Study establishes zebrafish as a model for flu study

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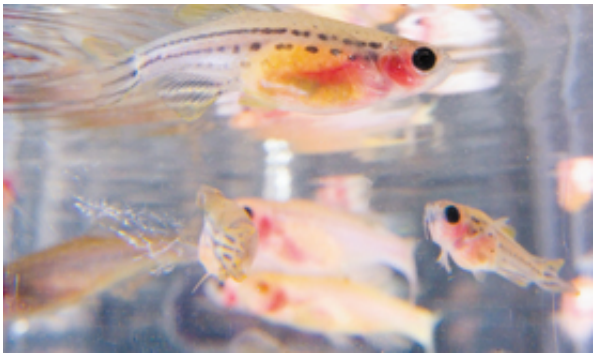

In the ongoing struggle to prevent and manage seasonal flu outbreaks, animal models of influenza infection are essential to gaining better understanding of innate immune response and screening for new drugs. A research team led by University of Maine scientists has shown that two strains of human influenza A virus (IAV) can infect live zebrafish embryos, and that treatment with an anti-influenza compound reduces mortality.

It is the first study establishing the zebrafish as a model for investigating IAV infection.

"A zebrafish model of IAV infection will provide a powerful new tool in the search for new ways to prevent and treat influenza," according to the

researchers, who published their findings in the journal *Disease Models & Mechanisms*.

The research team is led by professor Carol Kim and graduate student Kristin Gabor of UMaine's Graduate School of Biomedical Sciences and Engineering, and includes four other UMaine researchers and one from Ghent University.

Most studies of viral pathogens that can infect zebrafish have been limited to fish-specific viruses. However, in recent years, four human viral illnesses have been reported to be modeled in zebrafish—herpes simplex, hepatitis C and chikungunya and now influenza A.

For studies of flu virus infection, the researchers focused on specific sialic acids and cytokines comparable in zebrafish embryos and humans. For these studies the zebrafish embryos also were kept in a temperature range comparable to the human respiratory tract (77 to 91.4 degrees F).

"The transparent zebrafish embryo allows researchers to visualize, track and image fluorescently labeled components of the immune response system in vivo, making it ideal for immunological research," said Kim, a UMaine microbiologist and vice president for research and graduate school dean, writing earlier this year in the journal Developmental and Comparative Immunology.

In this study, visualization of a fluorescent reporter strain of IAV in vivo demonstrated that IAV infects cell lining surfaces of the zebrafish swimbladder, as it does in the human lungs.

In addition, the antiviral drug Zanamivir, known for being effective in treating influenza A and B in humans, was tested in vivo and was found to reduce IAV infection.

The researchers note that studies of IAV infection in adult zebrafish have the potential to provide valuable insights into infectious disease processes, particularly in understanding adaptive immune response and vaccine efficacy. This is critically important in light of the rapidly developing resistance of the influenza virus to drug therapies.

"This zebrafish embryo model of IAV infection will be an important resource for dissecting molecular mechanisms of host-pathogen interactions in vivo, as well as for identifying new antiviral therapies," write the researchers.

Provided by University of Maine