

Find may yield flu early warning

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For a decade, disease trackers have watched anxiously as avian influenza has migrated from Asia to Europe and on to Africa, devastating poultry flocks and wild birds. To humans, it has proved - so far - less of a widespread peril, lacking the genetic machinery necessary for efficient person-to-person transmission. Just 348 people have been infected worldwide since 2003.

But the germ, scientists agree, is a time bomb in search of the right fuse.

Viruses evolve rapidly, and a few genetic changes in the right places could enable the avian flu to easily infect people and ignite a firestorm of human illness akin to the 1918 global flu epidemic that killed tens of millions.

Even more worrisome, scientists fear the pandemic could be well underway before they realize it, unless they can develop an early warning system to detect when the germ has made a lethal change in its genetic clothing.

Now, scientists from the Massachusetts Institute of Technology have discovered new details about how the flu virus interacts with the human respiratory tract - research that could lead to better methods for monitoring the virus and even drugs to stop it in its tracks if it acquires the ability to infect large numbers of people, according to a federal scientist not involved in the research.

"It's a big step forward into new territory for helping us to understand another element of transmission," said Carole Bewley, a chemist specializing in the study of infectious diseases at the National Institute of Diabetes and Digestive and Kidney Diseases. "This would help to explain those things that didn't make sense before."

Scientists have long recognized that not all strains of the flu find humans attractive targets. Some prefer pigs or birds. It turns out that the flu virus is like a piece of Velcro hunting for a companion swatch of Velcro to attach itself to.

In scientific terms, it works this way: Before a flu strain can pose a broad threat to a species, a pivotal protein carried on the virus surface has to glom onto sugar that coats cells in the victim's upper respiratory tract. The virus "catches onto the sugar and uses the sugar as a way to gain entry into the cell," said MIT bioengineer Ram Sasisekharan, senior author of yesterday's report in the journal *Nature Biotechnology*.

The current strain of avian flu making the rounds doesn't have much affinity for humans' upper respiratory tract because it can't latch on very well to the type of sugar that coats the surface of human lungs. Flu strains that attack humans prefer a type of sugar known as alpha 2-6.

But not just any alpha 2-6. The MIT scientists, working with the Centers for Disease Control and Prevention, discovered that there are different versions of the important sugar. Some are shaped like cones. Others resemble an open umbrella - and they're the ones most susceptible to invasion by flu viruses that threaten humans. They have a length and shape more compatible with the wider proteins that populate human flu viruses.

The discovery, said University of Minnesota flu tracker Michael Osterholm, "could be an important piece relative to the whole avian flu puzzle. But it doesn't solve the whole puzzle."

By understanding that it's the sugars shaped like an open-umbrella that really matter, disease specialists can now consider developing tests to detect changes in the avian flu virus that would allow it to unite with that sugar.

"If we are able to recognize through monitoring that we're seeing that adaptation, then we need to obviously increase our vigilance," Sasisekharan said, "and seriousness of concern will go up."

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