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Scientists see Norwalk virus' Achilles heel

Using the Canadian Light Source synchrotron, an international team led by University of Calgary researcher Ken Ng has determined the detailed structure of the enzyme the Norwalk virus uses to make copies of its genetic code in order to replicate itself. The information is crucial to developing drugs that could be used to treat outbreaks of Norwalk and other related viruses.

The Norwalk virus uses the enzyme, RNA polymerase, to make new strands of RNA using an existing RNA strand as a template. The copying, which occurs within an area of the enzyme called an active site, can be blocked—or inhibited—with a drug molecule shaped to fit the site, like a key in a key hole.

“These are the first structures showing the enzyme doing its job interacting with RNA,” says Professor Ng. “These structures provide ideas of how we could develop new antiviral drugs that block the enzyme’s activity.”

The group includes scientists from the University of Calgary, University of Oviedo (Spain), Penn State University, the University of Kansas and the Canadian Light Source. Their work appears in the March 21 issue of the *Journal of Biological Chemistry*.

Outbreaks of Norwalk virus are notorious for the havoc they can cause to people living in close quarters, from cruise ships to hospital wards, often causing severe dehydration due to vomiting and diarrhea. The currently untreatable bug belongs to a superfamily of viruses that stores their genetic code as RNA, including polio, hepatitis C, foot-and-mouth disease and even the common cold. The problem with all of these viruses is the lack of effective treatments.

“The best doctors can do with Norwalk patients is treat the symptoms. We have the polio vaccine, but many other serious diseases, like hepatitis C, lack effective treatments,” explains Professor Ng. “This polymerase is closely related in all of these viruses, so an inhibitor drug that works against Norwalk virus could also work in treating hepatitis C.”

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The University of Calgary is ranked top 10 in Canada for research income, fundraising, endowment, research competitions and national awards. For more information, visit: www.ucalgary.ca

The Canadian Light Source is Canada’s national centre for synchrotron research. Located at the University of Saskatchewan in Saskatoon, the CLS is a powerful tool for academic and industrial research in a wide variety of areas including environmental science, natural resources and energy, health and life sciences, and information and communications technology. CLS operations are funded by the Government of Canada, NSERC, NRC, CIHR, the Government of Saskatchewan and the University of Saskatchewan. For more information: www.lightsource.ca/media/quickfacts.php.

Reference: Dmitry F. Zamyatkin, Francisco Parra, Jose M. Martin Alonso, Daniel A. Harki, Blake R. Peterson, Pawel Grochulski and Kenneth K.-S. Ng. 2008. Structural insights into mechanisms of

catalysis and inhibition in Norwalk Virus polymerase. *Journal of Biological Chemistry*, Vol. 283, Number 12, pp. 7705-7712. DOI: 10.1074/jbc.M709563200.

Media availability: Dr. Ng is available for interviews Wednesday, 19 March, from 10 to 11:30 a.m. MDT (12 to 1:30 p.m. EDT).

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