Discovery sets stage for vaccine against gastric cancer, ulcers

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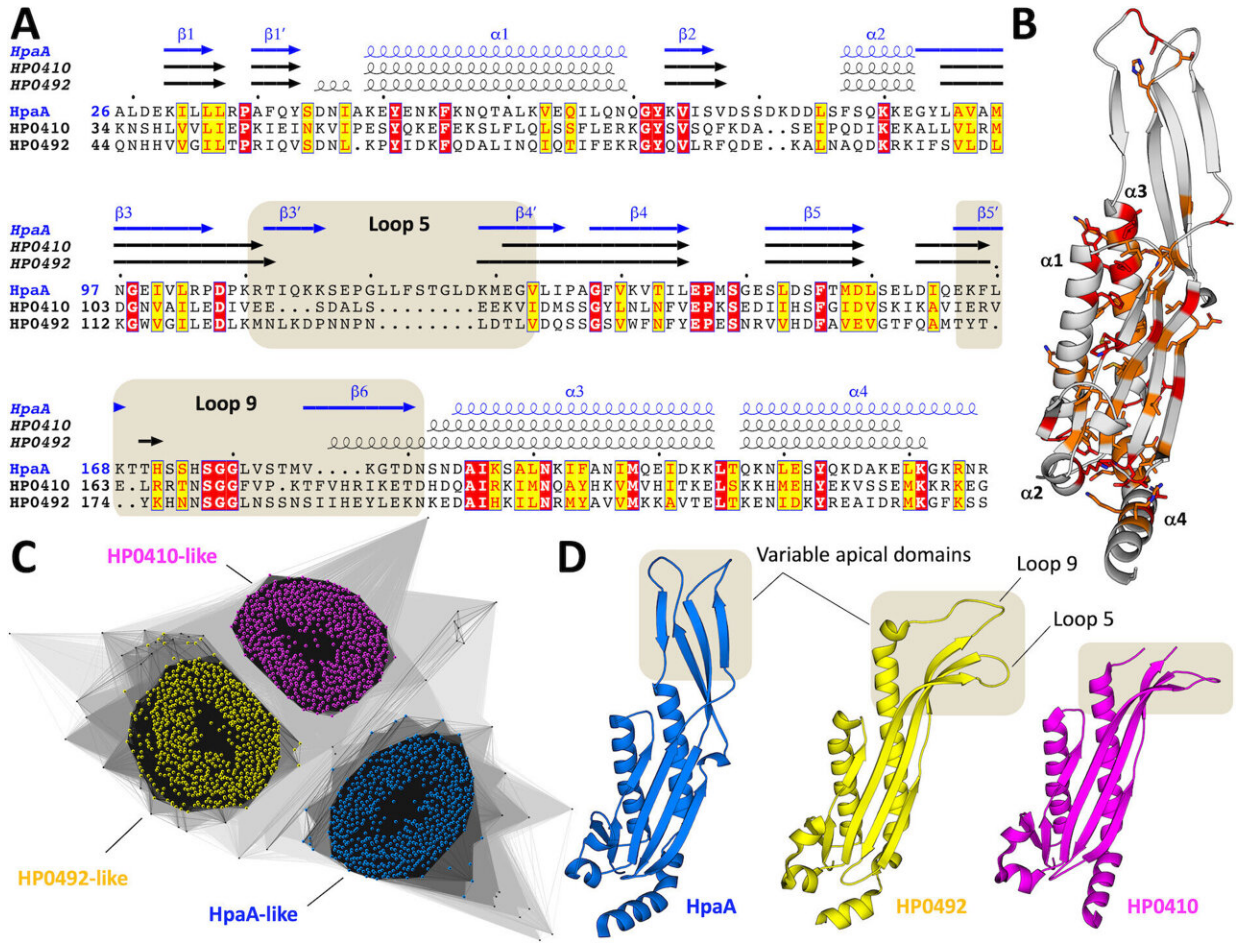

Structural alignment and cluster sequence analysis of the Neuraminyllactose-binding hemagglutinin superfamily. (**A**) Sequence alignment of HpaA, HP0410, and HP0492. The secondary structure elements and loops from the apical domain are shown above the sequences. Identical residues and conserved residues are highlighted and boxed in red and yellow, respectively. The apical domain is indicated with a brown background. (**B**) The sequence conservation

information is mapped onto the HpaA structure. Identical residues and conserved amino acids are colored in red and orange, providing insight into region of significant conservation within the protein. (**C**) To assess the broader context of HpaA, all sequences from the Neuraminyllactose-binding hemagglutinin superfamily (PFAM entry PF05211) were extracted and subjected to sequence-based classification using CLANS (34). The protein family comprises 2002 sequences, 1990 of them originating from the *Helicobacter* genus. The resulting plot depicts an all-against-all pairwise BLAST clustering of individual sequences in a two-dimensional space. Line connections are drawn between similar sequences based on a *P*-value cut-off of $1e^{-2}$, and the line distances represent proportional sequence similarities. The majority of sequences cluster into three distinct groups represented by HpaA, HP0410, and HP0492. These groups are not mutually exclusive and can coexist within *helicobacter* genomes. (**D**) Structural representations of HpaA, HP0410, and HP0492 are shown in the same orientation. The apical domain, which corresponds to the most variable region of the protein family in term of both sequence and structure, is highlighted and boxed in brown. Credit: *mBio* (2024). DOI: 10.1128/mbio.02952-23

H. pylori is one of the most common disease-causing bacteria. More than half of the world's population have the bacteria in their body; and while in Canada overall prevalence of H. pylori is between 20% and 30%, some groups—including Indigenous communities—have higher rates.

Using the Canadian Light Source at the University of Saskatchewan (USask) researchers from Quebec's National Institute of Scientific Research (INRS) have for the first time solved the structure of the protein that plays a key role in helping H. pylori stick to the lining of our stomach. Their research paves the way for developing a vaccine against the infection.

It is H. pylori's ability to bind to the inside of the stomach that helps it survive and cause health problems. The pathogen is responsible for nearly all gastric cancers and peptic ulcers. Around one in 10 people who

carry the common pathogen will develop an ulcer; almost 3% will get stomach cancer.

Professor Charles Calmettes, a biochemist at INRS, says that being able to see the structure of the protein HpaA helps scientists better understand H. pylori's "stickiness" and why our body reacts by causing certain immune cells to cause inflammation. His team's findings were published in the journal *mBio*.

"Investigating this bacterium is a way to help find new vaccine or drug targets, because there is some concern about antibiotic resistance," says Calmettes. "For the future, we will need to have some more tools to treat this infection."

Calmettes says the CLS's CMCF beamline was key in understanding how the protein binds a receptor on to a human cell. "Most of our studies rely on solving the atomic structure of bacterial virulence factors. And for this we need the synchrotron light," says Calmettes. "Without the CLS we are not able to solve the structure of HpaA."

More information: Cyrielle Martini et al, Unraveling the crystal structure of the HpaA adhesin: insights into cell adhesion function and epitope localization of a Helicobacter pylori vaccine candidate, *mBio* (2024). DOI: 10.1128/mbio.02952-23

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