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Scientists find burglary-ring-like mechanism in lethal 'Contagion' virus

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WSU virologist Hector Aguilar-Carreno and colleagues have discovered how efficient teamwork by proteins on the deadly Nipah virus help get the pathogen inside a healthy cell that's 10,000 times larger. Credit: Photo by Robert Hubner, WSU Photo Services

A team of scientists from Washington State University has discovered how one of the planet's most deadly known viruses employs burglary-ring-like teamwork to infiltrate the human cell.

Nipah virus is so menacing that the nation's top infectious disease experts served as consultants in the filmmaking of the 2011 medical thriller, "Contagion," which is based on a global Nipah outbreak.

The WSU researchers, led by virologist Hector Aguilar-Carreno, have found that two proteins on the surface of the virus communicate in a way similar to two skilled burglars – with one casing the human cell while the other waits for a signal to launch the break-in. Their findings were recently published in the medical journal *PLOS Pathogens*.

"Our study provides the most complete picture of what happens after Nipah virus attaches itself to the surface of the human cell to gain entry," said Aguilar-Carreno of WSU's Paul G. Allen School for Global Animal Health. "This is important not only to our understanding of how Nipah is transmitted, but also for viruses of the same family that can cause serious human and animal diseases."

Those include measles, mumps, respiratory syncytial virus in humans and distemper in dogs, he said.

Invasion from inner space

Working with disabled Nipah microbes that can't cause infection, Aguilar-Carreno and his colleagues determined that two proteins act as forward scouts, with protein G sensing an opportunity to activate the break-and-enter and then signaling the go-ahead to protein F to start the fusion process.

This signal exchange is so efficient that it helps explain how a single, miniscule virus can launch full-blown disease, said Aguilar-Carreno.

"The virus is able to fuse its own membrane with the membrane of a healthy cell and then invade with its RNA. Once inside its cell host,

Nipah multiplies by the thousands and the infection process begins," he said.

Flu-like, but worse

Nipah virus, identified 14 years ago during an epidemic in Malaysia, causes flu-like symptoms and convulsions due to swelling of the brain. Outbreaks of the virus inflict a high mortality rate, usually killing more humans than are spared.

Because the pathogen spreads from certain animals to humans and from person to person, the World Health Organization has identified it as a potential source of a global pandemic.

And it might start with a single cough.

As the movie "Contagion" portrays, the microbe is believed to have spread from the tropical fruit bat to pigs before making a leap to humans.

The disease hasn't been diagnosed outside remote areas of Southeast Asia. But the concern is that the pathogen could spread to other regions if an infected person travels on a plane or if the fruit bat - with its six-foot wing span - ventures farther in search of food and habitat. The virus doesn't sicken the bats; instead they are reservoir hosts.

Higher death tolls

"Since Nipah virus was identified, we've seen at least one outbreak each year, each resulting in a high percentage of deaths," said Aguilar-Carreno.

Most alarming is this year's outbreak in Bangladesh where the virus

killed 21 of the 24 people diagnosed, according to that country's Institute of Epidemiology, Disease Control and Research. Victims' ages were 8 months to 60 years.

Whether the virus is becoming more deadly or improved surveillance is finding more cases, "it's too soon to know," said virologist Paul Rota of the U.S. Centers for Disease Control in Atlanta, which classifies the pathogen in the same hot-agent category as Ebola and smallpox.

Not only does the virus spread among different species, but there is no vaccine or treatment. And that's where Aguilar-Carreno's work comes in.

"Our study reveals the intricate steps that one Nipah virus undertakes in order to enter a 10,000-times-larger healthy cell," he said. "The more we understand about Nipah's molecular mechanics, the more likely scientists can develop a drug to block it from infecting."

More information: www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1003770

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