

Yoshihiro Kawaoka

Even in a constant state of jetlag, Yoshihiro Kawaoka is a fiercely productive flu researcher. Wonder what he could accomplish with a little bit of sleep?

If Yoshihiro Kawaoka owned a country, its citizens would be well protected from a bird flu pandemic.

Confronted with a pandemic, Kawaoka says he would close his country's borders and release a vaccine based on the live, but weakened, bird flu virus. Some people might fall ill from the vaccine strain, but far greater numbers would benefit. "The immune response provided by live virus, that is going to be the one that really protects humans," Kawaoka says.

He is only half-serious. Kawaoka knows that closing borders is impractical and would at best only stall the pandemic. But when it comes to a vaccine, he knows of what he speaks.

Kawaoka engineered a method to generate entire viruses from genetic sequences, a technology that's now used to make flu vaccines. He has published paper after high-profile paper describing what makes certain flu viruses lethal and how they acquire resistance to available drugs. Most recently, he suggested that the H5N1 virus prefers to bind receptors far down in the lungs, making it more difficult for the virus to jump between people (*Nature* **440**, 435–436; 2006).

Since 1999, Kawaoka has juggled dual appointments at the University of Tokyo and the University of Wisconsin in Madison. Full-sized labs at each institution churn out top-notch publications, 27 in 2005 alone.

"I'm glad that I work with him and don't have to compete with him," says Heinz Feldmann, chief of special pathogen programs at Canada's National Microbiology Laboratory, and Kawaoka's collaborator on Ebola virus research.

Kawaoka became interested in Ebola after reading *The Hot Zone*, the only English novel he says he has ever read. But soon after he began working in the field, "Yoshi really came on the scene with a bang," recalls Tom Geisbert, chair of viral pathology at the US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland.

How Kawaoka has the energy to do so much is a mystery. He doesn't eat much, sleeps even less and is perpetually jetlagged. To keep up his dual appointment, he often travels to Tokyo, sometimes for just a day.

Even as a postdoc at St. Jude Children's Research Hospital in Memphis, Tennessee, Kawaoka was in the lab when the cleaning lady arrived in the early evening, would go home to sleep at some point and be back again, ready to start the next day, before she left. "We're all amazed at how he can physically manage to function so well in two different time zones," says Krisna Wells, who has worked with Kawaoka since 1987. "Personally, I don't think he sleeps."

Still, running two labs gives Kawaoka the best of both worlds.

His appointment at the University of Tokyo's prestigious Institute for Medical Sciences guarantees that his lab is always supplied with the best Japanese students. And Wisconsin allows those students to run experiments with recombinant DNA, which is under strict regulation in Japan.

But the dual appointment also has its share of headaches.

"Often I hear from Japanese that we, meaning Japanese, should do the work that sends a message to the world," says Kawaoka. "But it doesn't matter whether I do this work in Japan or the US or wherever. If people make comments, I don't say a word. I don't care what other people think."

Kawaoka began his career with a stint in veterinary school at frosty Hokkaido University, followed by graduate degrees in microbiology and bacteriology. After his mentor in Hokkaido introduced him to Robert

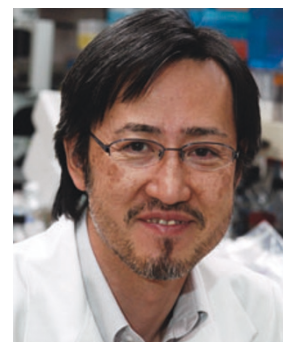
Webster, already a leader in influenza work, Kawaoka went to humid, mosquito-infested Memphis—and stayed there for 14 years.

In April 1983, four months before he arrived in the US, an H5N2 flu virus was sickening chickens in Pennsylvania. At first, the virus was only mildly pathogenic. But in October that year, it suddenly began killing chickens in large numbers.

Webster took Kawaoka to the early-morning poultry markets in New York City to sample the birds that were the source of the Pennsylvania virus. "[Speaking] as a mentor, he was the best student ever. He was brilliant," Webster says.

When the researchers compared the April and October strains, they found that the milder strain had become more pathogenic after just a single mutation in the hemagglutinin gene (*Virology* **149**, 165–173; 1986). That work, along with data from an outbreak in Mexico in 1993, established the concept that all highly pathogenic viruses are derived from nonpathogenic strains.

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Michael Forster Rothbart

Webster recalls that when Kawaoka and his family first arrived in the US, they were polite and proper, as most Japanese are. But the first time they visited Webster's house, their son, then two years old, picked up a duck-shaped cushion off the sofa and hurled it right at Webster. "We were highly amused. But they were embarrassed out of their minds," Webster recalls. "[Kawaoka] has since lost that formality somewhat."

One year, Webster's wife taught Kawaoka to wallpaper the rooms. Ever the eager student, Kawaoka mastered the skill and now inspects the wallpaper in his hotel rooms. "I watch the seams, you know, I can do it better. I can match the pattern," he says. "Even if lose my job some time, I can maybe put wallpaper up as a career."

Perhaps then he would work a little less.

Last year, on the twenty-fifth anniversary of his marriage, Kawaoka found himself once again on a plane to Japan. His wife, Yuko, whose father worked 9-to-5 shifts and came home for lunch, was less than thrilled. "She doesn't care about me publishing high-profile papers. What she wants is for me to stay home," he says.

Kawaoka promises to retire at 65 and stay home doing nothing, perhaps only listening to music and reading novels by the Japanese author Mangetsu Hanamura. Sensitive about his English speaking skills—regularly criticized by his students at the University of Wisconsin—he says he would probably want to die in Japan, where he wouldn't have to worry about making sense to the doctors.

Not surprisingly, Japanese would also be the language of his choice in any country he owns. Perhaps, Kawaoka says laughing, the country would be populated only with women. And what would it be called? "Yoshi's country, of course."

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