MedicalXpress

Scientists' studies combat health threats

May 25 2007

The outbreak of severe acute respiratory syndrome (SARS) in 2002 was a loud wake-up call for researchers studying infectious diseases. SARS infected more than 8,000 people, killed 10 percent of those infected and weakened most with pneumonia.

"The SARS outbreak was a strong reminder that new viruses can emerge – and, whether new or old, pathogens can cause not only significant disease and death, but they can also have a global socioeconomic impact," says Brenda Hogue, an associate professor in the Biodesign Institute's Center for Infectious Diseases and Vaccinology and in the School of Life Sciences.

Hogue has been involved in a big push to uncover some of the key clues behind coronavirus illness.

When SARS emerged, no one could have predicted that a new coronavirus – usually the culprit of nothing more than a common cold in humans – could become so harmful and spread so quickly through health systems from China to Canada.

Coronaviruses routinely cause about 30 percent of the common colds in humans and infect a large number of animals, where they cause significantly more severe diseases.

"We expect that some of what we learn about coronaviruses will no doubt be applicable to other viruses too," Hogue says. "Our long-term goals are to make use of this basic research to design better vaccines and

develop new targets for antiviral treatments."

One of the well-known characteristics of viruses is their uncanny ability to hijack the resources of its host. What made SARS such an alarming threat was that the symptoms were much more severe than had been seen before in human coronavirus infections. Even though the SARS virus has not reappeared in humans since the 2003 outbreak, Hogue remains cautious.

"Epidemiologists and those of us who work with these viruses think that it will reappear," she says.

As with other emergent threats, Hogue says that the outbreak of the SARS virus in Asia was linked to animals that live close to humans, including bats and cat-like animals called civets. So, while SARS may have been mitigated for now, Hogue and researchers hope that their efforts studying the basic science behind viral infection will apply to a variety of diseases, including the looming specter of pandemic flu.

Hogue and her Biodesign Institute colleagues have produced several insights into coronavirus biology that also could help pinpoint weaknesses in the viral armament. In a paper published in the March issue of the Journal of Virology, titled "Mouse Hepatitis Coronavirus A59 Nucleocapsid Protein Is a Type I Interferon Antagonist," lead authors Ye Ye and Kevin Hauns, graduate students in the Center for Infectious Diseases and Vaccinology, discovered a viral protein that may allow the virus to evade the immune system.

The suspected molecular cause is a nucleocapsid protein, whose primary role is to help assemble the viral genome into the virus particle that can readily infect the body. The nucleocapsid protein has been found to circumvent type I interferons, which are natural proteins that help mount the body's initial immune response against viruses.

Hogue and colleagues plan to focus their efforts on determining how the coronavirus nucleocapsid protein is able to act as an interferon antagonist, and also will continue to look for other viral proteins that could act as immune response antagonists.

Coronaviruses invade cells in the human body like spiny cockleburs by first attaching to cells with their “spike” proteins that stick out from the viral envelope. The spikes not only help cause infection, but they appear under the microscope as a halo, or “crown,” around the coat that gives coronaviruses their name. After it attaches, the virus then enters the cell and quickly uses the cell’s machinery to make copies of itself, thus spreading an infection.

Hogue is collaborating with Zhong Huang, an assistant research professor also in Biodesign’s Center for Infectious Diseases and Vaccinology, to express parts of the spike protein in plants. The scientists hope to develop a vaccine that can block the interaction of the spike protein with the host receptor and prevent infection.

Another important viral target of Hogue’s research is the role of the coronavirus envelope protein (E protein), described in “Role of the Coronavirus E Viroporin Protein Transmembrane Domain in Virus Assembly,” Journal of Virology (April). By creating mutants of the E protein in a mouse coronavirus model that infects the liver and other organs, Ye and Hogue found that the virus lost some of its ability to assemble and be released from cells.

Proteins similar to the E protein that can form channels in membranes are present in other viruses too, which would make the development of an antiviral that blocks the function of the E protein potentially applicable to a wide variety of diseases, Hogue says.

Teasing apart the cycle of coronavirus infection has helped Hogue’s

group identify new molecular targets and provided some exciting avenues to pursue. By continuing their fundamental research on viruses, the team hopes to refine their understanding of virus-host interactions.

Source: Arizona State University