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PIN1 as a Predictive Biomarker for *H. pylori* Infection–Associated Gastric Cancer

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ABSTRACT

Cancer is now one of the major causes of death across the globe. Peptidylprolyl cis/trans isomerase, NIMA-interacting 1 (PIN1), has recently emerged as a critical factor in various cancers. Numerous studies have shown that PIN1 is highly expressed in several cancer types and is significantly associated with the prognosis of patients with a certain type of tumor such as gastric cancer. Meanwhile, some studies have indicated that infection with *Helicobacter pylori* significantly increases the risk of developing duodenal and gastric ulcer disease and gastric cancer. In this article, we propose that PIN1 can play a vital role in the prognosis of *Helicobacter pylori* infection-associated with peptic ulcer disease and can be effective in order to provide the best cure and the choice for treatment.

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Main Body

Peptidylprolyl cis/trans isomerase, NIMA-interacting 1 (PIN1), has recently emerged as a critical regulator of cell proliferation and the DNA-replication checkpoint (1), which specifically interacts via its amino-terminal WW domains with a number of phosphoproteins through recognition of the pSer/ThrPro motif (2-4). It is interesting that pSer/Thr-Pro motifs in proteins exist in two distinct cis and trans conformations; their conversion rate is normally reduced upon phosphorylation, but the reaction is catalyzed by the prolyl isomerase PIN1. Consequently, it catalyzes the cis-trans isomerization of phosphorylated serine/threonine-proline (pSer/Thr-Pro) motif with its carboxy-terminal peptidylprolyl isomerase (PPIase) domain and induces conformational and functional changes of its substrates including protein stability, catalytic activity, phosphorylation status, protein–protein interaction, and/or subcellular localization (5, 6). PIN1 protein regulates centrosome duplication and its deregulation contributes to centrosome amplification, chromosome instability, and oncogenesis both in vitro and in vivo (7), and its overexpression is associated with poor clinical outcomes in several cancer types (8, 9). In contrast, depletion of PIN1 in cancer cells results in decreased tumorigenesis in vitro and prevents cancer development induced by overexpression of oncogenes such as Neu or Ras or by knockout of tumor suppressors including p53 in mice (6).

According to the study of Shi et al., PIN1 is highly expressed in gastric cancer and is significantly associated with advanced tumor stages, poor chemoresponse and clinicopathologic features, which might predict short overall survival and poor prognosis of gastric cancer patients (10, 11). Gastric cancer has cytologic, superior genetic and engineered heterogeneity compared to other types of gastrointestinal cancers. Numerous studies have shown that infection with *Helicobacter pylori* significantly increases the risk of developing duodenal and gastric ulcer disease and gastric cancer (12, 13). In fact, by impelling inflammation in the gastric, *H. pylori* would lead to gastric cancer via combining virulence factors with host factors (14). Half of the world's population is guessed to be involved in *H. pylori* which are classified as a type I carcinogen (15-17). It is interesting that PIN1 protein in the host involves two interacting modules, one a WW domain and the other a rotamase domain (cis/trans proline isomerase). The *H. pylori* proteins have also a rotamase domain which can interact with human WW domains (18).

Therefore, it can be hypothesized that PIN1 plays an important role in the prognosis of *H. pylori* infection-associated peptic ulcer disease and can be effective in order to provide the best cure choice for treatment. Indeed, if *H. pylori* infection is the cause of gastric ulcer disease, the presence of infection can be detected by PIN1 expression follow-up, therefore it can be treated before the gastric ulcer disease reaches gastric cancer. Thus, if the results confirm our hypothesis, PIN1 might be a possible biomarker in *H. pylori* infection disease leading to gastric cancer.

However, more in vitro and in vivo evaluations are needed to characterize the role of PIN1 in *H. pylori* infection and gastric cancer.

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Ethics approval and consent to participate

This article does not contain any studies with animals performed by any of the authors.

Conflict of interest

The authors declare that they have no conflict of interest.

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