

Whittemore Peterson Institute researcher makes major breakthrough in Chronic Fatigue Syndrome

Crippling disease may be linked to XMRV virus

Dr. Judy Mikovits, research director for the Whittemore Peterson Institute at the University of Nevada, Reno, vowed in childhood to find a cure for cancer following her grandfather's early death from lung cancer. Although she has yet to accomplish that lofty goal, in her quest to solve the riddle of one of the most pernicious and deadly diseases known to humankind, she has fortuitously made a major breakthrough in understanding the origins of Chronic Fatigue Syndrome, a debilitating disease that affects more than one million people in the United States.

In October, the Whittemore Peterson Institute announced that a recently identified retrovirus called the "XMRV virus" had been linked to the neuro-immune disease, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). An infection with XMRV virus was detected in 67 out of 101 patients tested in the study.

By Nicole Frost, freelance writer for the Whittemore Peterson Institute

Mikovits—whose patients affectionately call her "Dr. Judy"—along with Whittemore Peterson Institute colleagues and collaborators from the National Cancer Institute and the Cleveland Clinic, recently published their groundbreaking findings in the journal, *Science*, one of the world's leading journals of original scientific research, global news and commentary.

Researchers speculate that XMRV infection of certain immune system cells causes the chronic inflammation and immune deficiency that these patients exhibit, thereby resulting in their inability to mount an effective immune response to opportunistic infections.

"This is an incredibly significant discovery

for those with Chronic Fatigue Syndrome, and it has important implications for the world of science and medicine," said University President Milton Glick. "Scientific breakthroughs are often iterative, and a finding of this magnitude can lead to additional discoveries and new research frontiers."

In less than three years since she was hired as the research director at the Whittemore Peterson Institute, Mikovits and her team have identified a genetic susceptibility marker to Chronic Fatigue Syndrome, developed a cytokine signature describing Chronic Fatigue Syndrome as an inflammatory disease, produced a sensitive and accurate test for co-infections, and described an abnormal number of pathogens in this population. Taken together these biomarkers reveal the significant number of biological challenges that ME/CFS patients face.

These unique findings led Mikovits to encourage her team to keep looking for an underlying pathogen capable of producing the disease. She enlisted the help of eminent retrovirologist, Dr. Frank Ruscetti of the National Cancer Institute, Dr. Bob Silverman of the Cleveland Clinic, Dr. Vincent Lombardi '06Ph.D. (biochemistry) of the Whittemore Peterson Institute, and many other collaborators. Since that time, Mikovits' team has found that more than two-thirds of the samples are antibody positive.

This finding could be life-changing for the 17 million sufferers of ME/CFS worldwide. It not only creates the strongest link to a biological cause of disease in patients with ME/CFS but has implications for an untold number of other diseases as well. The discovery of XMRV as a human infectious pathogen may give rise to a new field of medicine. Finding XMRV to be infectious and replicating in blood samples supports the need for new diagnostic tools for its detection, and the development of effective treatments to end the destructive cycle of

disease, including the cancers that patients commonly suffer.

In contrast to HIV, which is a complex retrovirus, XMRV is a simple retrovirus, making it an easier target for the development of a preventative vaccine. "It's not going to be easy, but it's going to be easier," to find a vaccine or drugs to target XMRV compared to HIV, said Mikovits.

