Gut bacterium indirectly causes symptoms by altering fruit fly microbiome

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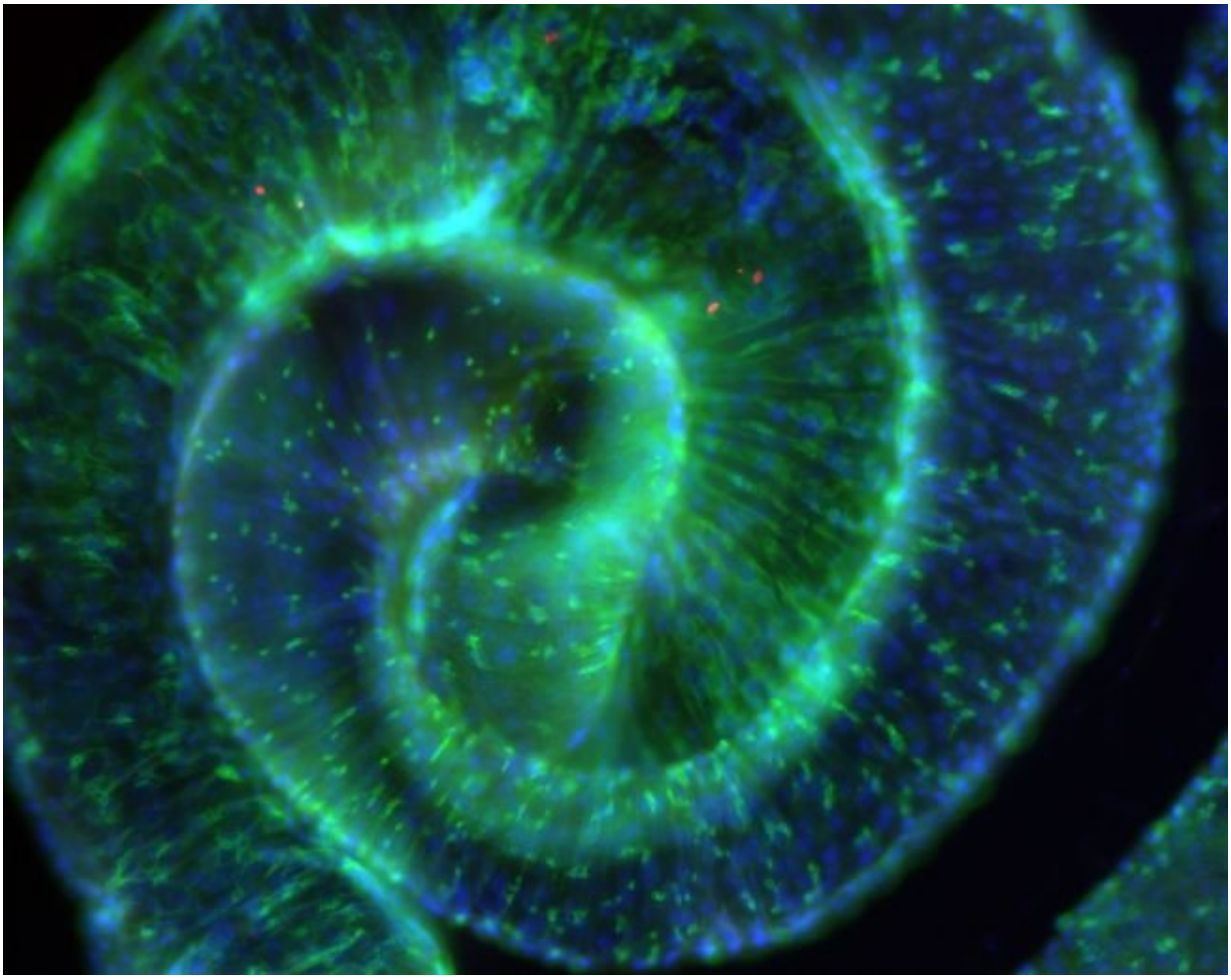

A fruit fly gut. Credit: Tiffani Jones

CagA, a protein produced by the bacterium *Helicobacter pylori*, can alter the population of microbes living in the fruit fly gut, leading to disease symptoms, according to new research published in *PLOS Pathogens* by Tiffani Jones and Karen Guillemin of the University of Oregon.

Microbes living in the human gut normally help keep people healthy, but disruptions to this microbial community can promote disease. Infections with specific microbial species can disrupt the gut microbiome, but it is unclear how such disruption occurs and whether it promotes disease.

In the new study, Jones and her colleagues used Drosophila fruit flies to test the effects of infection with *H. pylori*, which can cause gastric cancer in humans. They hypothesized that a protein associated with *H. pylori* called CagA disrupts the fruit fly gut microbiome and contributes to disease.

To test their hypothesis, the researchers genetically engineered fruit flies to express the CagA protein in their intestines, without being infected by *H. pylori*. This allowed them to disentangle the specific effects of CagA from the overall effects of *H. pylori* infection.

They found that CagA expression in the fruit fly gut caused excess growth of intestinal cells and promoted immune system responses that are associated with *H. pylori* infection. However, these symptoms did not occur in CagA-expressing flies that were raised without microbes, suggesting the importance of the gut microbiome.

Indeed, further investigation revealed that CagA expression was associated with a disrupted gut microbiome in the flies. Exposure to the CagA-expressing flies caused the same microbiome disruptions in normal flies, which was sufficient to cause the same symptoms of excess cell growth and immune response seen in the genetically altered flies.

Overall, these findings show that CagA can indirectly cause disease symptoms by altering the gut microbiome. This raises the possibility that the harmful effects of infection with *H. pylori*—and other microbes that may function similarly—could be mitigated by manipulating the balance of microbes in the gut.

"Our work demonstrates for the first time that a bacterial virulence factor like CagA can alter commensal microbial communities to cause disease," the author explain. "This work also reveals that commensal microbial communities may participate in the progression of *H. pylori* mediated gastric cancer."

More information: Jones TA, Hernandez DZ, Wong ZC, Wandler AM, Guillemin K (2017) The bacterial virulence factor CagA induces microbial dysbiosis that contributes to excessive epithelial cell proliferation in the Drosophila gut. *PLoS Pathog* 13(10): e1006631. doi.org/10.1371/journal.ppat.1006631

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