

The Impact of the Gastric Microbiome on Gastric Cancer Development

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Abstract: Although *Helicobacter pylori* infection is the most prevalent cause of gastric cancer worldwide, the molecular mechanisms leading to the development of malignancy as a consequence of infection remain unknown. The prevailing theory is that *H.pylori* infection results in a chronic inflammatory condition within the gastric mucosa, that leads to dysplastic mucosal changes over time, and that ultimately promotes malignant transformation. More recently, it is the realization that of a gastric microbiome that may also play an important role in chronic gastric inflammation and gastric cancer carcinogenesis. However, data regarding the relationship between *H.pylori* infection and the gastric microbiome and the concomitant changes in mucosal and adaptive immunity are lacking. In this proposal, we plan to examine the gastric microbiome in patients with and without *H.pylori* infection as well as in patients with and without *H.pylori* associated gastric cancer. We will couple this investigation with an examination of the mucosal immune infiltrate to provide data on the characteristics of both the microbiome associated with *H.pylori* infection as well as the consequences on host immunity. We will also examine genetic differences between gastric cancer that developed in the setting of chronic *H.pylori* associated inflammation and non-*H.pylori* associated gastric cancer. Together, these data will provide the necessary foundation for understanding the role the gastric microbiome plays in developing gastric cancer, and will form the basis for subsequent mechanistic and clinical studies for which NIH peer reviewed funding will be sought.