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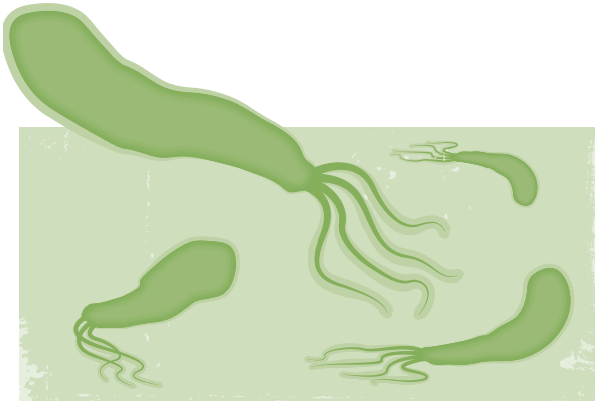
HELICOBACTER PYLORI

DARPP-32: a link between infection and gastric cancer



Neil Smith/NPG

Researchers have uncovered a novel pathway underlying the oncogenic effects of *Helicobacter pylori* infection in gastric cancer. The new findings show that *H. pylori* infection activates the pro-inflammatory transcription factor NF-κB, which in turn activates the oncogene *DARPP-32* (also known as *PPP1R1B*), promoting cell survival.

Gastric cancer is the third most common cause of cancer-related death globally, and onset is frequently associated with *H. pylori* infection, which promotes gastric inflammation. *H. pylori* infection induces cell death and DNA damage in the gastric epithelium. However, the development of apoptosis-resistant cells with damaged DNA enhances the risk of tumorigenesis. The mechanisms underlying this process are unclear.

"We previously reported overexpression of *DARPP-32* in about two-thirds of human gastric cancers," explains author Wael El-Rifai. "Therefore, we became interested in investigating the possible relationship between *DARPP-32*, *H. pylori* infection and inflammation."

The team found that *H. pylori* infection resulted in increased *DARPP-32* mRNA expression in a human gastric cancer cell line and in gastric tissue of infected mice, compared with non-infected controls. Using a luciferase reporter assay, the team also showed that *H. pylori* infection lead to upregulation of NF-κB-mediated transcriptional activity in cultured cells, which in turn increased expression of *DARPP-32*. Furthermore, human gastric mucosa samples showed increased NF-κB and DARPP-32 expression in cancerous tissue compared with normal tissue. Importantly, *H. pylori*-induced *DARPP-32* expression was associated with increased cell survival and activation of the pro-survival AKT pathway in the gastric cancer cell line.

> "…DARPP-32 is an important bridge between inflammation and cell survival"

"These results suggest that DARPP-32 is an important bridge between inflammation and cell survival," concludes El-Rifai. "The future development of potential inhibitors against DARPP-32 might be a novel strategy for treatment of gastric cancer."

Charlotte Ridler

ORIGINAL ARTICLE Zhu, S. *et al. Helicobacter pylori*-induced cell death is counteracted by NF-κB-mediated transcription of DARPP-32. *Gut* http://dx.doi.org/10.1136/gutjnl-2016-312141 (2016)