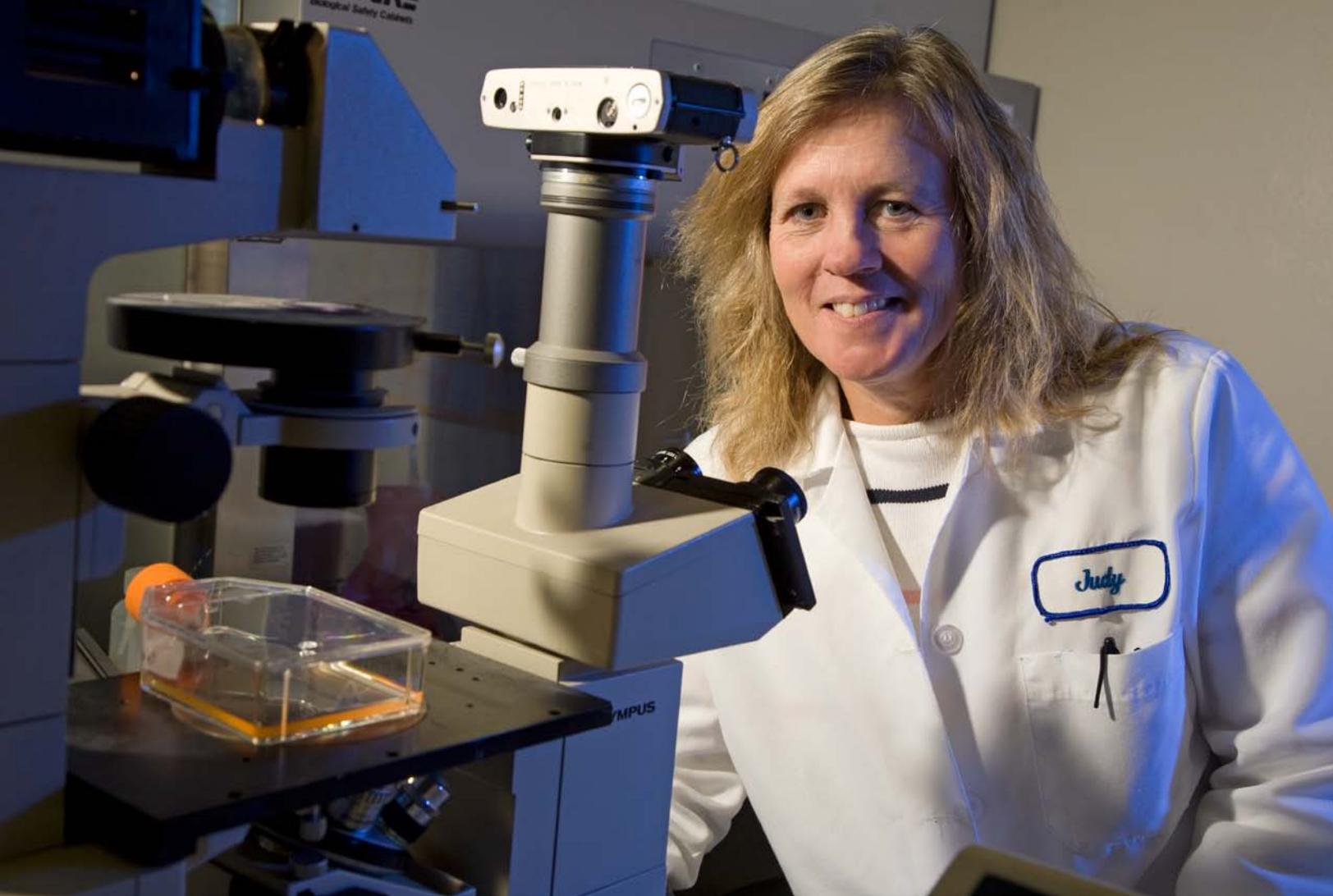
Mikovits spent more than 20 years at the National Cancer Institute in Frederick, Md., earning her doctorate in biochemistry and molecular biology and investigating mechanisms by which retroviruses dysregulate the delicate balance of cytokines—secreted substances that carry signals from cell to cell—in the immune response. Later in her career there, her work helped in the development of novel therapeutic agents for AIDS and AIDS-associated malignancies (Kaposi's sarcoma).

She agreed to work in Reno after attending a presentation by Dr. Daniel Peterson, medical director of the Whittemore Peterson Institute, in which he discussed an unusually large number of rare cancers that occur in patients with long-standing Chronic Fatigue Syndrome.

"I met and talked to several patients and I became convinced that I could help," Mikovits says. "I truly thought this work would not only lead to the answers to these patients' illnesses, but it might also lead us to the discovery of another new viral cause of cancer."

In addition, Mikovits was moved by talking to Annette Whittemore '74 (elementary education/special education), founder and president of the Whittemore Peterson Institute, whose daughter, Andrea, has suffered for many years from Chronic Fatigue Syndrome.

In the fall of 2006, the Whittemore Peterson Institute hired Mikovits to lead a unique program of translational research. She began forming a comprehensive research plan using her extensive background in immunology and virology. Armed with this intriguing



Dr. Judy Mikovits (above) and her colleagues at the Whittemore Peterson Institute are working to find the causes and potential treatments for debilitating neuro-immune diseases.

data, she began contacting her many friends at the National Institutes of Health to join in these efforts.

Mikovits realized that the field of neuro-immune disease lacked a comprehensive biological research program that could answer the many questions of patients and their doctors, but she faced longstanding prejudice in the medical community against even recognizing Chronic Fatigue Syndrome as a bona fide disease. “There’s a significant lack of federal funding and an institutional bias against biological research of ME/CFS and other neuro-immune diseases, which has created incredible hurdles to basic research for years,” she says. “We believe that situation will change with the knowledge of this important viral link.”

Nonetheless, she engaged the world’s best virologists, immunologists, microbiologists, geneticists and epidemiologists. Using the latest scientific technologies, which were acquired by the Whittemore Peterson Institute through

private and federal funding, she opened her lab on the University campus and set the research program in motion.

“I have a strong team of the world’s best scientists and the financial support of the Whittemore Peterson Institute, coupled with the University’s supportive environment,” she notes. “All of these factors allowed us to begin our research without waiting years for a federal grant to fund. I also work with a great team of young scientists from this University, including Dr. Vincent Lombardi, Katy Hagen, Max Miller and Dr. Isabel Silvestre.”

Formally trained as a cell biologist, molecular biologist and virologist, Mikovits has studied the immune response to retroviruses and herpes viruses. In addition, she has co-authored more than 40 peer-reviewed publications that address fundamental issues of viral pathogenesis, the production of blood cells and cytokine biology.

Ironically, Mikovits may soon realize her

childhood dream of curing cancer—since finding a cure for Chronic Fatigue Syndrome will also cure the cancers associated with it—while also helping millions of people who suffer from chronic neuro-immune diseases. When asked what’s next on her agenda, she says:

“In the world of science a new discovery brings more questions than answers. We will continue our studies to determine what other diseases are impacted by this virus and define the human immune defects related to XMRV infection. I am also interested in co-developing diagnostic tools and new effective treatments. Many of these studies are already underway in our lab. I tease Annette that I am going back to the beach [Mikovits lived in Ventura, Calif. prior to moving to Reno]. But she knows that I am committed to helping her find the answers for Andrea and all the other patients before I leave.” 