Lipid blocks influenza infection

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A natural lipid in the fluid lining the lungs inhibits influenza infections in both cell cultures and mouse models, according to researchers at National Jewish Health. These findings, combined with previous studies demonstrating effectiveness against respiratory syncytial virus, suggest that the molecule, known as POPG, may have broad antiviral activity.

"Supplemental POPG could be an important, inexpensive and novel approach for the prevention and treatment of influenza and other respiratory virus infections," said Dennis Voelker, PhD, Professor of Medicine, and senior author in the report, published online in the American journal of Respiratory Cell *and Molecular Biology*.

Influenza infects millions of people across the globe, killing 500,000 each year. Vaccines are highly effective, but must be reformulated each year to counter new viral strains. Two classes of drug are currently available to treat established influenza infections, although widespread resistance has developed against one class and is developing against the other.

Several proteins that inhibit viral activity have been identified in the fluid lining the lungs. Until recently, however, the antiviral role of POPG (palmitoyl-oleoyl-phosphatidylglycerol) has been unknown. Previous research by Dr. Voelker, Mari Numata, MD, PhD, and their colleagues demonstrated that POPG reduces inflammation in the lung and prevents infection by respiratory syncytial virus.

In the most recent study, the researchers looked at the ability of POPG

to inhibit infection by two strains of influenza, H1N1-PR8 and H3N2. They found that POPG suppressed inflammatory responses, viral propagation and cell death normally associated with influenza infection.

In mice, POPG also suppressed viral infection and replication, and markedly reduced the inflammatory response to the virus. There were no observable deleterious effects of POPG in animal behavior or histopathology.

"Lipids such as POPG, offer potential advantages over antiviral proteins, because they are less likely to elicit unwanted immune responses, are more chemically stable and less expensive to manufacture than proteins," said Dr. Numata, an instructor at National Jewish Health, and lead author on both the RSV and influenza papers. "Because POPG is effective against at least two different viruses, it also seems likely that a single mutation, which can make influenza vaccines and current drugs ineffective, is unlikely to have the same effect on POPG's action."

The researchers showed that POPG works by binding strongly to viral particles, which prevents attachment and infection of cells. This means that POPG works best if given before an infection occurs.

It has potential, however, to work after an infection has begun by inhibiting spread of the virus to uninfected cells. The success of POPG treatment after a virus infection has been established depends on keeping the lipid levels high for an extended period. At present it is difficult to maintain high levels of POPG in mice because of their rapid metabolisms and rapid respiratory rate.

"We believe POPG may prove effective both before and after an infection has occurred," said Dr. Voelker. "Our initial results suggest that it may be possible to maintain therapeutic levels in the body with a reasonable dosing scheme, and we are investigating that now."

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