, HTLV infections	43 HIV, 97 rheumatoid arthritis, 26 hematopoietic stem-cell or solid organ transplant, 95 patients presenting for medical care. (261 total)	112 MS (with fatigue), 40 healthy donors	42 (without CFS)	30 normal healthy controls	0	200 healthy volunteers
Number (%) CFS subjects positive	68/101 (67%) positive for XMRV	0/186	0/142 PCR 0/142 antibody 1/28 neutralizing activity	0/32	0/51	32/37 (86.5%) positive for genetically diverse group of MLV-related viruses	0/65	0/32	0/39	0/45	0/48 PCR 0/130 serology by ELISA	0/10 PCR (CSF) 0/43 RT-PCR or culture	0/100 PCR & serology 0/31 culture

Number (%) controls positive	8/218 (3.7%)	Not tested	0/157 PCR 22/157 serology	0/43	0/200	3/44 (6.8%)	0/85	0/261	0/152	0/42	0/30 serology by ELISA	Not tested	0/200 PCR & serology 0/34 culture
Positive test demonstrated by	PCR, culture	PCR	PCR, serology	RT PCR (integrase) Nested PCR (<i>gag</i>)	Nested <i>pol</i> /PCR, nested <i>gag</i> PCR, western blot, ELISA	<i>gag</i> nested PCR using protocols from Lombardi ¹ and Urisman ¹⁴	PCR	<i>gag</i> nested PCR using primers from Urisman ⁹ , Lombardi ¹ and Erlwein ²	<i>gag</i> and <i>env</i> -ELISA for antibodies; PBMCs stimulated with LNCaP cells tested by nested PCR for <i>gag</i> gene	PCR performed on PBMC DNA using two tests for <i>pol</i> (Urisman ¹² and Lombardi ¹) and one for <i>gag</i> (Lo ⁶). Antibody by western blot.	PCR primers described by Lombardi ¹ which bind to the XMRV <i>gag</i> and <i>env</i> open reading frames; ELISA to detect gp70 <i>env</i> protein	PCR for <i>env</i> ; RT PCR for <i>gag</i> and <i>env</i> ; co-cultivation with LNCaP cells in pools of 20 and 23 samples	4 quantitative PCR tests; 2 nested PCR tests; ELISA; Western blot. Culture in LNCaP cells (65 samples)
CFS criteria used (# subjects)	Fukuda ¹⁵ , Carruthers ¹⁶	Fukuda ¹⁵	Fukuda ¹⁵	Sharpe ¹⁷	Reeves ¹⁸ (up to 11 may have also met Fukuda ¹³)	Holmes ¹⁹ (25/25), Fukuda ¹⁵ (21/25)	Fukuda ¹⁵	Fukuda ¹⁵	Fukuda ¹⁵	Fukuda ¹⁵	Fukuda ¹⁵	Fukuda ¹⁵	Fukuda ¹⁵ and Carruthers ¹⁶
Other CFS characteristics	Some had cognitive deficits, immunological abnormalities and exercise testing abnormalities ^{20,21}			May have excluded patients who did not recover from viral illnesses	3 different populations; 3/33 acute onset; subjects selected on availability of banked specimens	25 were systematically evaluated with standardized history, physical exam and laboratory tests.		43-item CFS questionnaire administered; 75% had fever, lymphadenopathy at onset	All CFS patients had sudden onset	31 had severe CFS using Bell's assessment; 14 were "unclassified"	High levels of fatigue and disability based on standardized scales		72% had viral onset; low levels of physical function and energy based on RAND-36
Source of CFS samples	Collected from 25 patients identified during outbreak in Incline Village and 76 patients with sporadic cases from around U.S. (WPI) ¹⁶	Clinic attendees who had participated in studies of CBT and neuroendocrine measures	St. George's Univ., London and Glasgow Caledonian Univ.	Dutch clinic conducting CFS research (1991-1992)	Wichita population-based study (CDC); Georgia population-based study (CDC); Bibb County (Georgia) registry (CDC)	25/37 patients from practice of A.L. Komaroff. 8/25 patients provided fresh samples in 2010. Samples from 12/37 patients obtained from practices of P.R. Cheney and D.S. Bell in early 1990s ²²	Clinics at Peking Union Medical College Hospital	Adult patients presenting to outpatient clinics, or from preexisting repositories and cohorts at Boston area hospitals	Outpatient clinic for Adult Immunodeficiencies at the Charité.	Recruited by internet announcement; 26 had physician diagnosis; 5 were self-diagnosed	Consecutive referrals to the CFS clinic at King's College	Outpatient clinic of Benjamin Natelson, MD	Fatigue Consultation Clinic (100) and Whittemore Peterson Institute (14)
Source of controls	People visiting a doctor's office for routine tests and purchased from paternity clinic ¹⁶	n/a	Healthy blood donors, prenatal clinic; patients with blood disorders; liver patients and kidney clinic.	Matched neighborhood controls	Same as cases	Washington-D.C. area normal blood donors' samples collected in 2003-2006	Beijing blood center	Adult patients presenting to outpatient clinics, or from preexisting repositories and cohorts at Boston area hospitals	MS patients from Charité's NCRC outpatient clinic.	Recruited by internet announcement	National Health Service	n/a	Recruited via email from Salt Lake City area
CFS patient demographics	Age range 19-75 with a mean age of 55. 67% female ¹⁷	Unwell for a median of 4 years with high levels of fatigue and disability	Not described	Avg. age: 40 yrs (25-67 yrs) Avg. symptom duration: 7 yrs (2-45 yrs)	Avg. age: 47 85% female Avg. symptom duration: 13.9 years (3-40)	25/37 New England area; avg. age: 44 at time of initial sample collection; 84% female	Age range 20-55 yrs; men/women (35:30)	66% women; 76% daily symptoms; 69% stopped work as a direct result of CFS; 21% had household contacts with CFS symptoms	66% women; age range 17-56 yrs	69% women; avg. duration: 12 yrs; from 17 states in U.S.	Not described	Not described	68% women; avg. duration: 16 yrs; avg. at testing: 34.6 yrs.; unable to work full- or part-time: receiving disability: 13%;

								or diagnosis; 7% noted a tick bite prior to symptom onset. Avg. symptom duration: 11.6 years.					43%; past Ampligen study participant:17%
Institutional Review Board (IRB) approvals stated in paper	Leukopaks of PBMCs were collected according to a NIH approved 99-CC-0168 protocol. Patients' samples were obtained under NIH exempt status. No IRB approval reported.	South London and Maudsley NHS Trust Ethics Committee	Not reported	Commissie Mensgebonden Onderzoek from Radboud University Medical Centre (CMO-1991)	CDC IRB	Brigham and Women's Hospital IRB	Informed consent provided prior to study	Approved by the relevant Institutional Review Boards.	Written informed consent to test etiological theories of CFS and MS. Study approved by Ethics Committee of the Charité	Not reported	South London and Maudsley NHS Trust Ethics Committee	Not reported	University of Utah IRB protocol #7740

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