Loss of tight junction protein promotes development of precancerous cells

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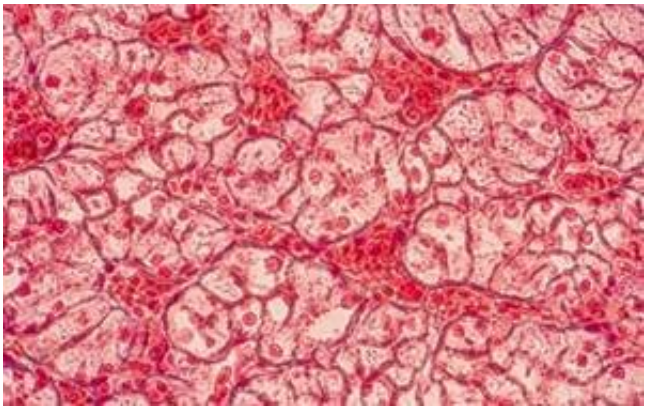

Credit: Beth Israel Deaconess Medical Center

Tight junctions are multi-protein complexes that serve as barriers in epithelial tissues such as the skin or lining of the gut. Loss of a specific tight junction barrier protein, claudin 18, occurs in the majority of gastric cancer patients and is correlated with poor prognosis in patients with advanced gastric cancer. Understanding how claudin 18 loss occurs and what pathways it regulates may provide new strategies to inhibit neoplastic progression in human gastric cancer patients.

In a first-of-its-kind investigation, researchers at Beth Israel Deaconess Medical Center analyzed gastric tissues from mice infected with the bacterium *H pylori* - which can cause stomach ulcers, gastritis and gastric cancer—as well as from mice genetically engineered to lack

claudin 18. The team demonstrated that mice infected with the bacteria lost claudin 18 overtime compared to uninfected mice. The team further showed that the lack of claudin 18 alone was enough to prompt the development of precancerous, abnormal cells and polyps in the engineered mouse model. Their findings were published in the journal *Gastroenterology*.

"The results were very surprising," said lead author Susan J. Hagen, Ph.D., an investigator at BIDMC and an Associate Professor of Surgery at Harvard Medical School. "Epithelial cells express numerous varieties of claudin proteins at the tight junction. We thought that other claudin molecules would compensate for the loss of claudin 18. It is incredible that manipulating only one protein in the stomach results in gastric cancer development."

Provided by Beth Israel Deaconess Medical Center