

Homing in on how H pylori aids in the development of stomach cancer

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Video Abstract

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Abstract

Residing in the stomachs of over half the human population, the bacterium *Helicobacter pylori*, also known as H pylori, has become a major cause of digestive complications, ranging from peptic ulcers to stomach cancer. But despite this link, scientists still aren't sure how these disorders arise after infection. Now, researchers have homed in on a single protein produced by H pylori that seems to rev up the immune system, causing a state of inflammation that may pave the way for cancer growth or other types of gut breakdown. The protein, HP1454, is naturally released from H pylori – both actively by living cells and passively as cells die. The scientists found that when special immune cells known as T cells encounter this secreted HP1454, they kick into action, mounting an inflammatory response. This relationship was particularly strong in people with stomach cancer. The team showed that patients with a form of cancer known as gastric adenocarcinoma had significantly higher levels of T cells that recognize the protein than patients with less serious disorders, such as chronic gastritis. In line with these findings, exposing T cells to the protein caused the cells to multiply. To work out the details of how this response happens, the researchers looked at the effects of HP1454 on T cell gene expression. They found that the protein boosted the levels of a gene linked to T cell activation as well as genes known to morph T cells into a phenotype associated with pathological consequences such as gastric atrophy. As a result, HP1454-positive cells were primed to promote the type of inflammatory state in which cancer cells thrive. HP1454 also affected genes related to T cell homing and migration. One possible result of these changes is that HP1454-positive cells may be better equipped to travel to and breach the stomach's protective lining. Overall, the work suggests that HP1454 plays a crucial role in the development of gastric disorders stemming from H pylori infection due to the protein's ability to amplify T cell dependent inflammation. Future work with HP1454 may help reveal new ways to monitor or prevent the dangerous complications that can arise from long-term exposure to the bacterium.