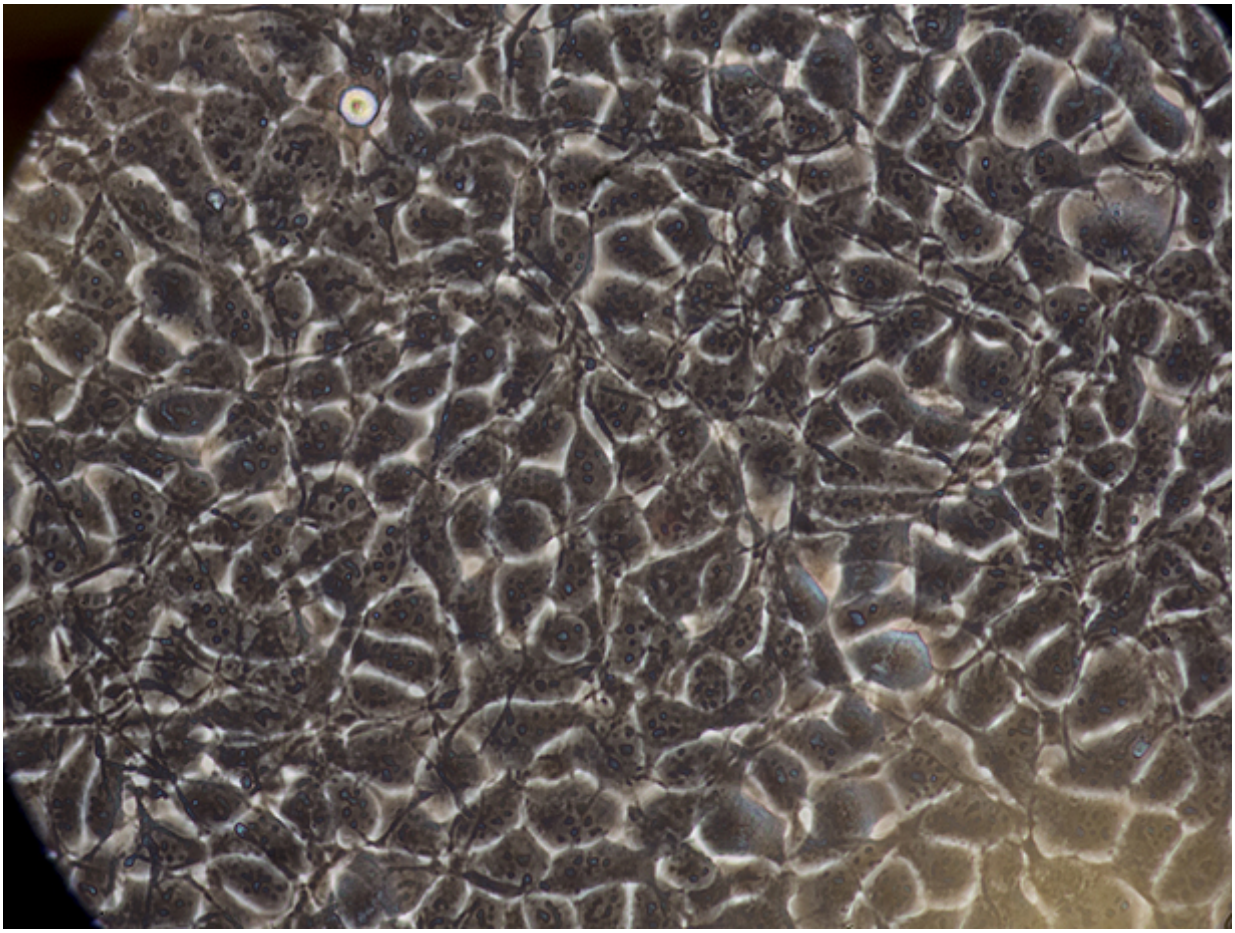
MedicalXpress

Compound found to trigger innate immunity against viruses

December 17 2015, by Bobbi Nodell



Cells under a microscope in a UW Medicine immunity lab. Credit: Dennis Wise

Research from UW Medicine and collaborators indicates that a drug-like

molecule can activate innate immunity and induce genes to control infection in a range of RNA viruses, including West Nile, dengue, hepatitis C, influenza A, respiratory syncytial, Nipah, Lassa and Ebola.

The findings, published today in the *Journal of Virology*, show promising evidence for creating a broad-spectrum antiviral.

"Our study shows that our compound has an antiviral effect against all these viruses," said Michael Gale Jr., UW professor of immunology and director of the UW Center for Innate Immunity and Immune Disease.

Gale said the findings are the first he knows of which show that a small molecule can trigger innate immunity through a molecule present in all our cells known as RIG-I.

RIG-I is a cellular protein known as pathogen recognition receptor. These receptors function to detect viral RNA and signal an innate immune response inside the cell that is essential for limiting and controlling viral infections. This signaling then induces the expression of many innate immune and antiviral genes and the production of antiviral gene products, pro-inflammatory cytokines, chemokines and interferons.

"These products act in concert to suppress and control virus infection," the researchers wrote.

The researchers said inducing signaling to activate the innate immune response to control virus infection has been tested successfully in cells and in mice. The next step would be to test dosing and stability in animal models and then in humans - a process that could take between two and five years, said Gale.

Currently, there are no known broad spectrum antiviral drugs, and few cures for infection by RNA viruses, much less much effective

treatments. RNA viruses pose a significant public health problem worldwide because of their high mutation rate that allows them to escape the immune response, and they are a frequent cause of emerging and re-emerging viral infections. West Nile virus infections, for example, started in the USA in 2000 and remerged again in 2012. Moreover, the World Health Organization reports about 50 million to 100 million new cases of dengue fever yearly and 22,000 deaths caused by the related dengue virus. Dengue is now present in the southern U.S.

Michael Gale, UW professor of immunology and director of the Center for Innate Immunity and Immune Disease, talks with staff. Credit: Dennis Wise

Hepatitis C, which is transmitted through the blood, infects about 3 million-4 million people each year and about 150 million people are chronically infected and at risk for developing liver cirrhosis or liver cancer, according to the paper. Researchers said direct acting antiviral drugs have been developed to control hepatitis C and show promise of long-term cure of infection but treatment of disparate hepatitis C genotypes remains a concern, and viral mutation to drug resistance is an underlying concern with prolonged use of these drugs. Also, the researchers noted, the cost of the drugs are exorbitant, which make them unaffordable to most patients.

Shawn Iadonato, the chief scientific officer at Kineta, a Seattle-based biotechnology firm, said there is tremendous interest in triggering innate immunity for a number of reasons. One, he said, is because some viral infections can't be treated by traditional antivirals, such as chronic hepatitis B infection. Also, by triggering innate immunity, the viruses will be much less likely to resist the drug actions because they are targeted to the cell through the actions of many different genes and not to the virus itself, thus making drug resistance much harder if not impossible to achieve.

The span of viruses that could be treated would also have a huge benefit globally since many RNA viruses - Ebola, Nipah, Lassa and dengue - affect mainly developing countries.

"It's routine for us to think of broad-spectrum antibiotics, but the equivalent for virology doesn't exist," said Iadonato.

More information: hsnewsbeat.washington.edu/site …lt/files/documents/J.%20Virol.-2015.pdf

Provided by University of Washington