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Flu virus trots globe during off season

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The influenza A virus does not lie dormant during summer but migrates globally and mixes with other viral strains before returning to the Northern Hemisphere as a genetically different virus, according to biologists who say the finding settles a key debate on what the virus does during the summer off season when it is not infecting people.

"Nobody really knows why flu is a winter disease in the temperate regions and more continuous in the tropics," says Edward Holmes, professor of biology at Penn State. "The big question is, ‘Why is flu seasonal?’"

Flu infections in the Northern Hemisphere typically follow a familiar pattern. Some time before the start of the winter infection season, the virus evolves, changing enough to evade the previously primed immune system. Then, just before summer, the virus disappears, only to resurface the next fall with a completely different genetic makeup, ready to fool the immune system anew.

But little is known about what happens to the virus between two successive winters, or how and where it is able to sustain itself.

The key question, Holmes explains, is whether the virus settles into a dormant state waiting for the right cues of temperature and sunlight to reactivate, or whether it migrates to viral reservoirs in the tropics, from where it is later reintroduced.

It is thought that places in Southeast Asia, where humans and animals

live in close proximity, might be the permanent melting pot where viruses continually circulate and exchange genetic information.

To test the migration theory, Holmes and Martha Nelson, graduate student at Penn State, and their colleagues at the National Institutes of Health, Lone Simonsen, Cecile Viboud, and Mark A. Miller, analyzed the influenza A virus genomes of 900 virus samples from New Zealand, Australia and New York state dating between 1998-2005.

Their findings, outlined in this month's issue of *PLoS Pathogens*, reveal that the genomes of 52 viruses from New York are closely related to viruses that circulate during the winter (April to October) in New Zealand and Australia. These mixed family trees of viruses from both the north and south suggest there is widespread viral traffic across the equator each season, which contributes significantly to new epidemics in both hemispheres, the researchers note.

"If the viruses had been dormant, samples from successive seasons in each region would only be closely related to other viruses of that same region," said Holmes, who is also affiliated with Penn State's Center for Infectious Disease Dynamics (CIDD). "The fact that they are, instead, interspersed clearly tells us that the viruses are seasonally migrating across both hemispheres."

However, it is still fully unclear where and when the viruses are evolving to beat the immune system. According to Nelson, the virus changes its entire genetic makeup somewhere during the summer off-season, and it likely does this in the tropics, where the virus is found year-round.

"But we cannot say for sure at this point. To test this theory, we need viral samples from the tropics," Nelson added. The authors anticipate that samples from these regions will become available in the next few years.

The researchers are also not sure why the virus seems to die out during summer and what exactly triggers its return.

"It could be anything from human migration, aspects of climate, levels of sunlight, seasonal susceptibility of people or a combination of all these and more factors. That is another big question," said Holmes, whose work is funded by the National Institutes of Health.

What is certain, the Penn State researcher noted, is that multiple viruses arrive in New York state each season. In a connected world where emerging viruses can spread globally very quickly, Holmes says that the best way to protect communities is to have an extremely good system of disease surveillance in place and to develop universal vaccines that can protect against all kinds of influenza virus.

Source: Penn State