💉 Retroviral Plague: An interview with molecular biologist Judy Mikovits

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I had the rare pleasure of interviewing Dr. Judy Mikovits at the IACFS/ME conference in San Francisco last March. Dr. Mikovits is best known for her involvement with XMRV research.

Dr. Mikovits is a cellular and molecular biologist with over 30 years of scientific expertise. She has directed programs on HIV, cancer, epigenetics, and neuroimmune disease, with a focus on development of novel drug and diagnostic technologies. Dr. Mikovits holds a PhD in Biochemistry and Molecular Biology from George Washington University. Her dissertation was on HIV latency and mechanisms of immune activation in monocytes. Dr. Mikovits was a Postdoctoral Scholar in Molecular Virology at the Laboratory of Genomic Diversity, National Cancer Institute under Dr. David Derse. Over the past 26 years, she has published 51 scientific papers in peer-reviewed journals.

The riveting story of XMRV, and the subsequent scandal which left her career in ruins, is told in Dr. Mikovits' forthcoming book, *Plague: One Scientist's Intrepid Search for the Truth about Human Retroviruses and Chronic Fatigue Syndrome, Autism, and Other Diseases*. **It was a journey that took Dr. Mikovits through the process of scientific research, the thrill of discovery, and ultimately to the high-level corruption which eventually led to her arrest, and the conviction and sentencing to federal prison of her employer, Harvey Whittemore, for federal crimes that, in the words of Nevada's highest court, reflected badly on his "honesty, trustworthiness or fitness as a lawyer."**

In spite of the notoriety surrounding XMRV, Dr. Mikovits remains committed to helping people who suffer from ME/CFS and is determined to discover its cause. "To me," she says, "it's the patients who matter."

Dr. Mikovits continues to work on neuroimmune disease and cancer at MAR consulting, an endeavor she shares with Dr. Francis W. Ruscetti.

"Plague: One Scientist's Intrepid Search for the Truth about Human Retroviruses and Chronic Fatigue Syndrome, Autism, and Other Diseases" will be released on July 1. You can pre-order it now from Amazon at a guaranteed 30% discount. (Note: This discount will not be available after the release date.) *Order here*. For more information, visit Plague the Book.

How did you get involved in ME/CFS research?

That's a good story. In late November of 2005, I met Kristin Loomis, the head of the HHV6 Foundation. Kristin visited my lab and got excited. Her daughter, who was very sick, had been diagnosed with CFS, but Kristin thought she had HHV6. What I saw in Kristin Loomis' daughter was an astounding loss of intelligence and cognitive function, which was striking in such a young person.

At the time, my company, EpiGenX Pharmaceuticals, was being sold, and I didn't have much to

2006, Kristin sent me to the HHV6 meeting in Barcelona where I met Dan Peterson. He gave a very compelling talk. His data showed clonal rearrangement of gamma delta T cells; you don't get clonalities like that unless you've got a frank cancer. He said, "I don't see where all this cancer is coming from. I don't know what it means. If anybody can help me, see me after the talk." I took one look at the slide, and I could not get to him fast enough. He invited me to Reno, where I met the Whittemores.

So, you got hooked because you saw something very strange.

It was the mantle cell lymphoma that was the red flag. Dan Peterson had five patients with mantle cell leukemia in a group of 100, which appeared to be a cluster. The way I've been trained, I look at cancers and I look at clusters. So, I thought, "There's something going on," because mantle cell lymphoma is incredibly rare.

Did you know anything about ME/CFS before you met Dr. Peterson?

At that time, CFS was really nothing to me, because when I looked at the literature I thought, "Fine, they've got an NK problem." That makes sense, because NK [natural killer] cells only do two things, they recognize viruses and they recognize tumor cells. So, if you can't clear viruses, you're going to have NK cell disturbances. After I met Dan, I purposely didn't read the research, because I wanted to discover what was going on without being influenced by previous research.

The one exception I made was a paper by Paul Levine. His paper was about families that had children who had cancer and CFS. NK function was lowest in the children with cancer. But CFS patients had only slightly more NK function. I carried that paper in my backpack wondering why.

How did you begin working with him?

To me, it's the patients that matter. I basically saw a sick patient population - and they were so sick. These were young people, the promise of the country. Something had to account for it.

From the day I went into the field, I saw a crippled immune system. That's what Dan Peterson showed me - a crippled immune system.

