# A bacterium which triggers cancer

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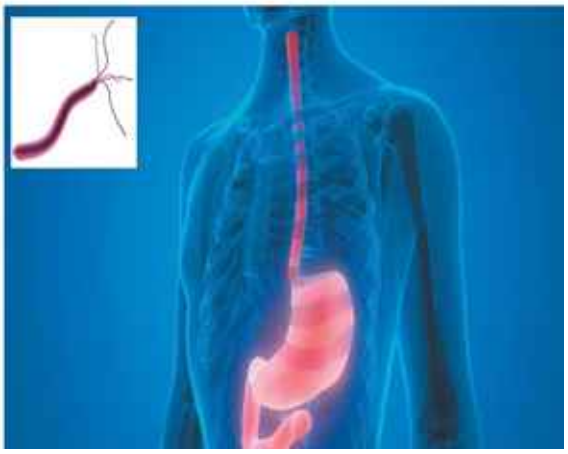
*The results of a recent study allow us to better understand how the bacterium H. pylori infects the cells of the stomach lining and triggers the development of cancer.*



## A BACTERIUM WHICH LOVES ACIDITY

*Helicobacter pylori* is a very particular bacterium which has the characteristic of specifically infecting the stomachs of primates, including humans. This infection is made possible by certain unique properties of this bacterium, notably its spiral form which allows it to burrow through the mucus which overlays the lining of the stomach, its flagellae which make it quite mobile and its production of ammonia which protects it from the extremely acidic conditions which exist inside the stomach (the bacterium secrets an enzyme, urease, which transforms urea into ammonia and thus forms an alkaline shield which neutralizes the acidity around the bacterium). These comprise an assembly of highly effective adaptations, because genetic analysis indicates that this bacterium has cohabited with humans for at least 100,000 years, and even today about half of the world population is infected by *H. pylori*.

## INFLAMMATORY LESIONS

The presence of *H. pylori* within the stomach is threatening because this bacterium provokes the formation of inflammatory lesions (chronic gastritis) which can evolve into ulcers or, even worse, into stomach cancer. This role, discovered in 1983 by Australian researchers (Drs. Barry Marshall and Robin Warren) was ridiculed for several years because the medical dogma at the time attributed the responsibility for gastric ulcers to stress. However, the truth always triumphs in the end in science and the discovery by Drs. Marshall and Warren was shown to be a major advance in our understanding of stomach pathologies, which brought them the Nobel Prize in Medicine in 2005.

## A CARCINOGENIC BACTERIUM

One of the most serious consequences of *H. pylori* infection is, of course, the increased risk of stomach cancer, a risk which is about 6 times higher in infected persons than in uninfected individuals. This carcinogenic effect of the bacterium is caused by the secretion of a toxin called CagA (cytotoxin-associated gene A), which penetrates into the cells of the gastric mucosa and modifies their structure and activity.

A recent study sought to elucidate the mechanism used by *H. pylori* to inject this carcinogenic toxin into the stomach cells and thus promote the development of cancer[1]. It turned out to be a very elegant mechanism, which can be separated into two distinct phases:

1. The scientists initially observed that the bacterium produced an enzyme (HtrA) which acts as a sort of molecular scissors for breaking through the "seal" binding the mucosal layer. Under normal conditions, the cells of this mucosa tightly adhere to each other as a way of preventing the gastric acidity from damaging the stomach. Upon infection by *H. pylori*, production of the HtrA enzyme leads to the destruction of three proteins involved in the formation of this barrier (occludin, claudin-8 and E-cadherin), which allows the bacterium to infiltrate amongst the cells.

2. Once established deep within the mucosa, the bacterium uses its surface proteins like molecular antennae, in order to bind to a cellular protein (integrin) and inject its carcinogenic toxin. The toxin can then perturb the normal activity of the cells and creates an instability which promotes the acquisition of cancerous mutations.

In general, infection by *H. pylori* remains asymptomatic for several years before generating clinical symptoms (gastric pains). It is important to rapidly seek medical care when these signs appear, particularly if the patient has a family history (father, mother or sibling) of stomach cancer (the infection is often transmitted during childhood). Additionally, it is interesting to note that some studies have shown that sulforaphane, a molecule contained in broccoli, is an active antibiotic against *H. pylori* and that regular consumption of this vegetable could have a protective effect against this bacterium. For example, a clinical study performed in Japan showed that consumption of broccoli sprouts, an exceptional source of sulforaphane, led to a decrease by half of the quantity of *H. pylori* present in the mucosa of infected individuals[2].

(1) Tegtmeyer N et al. *Helicobacter pylori* employs a unique basolateral type IV secretion mechanism for CagA delivery. Cell Host Microbe 2017;22:552-560.

(2) Yanaka A et al. Dietary sulforaphane-rich broccoli sprouts reduce colonization and attenuate gastritis in *Helicobacter pylori*-infected mice and humans. Cancer Prev. Res. 2009;2:353-360.

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