

NATION & WORLD

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Hope fades on chronic fatigue syndrome

Retroviral link to illness looks shaky, but researcher still backs finding

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A high-profile scientific paper that gave enormous hope to patients diagnosed with chronic fatigue syndrome, and even prompted some to take potent anti-HIV drugs, has been largely discredited by later research.

Evidence is mounting that a retrovirus called XMRV is not a new human pathogen infecting millions, as was feared, but a laboratory contaminant.

Cancer biologist Robert Silverman, a key researcher at Cleveland Clinic's Lerner Research Institute who worked on studies that linked XMRV to chronic fatigue syndrome and prostate cancer, told the Tribune his lab had stored a cell line known to harbor XMRV and he was working to tell if contamination occurred. Virologists who examined work by Silverman and others have raised serious questions about contamination, an unfortunate but not unusual mishap.

"I am concerned about lab contamination, despite our best efforts to avoid it," Silverman wrote in an e-mail, adding that similar cell lines "are in many, many labs around the world. Contamination could come from any one of a number of different sites."

A European research team this week reported being unable to find any evidence of XMRV in the blood of people diagnosed with chronic fatigue syndrome and their healthy peers, the latest in a stream of studies in which researchers looking for the retrovirus in the blood of both sick and healthy people have come up empty. Others have reported no evidence of the retrovirus in the blood of patients who were previously found to be XMRV-positive.

The Tribune reported last year that the original research on chronic fatigue syndrome and XMRV had led some patients to get tested for the retrovirus and take anti-retroviral drugs intended to treat HIV, which causes AIDS. The situation highlights the danger in putting too much stock in one scientific study, even one in a prestigious journal. Studies need to be replicated, and



Judy Mikovits stands by her paper about chronic fatigue syndrome, which raised hopes for a cure. But her results have been questioned.

early research is often proved wrong.

The original study published in *Science* in 2006, was led by retroviral immunologist Judy Mikovits of the private Whittemore Peterson Institute for Neuro-Immune Disease in Reno, Nev. The institute plans to open a clinic that in May would begin treating patients diagnosed with chronic fatigue syndrome and other neuro-immune diseases. Despite the newer research, its leaders strongly deny that contamination could account for their findings.

"It is clearly a human infection," Mikovits, the institute's director of research, told an audience at a January presentation hosted by a California alternative medical practice. "It is clearly circulating through the population as is our fear and your fear."

Scientists say there is no evidence to support her statement.

"Saying that is just inciting fear," said Columbia University virologist Vincent Racaniello.

Mikovits, who once worked at the National Cancer Institute in Frederick, Md., has made increasingly broad statements about XMRV. At the January talk, she showed a slide connecting XMRV to a list of frustrating medical conditions like ALS, Parkinson's disease, multiple sclerosis and dementia. She also linked it to autism. But no published data exist to support those links.

Mikovits also talked about potential treatments, including the powerful anti-retroviral drugs used to treat people who have HIV. These have not been proved safe or effective for people with chronic fatigue syndrome or any of the other conditions listed.

The WPI's director of clinical services, Dr. Jamie Deckoff-Jones, who has chronic fatigue syndrome and has taken anti-retroviral drugs for a year, is using a personal blog to allege a cover-up by researchers seeking to discredit the XMRV link.

"So is there motivation for the cover-up and baseless attacks against Dr. Mikovits?" she wrote in a posting that has been widely circulated on patient forums. "They cannot attack the data because it is impeccable."

WPI President Annette Whittemore, whose daughter has been diagnosed with chronic fatigue syndrome, said in an interview that she thinks politics are at play.

"I thought we were going to solve my daughter's illness or at least fund more significant treatments," said Whittemore, who founded the institute. "I didn't think we would have such political pushback. That was so naive of me."

Whittemore also defended patients trying anti-retrovirals, saying they are safe if used under an experienced doctor's care.

"Patients choose to try these drugs because they are so sick they have lost their entire lives to this

illness," she wrote in an e-mail. "As far as I am concerned, they are the pioneers paving the way forward for other sufferers."

In her presentation, Mikovits also described the antiretroviral drugs as "very well tolerated" by patients trying them for chronic fatigue syndrome. "Very clearly something is going on in the majority of people being treated," she said. "Most don't notice they are taking them."

Physicians who work with HIV patients say antiretroviral drugs can cause significant side effects and that efficacy cannot be determined through anecdotes.

The chasm between the WPI and its supporters and many in the scientific community is emblematic of a new, modern-day dynamic in which patients keep close tabs on the work of researchers and feel empowered to challenge that work and form strong opinions about the quality of it.

Early on, many in the online chronic fatigue community threw their support behind WPI, believing strongly that XMRV was the cause of their illness. More than 1,000 people have paid for non-FDA-approved XMRV blood tests from a commercial lab associated with WPI and headed by Whittemore's husband, Harvey, according to state records. The tests range from \$249 to \$450, according to the lab website.

Patients' ardent support for XMRV as a cause has continued as other research teams have failed to find evidence that it was true.

On one patient message board, a commenter wrote in February about not only having contributed multiple times to WPI but also having "sent letters, e-mails, tried to contribute ideas, talked with both Judy M. and Annette, considered whether there's an opportunity for venture capital funding, am willing to protest, knit a pair of socks, etc."

This month, a retroviral conference for 4,000 in Boston included 10 presentations offering evidence that XMRV is a lab contaminant. Mikovits did not attend.

Retrovirologist Jonathan Stoye, who co-wrote a supportive commentary that accompanied Mikovits' original study linking chronic fatigue syndrome and XMRV, said he has since changed his mind. "I think there are serious problems," said Stoye, of the MRC National Institute for Medical Research in

London.

His co-author, John Coffin, a retrovirologist at Tufts University, agreed the evidence for a link between XMRV and human disease had been seriously hurt.

"I think most people are reasonably convinced that there is not much left anymore," Coffin said. But, he said, "I don't think everything has been nailed down."

Coffin began having doubts about Mikovits' study as negative evidence piled up and after he, researcher Vinay Pathak at the National Cancer Institute and their colleagues believed they found the parent viruses of XMRV.

The viruses, according to researcher Pathak presented at the Boston conference, recombined in a cell line called 22RV1 to create a new retrovirus — XMRV — sometime in the 1990s. The work is in the publication process.

That widely used cell line had been stored in Silverman's lab before he found evidence of the retrovirus in prostate tissue with a form of prostate cancer.

"22RV1 cells were once previously (more than a year earlier) grown in my lab but were being stored in a liquid nitrogen freezer at the time, and not the same freezer used to store prostate tissues," Silverman wrote in an e-mail. "At the time it was unknown that 22RV1 cells were infected with XMRV."

In the field of virology, contamination has sometimes been mistaken for real results. Greg Towers, a virologist from University College London, notes that the technology is so sensitive that only one molecule of genetic material can contaminate a sample.

Scientists have been reluctant to shut the door completely on the possibility that XMRV really is tied to human disease. Some questions remain unanswered, said Racaniello, of Columbia University. "I don't think it is time to put a lid on it," he said. "You have to carry the whole thing to its conclusion."

The XMRV story is, to Racaniello, an amazing opportunity for people to watch how science works in real time.

"It is like Watergate," he said. "You saw the Constitution work. You think, oh my gosh, it works! And this is science working. Science determines the truth. ... It always sorts it out in the end."

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