So, all that summer I worked with Dan Peterson. We took multiple samples of the most severely ill patients. We took samples every six weeks, so we developed a very good database. It's important to have a database like the one we were creating, because if you do a snapshot of an immune profile, you capture only one day. You might miss something. The virus(es) may be latent, so you have to take repeated samples over several time points, months apart.

That was how we found XMRV. We didn't see it in of 67/101 samples, we saw it in 67/101 *patients*. And we had multiple samples from every patient taken over a two-year period. The reason we needed so many samples was that there could be DNA silencing of the virus by methylation, the very mechanism that was the basis of my startup, EpiGenX.

For me it made perfect sense based on my decades-long work on HIV and HTLV-1. I had published a paper on how methylation of immune modulators in HIV-infected people silenced the virus, and now I was finding something similar with CFS. [DNA methylation suppresses the expression of endogenous retroviral genes. It plays a crucial role in the development of nearly all cancers.]

We never said *cause*. It was the adversaries that said cause. What we said was that there was an association. Everyone wanted to make this virus like HIV, but it's not like HIV. It's not crippling the immune system so badly that people are dying quickly. And it's not a large visible cell component that is being crippled, like the CD4 T cell.

If you want to find a retrovirus you've got to grow it in a dividing cell, because it needs cellular genes to multiply, and it's not easy to find. So we used the classic techniques. And the association with XMRV was very strong. We had a transmissible retrovirus from the third family of retroviruses. It was first associated with a cancer, and now we found it was associated with a neurological disease, just like HTLV-1.

If XMRV was a lab artifact, why wasn't it in all the samples - those from healthy people as well as from those who were sick?

Only the samples we sent to Silverman's lab got contaminated, but these were all samples from patients. So samples from healthy controls didn't get contaminated.

In our paper, the hypothesis was that we would find a retrovirus. We did experiments in 2008 that did not quite match Silverman's XMRV plasmid sequence. Because we couldn't make the match with Silverman's XMRV, we modified the parameters. We changed the PCR reaction to capture everything that wasn't an exact match. This is what we call "wobble" or "variation." Max Post was the person who captured the variation in our samples.

When we pulled those pieces out and sequenced them, we were getting similar, but not exact matches with Silverman's XMRV.

Silverman asked for 30 samples, which we provided. But he wouldn't do his work blinded, so he knew they were from patients. Our work was blinded, but my notebooks were the only way you could figure out which sample was associated with which patient. Silverman provided his own controls.

So, after three tries Silverman still couldn't get a full-length sequence of the virus we were looking at. That meant that what we sent him simply was not XMRV Silverman. He said in March 2009, "Let me try again." We replied, "No, there's too big a chance of contamination." But Lombardi cultured the virus and sent Silverman the samples anyhow without telling me. That was a mistake. When Silverman sequenced those samples - which were not blinded - in his laboratory, they got contaminated. Silverman had lots of plasmid in his laboratory, as he had been doing all the sequencing. He notified us in July of 2011 that our samples were contaminated with his VP62 plasmid.

But even if what we found wasn't Silverman XMRV, it was still associated with two diseases - the lymphoma in Dan's patients and CFS. It could have been a family of viruses, or a different strain. For example, there are five strains of HTLV, and only one is pathogenic. What we found could have been just one in a family of retroviruses.

A good example of this problem is Dr. Lipkin's research. Dr Lipkin says he has found evidence of retroviruses in Montoya's samples of ME/CFS patients, but he claims this probably doesn't mean anything because he also found them in the controls. But what if the controls have a non-pathogenic strain? No one has a detailed sequence that would enable anyone to know those answers. And only 5% of the people infected with HTLV-1 ever get disease.

After 40 years we still don't know the exact mechanisms of how HTLV-1 or HIV cause disease and why the other very closely related strains do not. The point is that healthy people do not

abandon a line of research that could help millions of people is just bad science.

So, if it wasn't Silverman's XMRV plasmid, what virus did you find in Dan Peterson's patients?

We isolated a gammaretrovirus from at least one person. And I believe beyond a shadow of a doubt that it was a new gammaretrovirus that could infect humans. The way we found it was by using a reagent called a 7C10 monoclonal antibody, which was an antibody to murine gammaretroviruses. That antibody recognized all known murine gammaretroviruses.

The problem was that every time we put our sequence in the database it came up with XMRV, because that's all there was. There was nothing else to compare it to. When De Freitas did her work in 1990 she had the same problem. She found HTLV-1 and HTLV-2-like virus because, back then, that's all there was in the database.

So, every time we put a sequence in the database, it came up with XMRV because there was nothing else to check it against. But you have to remember that XMRV isn't a single virus, it's a family of viruses. And there may be many other retroviruses that are similar to it that may be pathogenic to humans. We just don't have a way of identifying them through a database right now.

