New world Helicobacter pylori genome sequenced, dynamics of inflammation-related genes revealed

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An international team of researchers led by scientists at the Virginia Bioinformatics Institute (VBI) at Virginia Tech have sequenced the genome of an Amerindian strain of the gastric bug *Helicobacter pylori*, confirming the out-of-Africa migration of this bacterial stowaway to the New World. Experiments in animals have highlighted how specific genes in the bacterial strain may be crucial to the onset of inflammation and disease.

H. pylori is a bacterium that colonizes the stomachs of over half the world's human population. Different strains of the bug have lived with, evolved and followed humans on their travels since ancient times. *H. pylori* is now recognized as a major risk factor in the development of stomach cancer and ulcers. However, the details of what make some strains of the bug trigger disease and others not need to be fully worked out.

Martin Blaser of the New York University Langone Medical Center, one of the authors of the study, remarked: "Most sequencing efforts for *H. pylori* have focused on the bacterial genomes from individuals of European descent. The new sequence information helps to redress the geographic bias of earlier work and reveals important clues about the evolution and migration of the bacterium and its human host into the New World."

To help visualize the evolutionary relationships among the different *H. pylori* strains, the team built a robust phylogenetic tree that helps show the evolutionary relationships among the different biological strains. The tree of life that the scientists were able to piece together reflected the major human migration out of Africa, through Asia and into the New World. Consistent with earlier findings, similarities between the genetic make-up of the Amerindian strain and the genome of a strain from East Asia suggest that the first colonizers of the New World brought *H. pylori* with them.

Josep Bassaganya-Riera, associate professor and leader of the Nutritional Immunology Group at the Virginia Bioinformatics Institute at Virginia Tech, senior author on the paper, commented: "In addition to building a picture of the *H. pylori* genome, we have been trying to find out what features of the Amerindian strain of *H. pylori* might be responsible for the low incidence of gastric cancer and other related conditions that have been reported in some geographic areas, including parts of South America. Our experiments show that a cytotoxin-associated gene known as cagA is essential to induce inflammation." He added: "Further experiments in mice have revealed that an unusual arrangement of these inflammation-related genes are lost when the organism interacts with its host in the stomach, which may explain the low incidence of gastric cancer and peptic ulcers in some populations of the New World. Further experiments are in progress to establish the causality of these observations and to develop computational and mathematical models of immune responses to *H. pylori*."

The scientists hope to use the insights gained from the analysis of the *H. pylori* genome to help in the development of diagnostic tools and therapies for inflammation-related diseases and conditions.

More information: Mane SP, Dominguez-Bello MG, Blaser MJ, Sobral BW, Hontecillas R, Skoneczka J, Mohapatra SK, Crasta OR,

Evans C, Modise T, Shallom S, Shukla M, Varon C, Mégraud F, Maldonado-Contreras AL, Williams KP, Bassaganya-Riera J. (2010) Host-Interactive Genes in Amerindian Helicobacter pylori Diverge From Their Old World Homologs and Mediate Inflammatory Responses. Journal of Bacteriology 192(12): 3078-3092. Available on-line at jb.asm.org/cgi/reprint/JB.0006 … w=long&pmid=20400544