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Rice University researcher Jane Tao crystallized viral pieces in her quest to find flu medications.
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Finding may be tool in flu fight
Scientists at Rice and UT discover promising target for class of drugs
By LEIGH HOPPER
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Think of it as birth control for flu viruses.

Scientists at Rice University and the University of Texas at Austin have discovered a promising target for a new class of drugs that could cripple influenza A — including bird flu — as well as the common strain that sickens millions each flu season.

The discovery could lead to another weapon in the arsenal of flu-fighting drugs, of particular importance because of influenza's rapidly mutating nature.

"Some H5N1 (bird flu) strains are resistant to Tamiflu," said lead researcher Jane Tao, an assistant professor of biochemistry and cell biology at Rice, whose findings were published online Wednesday by the journal Nature. "That's the reason why it's very important that we come up with new types of antivirals."

Changing structure

Baylor College of Medicine flu expert Paul Glezen applauded "the fact they are thinking about new approaches to antivirals. We need more research into that."

The potential drug target is a long, flexible "tail loop" on a flu virus protein called nucleoprotein, or NP. Tao and her colleagues found that even minor changes to the tail prevent NP proteins from stacking together and forming the physical structure necessary to turn a host cell into a virus-replicating factory.

A deep "binding pocket" on the tail loop — nearly identical across many strains of influenza A — could be the flu virus's Achilles' heel, Tao explained.

"We are collaborating with others to identify possible antivirals," Tao said. Such a compound would "dock" in that binding pocket and prevent the NP protein from binding with other NP proteins.

She said the next step is to look through a computer database containing the atomic structure of more than 10,000 compounds to see which best fits the NP's binding pocket.

Overcoming resistance

The tail-loop discovery was based on a series of experiments done to reveal the atomic structure of NP. Biochemists used a method called X-ray crystallography to discern, in three-dimensional
form, the position of a biomolecule's atoms in a crystal based upon the diffraction patterns of X-rays that pass through it.

But NP resists crystalization and many researchers have been stymied in their efforts. Tao's ability to pull it off, said her collaborator Robert M. Krug, a professor at the Institute for Cellular and Molecular Biology at UT Austin, was an impressive feat.

"Many well-established people in the past have tried to crystallize and get the structure of the flu virus NP protein and failed," he said. "Here, you have this young structural biologist succeeding. It's quite an accomplishment."

Tao, 34, gave credit to postdoctoral research associate Qiaozhen Ye, estimating Ye prepared about 1,000 jars to get the 100 or so crystals needed for the experiments. "She was amazing," said Tao of Ye, who earned a raise for her efforts.

leigh.hopper@chron.com