If you found a new retrovirus, why was the paper you published in *Science* retracted?

The paper should not have been fully retracted. It should have been partially retracted. The only reason the paper was fully retracted was because I was jailed and had no access to our data.

One of the things that was so wrong about what happened is that they threw out *all* my research. They destroyed it all. And this is the saddest part; we came up with a study that showed who would do well on Ampligen. 30% of the people with ME/CFS had antibodies to spleen focus-forming virus (SFFV), and these were the patients who responded to Ampligen.

What we had found was a biomarker - the antibody to SFFV-env recognized by 7C10. This finding was later validated in the Lipkin multicenter study. The assay in our original paper was replicated in every study we did, but now all of that original data is lost. If I hadn't been so thoroughly discredited, and my research destroyed, Ampligen could have been approved.

But I look at it this way, if that *Science* paper on XMRV had never come out, would we have the research that is being done today?

Why did you call your book "Plague"?

One of the reasons we called it *Plague* was not so much because of the disease itself, but because of the **increasing numbers we are seeing of people developing related health problems, such as autism, neuroimmune disease, and cancer.** If we do nothing, in another decade one in two families will have one of these neuroimmune diseases.

From another standpoint, the title refers to the plague in science. **There is a plague in medical research. We don't want to believe that medical research is corrupt.** We don't want to think that if they saw a child who was sick, researchers wouldn't do something. But yet, the government is corrupting science - just as they did with ME/CFS and XMRV - by controlling the funding and the message, which ultimately determines what the journals publish.

That is the question I ask myself.

XMRV was made in recombination with mouse cells. Before we could grow cells in labs we would pass cells through mice in order to attenuate them. But we found that by passing cancer cells through mice we could grow tumors; the cells had recombined with a retrovirus. Everyone before 1980 did this. It was standard laboratory procedure. We learned that anything we passed through animal tissues could make replication competent recombinant retroviruses in only ten days. All of our NIH research is based on mouse research. And those cell lines I worked with daily for more than 30 years have the potential to produce novel retroviruses.

So, here's the question: How many of these recombinant retroviruses are now in our environment and playing a role in all of these neuroimmune diseases?

If XMRV had mutated only two amino acids in its genetic envelope we could have had a true plague. **Nobody could have predicted that XMRV could remain stable on a bench for months, or that it could be aerosolized and transmitted in dust, in saliva.** But because our immune systems spotted it, we developed an antibody. (Many of the lab workers such as Max and myself seroconverted, meaning we developed the antibody from our lab exposure.)

How many people did we save by learning that XMRV could be aerosolized and spread to immune-compromised individuals or lab workers? We may have avoided something that could have infected everyone, because Silverman was sending XMRV all over the world.

But, exposing Silverman's XMRV as a lab artifact should not have ended the research. work Frank Ruscetti and I did to find the epitope that the antibody recognizes in humans should have been completed. Currently 6% of the population carries an antibody that recognizes a gammaretrovirus envelope protein. Six percent is 20 million Americans!

Last year, Gary Owens published a research paper that showed the envelope protein of MLVs alone could cause vascular leak and aggressive tumors. He had previously published data identifying XMRV-2, now called B4RV, on November 10, 2009. That was only one month after our paper was published. We worked with Gary and found those sequences and proteins in some of our original patient samples. The virus Gary Owens found causes the very things I saw in Dan Peterson's patients and which are found in so many of the complex chronic diseases that affect our population today. **So why was this work suppressed for three years, and why is it being downplayed now? How many new retroviruses have we created through all the mouse research, the vaccine research, gene therapy research? More importantly, how many new *diseases* have we created?**

When they destroyed all of our work, and discredited everything I or Frank Ruscetti had *ever* published, and arranged for the publication of my mug shot in *Science*, the NIH very deliberately sent the message to researchers everywhere about what would happen to any honest scientist who dared ask those important questions.

If HHS gave you the power to re-name CFS, what would you call it?

Non-HIV AIDS. It is an acquired immune deficiency, beyond a shadow of a doubt.

Comment: XMRV = Xenotropic murine leukemia virus-related virus
So, for years the biotech labs involved in vaccine and gene therapy research have bred countless new retroviruses. But instead of researching their biology and distribution, one

equally at risk of being infected and falling ill. Unless they know more than we do and have used this information for more sinister purposes - like subjugating humans to all sorts of debilitating diseases, and possibly population reduction.

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