H5N1 virus targets pulmonary endothelial cells

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The H5N1 virus has killed roughly 60 percent of humans infected, a mortality rate which is orders of magnitude higher than that of seasonal influenza virus. Many victims of the former fall heir to acute respiratory distress syndrome—the inability to breathe. Now researchers from the Centers for Disease Control and Prevention, and the University of South Alabama show that the highly pathogenic avian influenza H5N1 virus, but not seasonal influenza viruses, can target the cells of human lung tissue, where they replicate fast and efficiently, and induce inflammation, which correlates with H5N1-induced acute respiratory distress syndrome that is observed in humans. The research is published in the January *Journal of Virology*.

"The pulmonary endothelium is strategically located within the lung and its function and structural integrity are essential for adequate pulmonary function," says coauthor Terrence Tumpey of the Centers for Disease Control and Prevention. "We compared the infection rate of different subtype influenza viruses in human lung endothelial cells, and assessed the host response to infection," he says. "We found that the H5N1 virus, but not common seasonal influenza viruses, can target human pulmonary endothelial cells." There, the viruses replicate rapidly, creating an overwhelming inflammatory cytokine response, essentially causing an immune response so powerful that it kills the pulmonary endothelial cells, results which Tumpey says correlate with the H5N1-induced acute respiratory distress syndrome that is observed in humans where the production of cytokines, immune system compounds, has been detected in lung endothelial cells.

The Spanish influenza pandemic of 1918 is thought to have resulted in a similarly high influx of inflammatory cells and profound vascular leakage in the lower respiratory tract, often precipitating the same acute respiratory distress syndrome seen in H5N1 influenza cases. That pandemic, estimated to have sickened 350 million, killing roughly 50 million, had a mortality rate of approximately 14 percent—far less than that of H5N1, but still shockingly high.

“Although the mechanism of H5N1 pathogenesis is not entirely known, our research identified one virulent factor, the cleavage site of the viral surface glycoprotein hemagglutinin, which we found to be critical for the production of infectious progeny H5N1 virus in pulmonary endothelial cells,” says Tumpey. Other unknown virulence factors undoubtedly exist, and require further study, he says.

“Treatment with anti-inflammatory drugs has been proposed as a therapeutic option for patients infected with H5N1 viruses,” says Tumpey. “The development of new, more targeted therapies for H5N1 disease along with combination antiviral drug treatment could be an effective approach in reducing acute lung injury and mortality caused by H5N1 virus.”

More information: H. Zeng, et al., 2011. Human pulmonary microvascular endothelial cells support productive replication of highly pathogenic avian influenza viruses: possible involvement in the pathogenesis of human H5N1 virus infection. *J. Virol.* 86:667-678.

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