New research shows virus previously linked to chronic fatigue syndrome is a lab contaminant

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A virus previously thought to be associated with chronic fatigue syndrome is not the cause of the disease, a detailed study has shown. The research shows that cell samples used in previous research were contaminated with the virus identified as XMRV and that XMRV is present in the mouse genome.

XMRV was first linked to chronic fatigue syndrome – also known as myalgic encephalomyelitis (ME) – in a study published in October 2009, where blood samples from chronic fatigue syndrome patients were found to have traces of the virus. XMRV had also been identified previously in samples from certain prostate cancer patients.

The new study, published in *Retrovirology*, identifies the source of XMRV in chronic fatigue syndrome samples as being cells or mouse DNA rather than infection by XMRV. The research does not rule out a virus cause of chronic fatigue syndrome - it is simply not this virus.

The research team developed improved methods to detect XMRV against the genetic noise of other sequences and make recommendations for future study of virus causes of human disease.

"Our conclusion is quite simple: XMRV is not the cause of chronic fatigue syndrome," says Professor Greg Towers, a Wellcome Trust Senior Research Fellow at University College London (UCL). "All our

evidence shows that the sequences from the virus genome in cell culture have contaminated human chronic fatigue syndrome and prostate cancer samples.

"It is vital to understand that we are not saying chronic fatigue syndrome does not have a virus cause – we cannot answer that yet – but we know it is not this virus causing it."

The team, from University College London, Wellcome Trust Sanger Institute and University of Oxford, showed clearly that the experimental design of previous studies would pick up sequences that resembled XMRV; however, in this improved study, they could prove that the signal was from contamination by a laboratory cell line or mouse DNA. The sequences from the contaminated cell line and chronic fatigue patient samples were extremely similar, contrary to the pattern of evolution expected during the infectious spread of a virus in a human population.

They also showed that the existing methods would indicate that one in fifty human cell lines they examined were infected with XMRV-related viruses: they showed that contamination of human tumour cells with XMRV-related viruses is common and that a principal prostate cancer line used is contaminated.

"When we compare viral genomes, we see signs of their history, of how far they have travelled in space or time," says Dr Stéphane Hué, Post Doctoral Researcher at UCL. "We would expect the samples from patients from around the world, collected at different times, to be more diverse than the samples from within a cell line in a lab, where they are grown under standard conditions. During infection and transmission in people, our immune system would push XMRV into new genetic variants.

"Viral infection is a battle between the virus and the host and XMRV does not have the scars of a virus that transmits between people."

Together the results demonstrate that XMRV does not cause chronic fatigue syndrome or prostate cancer in these cases. The team's methods suggest ways to ensure that virus contamination does not confound the search for a cause of disease in future work.

The authors propose that more rigorous methods are used to prevent contamination of cell and DNA samples. They also suggest that consistent and considered standards are needed for identifying viruses and other organisms as cause of a disease.

"Increasingly, we are using DNA-based methods to accelerate our understanding of the role of pathogens in disease," explains Professor Paul Kellam, Virus Genomics group leader from the Wellcome Trust Sanger Institute. "These will drive our understanding of infection, but we must ensure that we close the circle from identification to association and then causation.

The strongest lesson is that we must fully use robust guidelines and discriminatory methods to ascribe a cause to a disease."

More information: The research paper can be found online at www.retrovirology.com/content/7/1/111

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