**Helicobacter pylori** is a spiral-shaped, gram-negative rod that has motility due to its flagella. As it resides in the host’s stomach, usually too acidic for most bacteria, it is able to thrive due to the presence of a urease enzyme. This enzyme creates a neutral environment for the bacteria by producing ammonia. Its multiple adhesion molecules allow **H. pylori** to interact with the stomach’s epithelial lining and promote an inflammatory response. It is this increase in inflammation which has been linked to the formation of gastric adenocarcinomas and mucosa associated lymphoid tissue (MALT) lymphoma. However, because of the many different strains of **H. pylori**, not everyone infected with **H. pylori** is equally at risk of developing gastric cancer from the bacteria. Someone who has **H. pylori** that is positive for the cytotoxic-associated gene A (CagA) protein has a greater risk of developing gastric cancer than someone who is negative. CagA is a virulence factor that is translocated into epithelial cells using the type 4 secretion system (T4SS). T4SS, which acts as a needle appendage, injects CagA into the epithelial cells where it undergoes tyrosine phosphorylation. This induces an oncogenic reaction as it causes proinflammatory cytokines to be produced. Thus, the introduction of CagA into the epithelial cells causes the cells to grow and transform leading to the development of gastric cancer.

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**Introduction**

Helicobacter pylori (H. pylori) is a carcinogenic stomach bacterium that is present in more than 50% of the world’s population. The bacteria infect the stomach’s epithelial lining and, as a result, most people develop gastritis which causes burning abdominal pain and can lead to stomach ulcers. However, those infected are also at a greater risk of developing gastric cancer, the third leading cause of cancer deaths worldwide and the fifth most diagnosed cancer as of 2018. **H. pylori** is responsible for about 3% of those cases, making up about 30,000 gastric cancer diagnoses annually. As a result, H. pylori, a class I carcinogen, has been identified as one of the most common causes of gastric cancer.

**Hypothesis**

The inactivation of the CagA protein decreases the risk of developing gastric cancer caused by CagA positive H. pylori.

**Aims**

To establish a causal relationship through an in-vivo study

**Possible Future Treatment Methods**

To control the negative effects of CagA positive H. pylori, the use of a Tet inducible system was explored. The Tet-On system uses a tetracycline repressor (TetR) to regulate gene expression. Whether TetR affects gene expression is dependent on the presence or absence of an inducer (tetracycline). When the inducer is present, the transcription of certain gene is allowed as the tetracycline blocks the TetR from binding to specific tet operator (tetO) sequences located in the promoter region of the target gene. When the inducer is absent, the transcription of certain gene is repressed due to the binding of Tet to tetO.

This can stop the expression of a certain gene and thus, inhibits the translation of the protein encoded by that gene. The purpose of this study would be to test whether blocking the expression of the CagA protein decreases the risk of developing gastric cancer. The Mongolian gerbil model would be the most suitable animal model to use due to its ability to develop gastric cancer, unlike the mouse model.

This study would help verify the etiology of gastric cancer in patients with CagA positive H. pylori. It also provides proof of concept for a new treatment for this widespread bacteria which could possibly reduce the chances of people getting gastric cancer before serious symptoms present themselves. The study of gene regulation through the use of Tet inducible systems in relation with the knockdown expression of the CagA protein can provide valuable information for possible treatments in the future. The results of this study may be influential for the creation of future drugs to treat CagA positive H. pylori, as well as other gene regulatory treatments for varying diseases.