

Insights gained from growing cold-causing virus on sinus tissue

April 10 2011

Using sinus tissue removed during surgery at University of Wisconsin Hospital and Clinics, researchers at the University of Wisconsin-Madison have managed to grow a recently discovered species of human rhinovirus (HRV), the most frequent cause of the common cold, in culture.

The researchers found that the virus, which is associated with up to half of all HRV infections in children, has reproductive properties that differ from those of other members of the HRV family.

The accomplishments, reported in <u>Nature Medicine</u> on April 11, should allow antiviral compounds to be screened to see if they stop the virus from growing.

The report sheds light on HRV-C, a new member of the HRV family that also includes the well-known HRV-A and HRV-B. Discovered five years ago, HRV-C has been notoriously difficult to grow in standard cell cultures and, therefore, impossible to study.

"We now have evidence that there may be new approaches to treating or preventing HRV-C infections," says senior author James Gern, professor of medicine at the UW-Madison School of Medicine and Public Health and an asthma expert at American Family Children's Hospital.

Future drugs could be especially useful for children and adults who have asthma and other lung problems, Gern says.



Recent studies have shown that in addition to its major role in the common cold, HRV-C is responsible for between 50 percent and 80 percent of asthma attacks. HRV-C is a frequent cause of wheezing illnesses in infants and may be especially likely to cause asthma attacks in children. HRV infections of all kinds also can greatly worsen chronic lung diseases such as cystic fibrosis and chronic obstructive pulmonary disease.

Like other scientists, Yury Bochkov, a virologist in Gern's lab, was unable to grow HRV-C in standard cell lines. So he turned to nasal tissue he collected following sinus surgery-and was surprised to find success. He grew significant amounts of two forms of HRV-C, then sequenced the complete virus genome and engineered an identical copy of it in a plasmid vector.

Studying the reproduction of the living, growing virus, he found that HRV-C replication appeared to occur in specific kinds of cells localized in nasal epithelium tissue.

"We also found that HRV-C does not attach to the two receptors that HRV-A and HRV-B use," Bochkov says. "HRV-C uses a distinct, yet unknown, receptor that is absent or under-expressed in many cell lines."

HRV-C also responded differently to antibodies that block receptor binding.

"Antibodies that normally keep HRV-A and HRV-B from binding to their receptors did not prevent HRV-C from binding to them," Bochkov says.

The findings suggest that new approaches are needed to treat HRV-C, says Gern.



"Previous drug candidates for the common cold were tested only against HRV-A and HRV-B," he says. "For more effective medications, we need to also target HRV-C."

Bochkov will continue to use the organ culture system to study details of HRV-C biology.

"It's now clear that these viruses have unique growth requirements," he says.

Provided by University of Wisconsin-Madison

Citation: Insights gained from growing cold-causing virus on sinus tissue (2011, April 10) retrieved 10 July 2023 from https://medicalxpress.com/news/2011-04-insights-gained-cold-causing-virus-sinus.html

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