UW-Madison scientist on front lines in fight against Ebola

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University of Wisconsin-Madison scientist Yoshi Kawaoka was researching influenza viruses that were killing chickens in the mid-'90s when he picked up a new bestseller, "The Hot Zone."

Richard Preston's 1994 chiller — based on scientific evidence but with fictionalized details — revealed the genesis of viral hemorrhagic fevers, particularly Ebola and Marbug. It described a true-life secret Army mission to wipe out a colony of sick African monkeys housed in Reston, Va. — monkeys that had been imported for research, but that arrived infected with a mysterious rain-forest virus thought to be the deadliest ever known.

An associate member at St. Jude Children's Research Hospital at the time, Kawaoka realized as he read "The Hot Zone" that he could advance the world's understanding of the little-known virus. He could apply to Ebola his knowledge about how influenza replicates in the cells of chickens and how their bodies respond to being infected.

"I knew the pathology," Kawaoka, now a professor of pathobiological sciences at UW-Madison's School of Veterinary Medicine, explained in a rare interview this week. "I've done lots of dissection of chickens infected with highly pathogenic viruses."

Kawaoka contacted the federal Centers for Disease Control and Prevention in Atlanta, telling the nation's top health officials he wanted to work on Ebola. Back then, it was the work of a much smaller cadre of scientists than today.

Before working on Ebola, Kawaoka first had to figure out how to alter the deadly virus so it was safe enough by federal government standards to work within a St. Jude lab that, in terms of safety and security, was a notch below the CDC's top lab in Atlanta. He consulted with a scientist in Tennessee who had figured out how to disarm a vesicular stomatitis virus found in pigs that causes flu-like symptoms in people.

Kawaoka became the first scientist using the same reverse genetics to render a vesicular stomatitis virus containing an Ebola virus surface protein that does not grow in normal cells.

He also began doing research at a top-level National Institutes of Health biomedical research facility in Montana, using a type of Ebola not disarmed.

Kawaoka published his first Ebola paper in 1997, and would go on to develop a candidate vaccine that was still too early in development to discuss clinical trials when government funds were terminated about three years

ago, roughly 10 years into the research.

The vaccine protected two non-human primates from Ebola — the gold standard — but Kawaoka never got to expand the number of monkeys given the vaccine to determine why it protected them. He needed that information to make a case for clinical trials.

When government funding dried up, he didn't allow himself to be upset.

"In this business, I don't put any emotion into it. Frustration doesn't help," he explained.

Had the funding been there, Kawaoka said, "I would have known by now whether it was a promising candidate."

Work in Madison, Montana

Kawoaka is well-known for his work with H5N1 avian influenza viruses to determine whether those viruses may be mutating to gain the ability to jump from birds to people, which could cause great loss of life. A subset of enabling mutations identified by Kawaoka's team already has been detected in viruses circulating in poultry flocks in Egypt and parts of Southeast Asia, he says.

Kawaoka's research has explored how many mutations — and which ones — could make the jump from birds to people happen. The work is so sensitive, it's been in the news because of fears it could fall into the wrong hands and pose a threat.

In a new development Friday, the White House announced that it was pulling funding for all gain-of- function research, including Kawaoka's influenza studies, as the result of a review of recently revealed biosafety slips at federal research facilities.

On the Ebola front, Kawaoka currently is leading a team of top researchers that last year received an $18 million grant from the NIH to develop a detailed molecular understanding of what happens when lethal viruses such as Ebola, influenza and West Nile infect their hosts. That's useful for developing anti-viral drugs and to potentially enhance the body's immune response and better treatments and prevention, he said.

The Ebola work is being done at UW-Madison and a federal lab in Montana. The live virus is only studied in the Montana lab with pre-eminent virologist Heinz Feldmann, who has spent most of his career studying Ebola and co-developed one of the Ebola vaccine candidates scheduled to be tested in 2015.

At the time "The Hot Zone" was written, three of Ebola's seven known proteins were vaguely understood and four were "completely unknown." Their structure and function were a mystery.

Today, Kawaoka said, "We know the functions of most of the proteins to some extent, but not completely. We are looking for additional proteins made by Ebola virus, but not found yet."

Secrets to unlock

While Ebola no longer is a complete mystery, it still has secrets to unlock. Evidence supports that Ebola is

transmitted through direct contact with body fluids; there is no hard evidence that Ebola can mutate and become airborne like influenza — a much better understood virus with properties that allow it to be widely spread through airborne particles.

Kawaoka said he doesn't know of another virus that has changed its mode of transmission — in this case, from body fluids to aerosolized particles suspended in the air.

Asked whether he would be comfortable flying on a plane with someone infected with Ebola, Kawaoka chose his words carefully.

"If the person is known to be infected with Ebola virus and is not isolated properly, I would be uncomfortable."

Asked whether researchers know with scientific certainty that someone infected with Ebola can or cannot spread the virus before showing symptoms, he was equally precise: "I do not think we have data on this."

Kawaoka declined to comment on whether he would be comfortable working in a hospital with an Ebola patient without the biohazard suit and special respirator he wears in his lab.

"If you do the protection right, there's no way one can get infected," he said. "If the entire body is protected and covered, everything is isolated. … A patient's (bodily) fluid may touch you, but then you disinfect the surface before you remove the clothes" and don't touch your eyes, nose or mouth, he said.

Kawaoka offers some perspective to those panicking over Ebola.

In "The Hot Zone," Preston wrote that when infected, vital organs such as the liver "begin to liquify," skin "bubbles up" into a rash "likened to tapioca pudding," and "you may weep blood."

"This is too exaggerated," said Kawaoka, underscoring that details in the book are fictionalized.

He also suggested not getting caught up in the book's description of one emerging virus' ability to jump from one primate to another.

"It did not know boundaries," the author wrote. "It did not know what humans are; or perhaps you could say that it knew only too well what humans are: it knew that humans are meat."

For all their dangers, Kawaoka said giving viruses human characteristics is a mistake. He is the scientist; they are the subjects.

"They do not think," he said.

Four facts about Ebola

Can Ebola be spread by coughing or sneezing?

Ebola is transmitted by direct contact with body fluids of a person who has symptoms. Coughing and sneezing

are not common symptoms of Ebola, but if a symptomatic patient with Ebola coughs or sneezes on someone, and saliva or mucus come into contact with that person's eyes, nose or mouth, these fluids may transmit the disease.

What is a body fluid?

Ebola has been detected in blood and many body fluids. Body fluids include saliva, mucus, vomit, feces, sweat, tears, breast milk, urine and semen.

What does "direct contact" mean?

Direct contact means that body fluids (blood, saliva, mucus, vomit, urine or feces) from an infected person (alive or dead) have touched someone's eyes, nose, or mouth or an open cut, wound or abrasion.

How long can Ebola live outside the body?

Hospital-grade disinfectants such as household bleach kill Ebola. Ebola on surfaces such as doorknobs and countertops can survive for several hours; however, virus in body fluids (such as blood) can survive up to several days at room temperature.