# Therapeutic relevance of gastric mucus as an 'external' protective host barrier and a preferred niche of *Helicobacter pylori*

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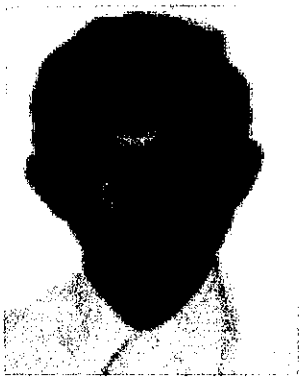

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|---|---|
| 1957年 | フィリピンに生まれる |
| 1981年 | フィリピン大学獣医学科博士号 |
| 1988年 | ㈱ゲン・コーポレーション研究員 |
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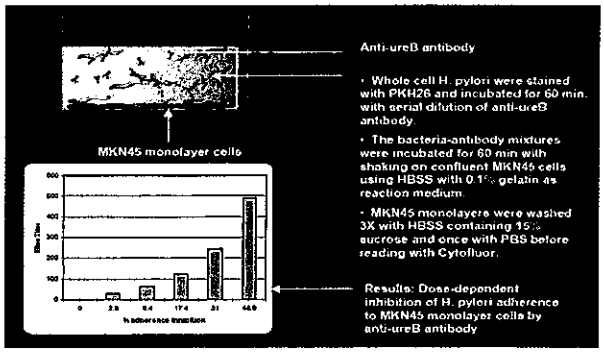
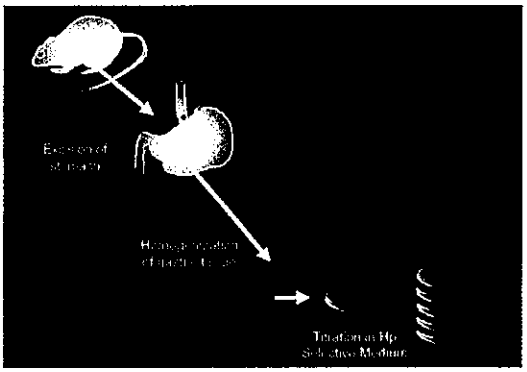
*Helicobacter pylori* has evolved into a pathogen with a singular niche that favors long-term colonization of the host. The acidic gradient of gastric mucus is basically a defensive host barrier to invasive organisms and a site that is otherwise inhospitable to the vast majority of other microorganisms, but has been converted into a natural habitat by the acid-resistant *H. pylori* allowing for host colonization with infrequent direct contact with host cells. Survival in acidic mucus presupposes abundance of acid compatible lectins or adhesins on the part of the pathogen and this has been confirmed with the demonstration of urease as a major acid-dependent adhesive or colonization factor on the cell surface of *H. pylori*. In view of this unique biology, the gastric mucus as a target site for anti-*Helicobacter* interventions acquires particular relevance. The efficacy of urease-binding molecules in the form of exogenous orally administered antibodies (in the form of IgY), soluble forms of acidic polysaccharides, as well as Maillard reaction products, have been explored in animal models and have been extended to human clinical trials. Passively administered antibodies basically exert their effect via agglutination and immobilization of bacterial cells with resulting inability to maintain their position in the mucus layer leading to clearance from the gastric mucosa. Such antibodies are designed to act locally upon introduction to the gastric lumen without being absorbed into the systemic circulation. Since the acid hydrolyzable antibodies may act mainly on the epithelial side of gastric mucus, they are specially suited for dislodging bacterial cells that are in direct contact with or near the epithelial cell surface where pH is neutral or only slightly acidic. On the other hand, acidic polysaccharides and melanoidins or Maillard reaction products likewise diffuse through the mucus gel as much

as the antibodies and scavenge the free forms of urease or 'capture' and immobilize urease-decked *H. pylori* cells by acting as surrogate mucus in the acidic side of the mucus gel. These urease-binding materials are eventually washed out onto the gastric lumen carrying with them the adherent urease and/or bacterial cells, and some are excreted by the host as part of non-digestible bolus. The predominating mindset regarding eradication of *H. pylori* infection have largely followed the traditional systemic approaches (active immunizations and conventional multi-drug combination therapies) with very little attention to the luminal side of the gastric mucus, which may thus explain the voluminous literature on these conventional approaches. It is now clear that these approaches have their limitations as borne out by recent clinical studies most likely because the potential role of the acidic side of gastric mucus has been largely overlooked. Considering that most *H. pylori* cells reside within a niche 'external' to host cells, namely, the surface mucus gel layer (more than 80% in humans, and more than 96% in animal models) where host-generated antibodies and systemically acting anti-microbials can barely gain access, a luminal approach to *H. pylori* eradication, such as the use of counter-adhesive molecules, deserves closer scrutiny. Further experiments on the use of combinations of agents targeting urease or non-urease adhesins and *H. pylori* itself on both sides of the electrochemical gastric mucus gradient are clearly needed in order to exploit their additive effects. There is also a need to expand the list of cost-effective foodstuff-derived molecules with natural affinity for *H. pylori* surface proteins (including acid-activated non-urease adhesins) which can have a major impact on eradication of *H. pylori* and prevention of its relapse or pathologic sequelae in third World countries.

IgY による *H.pyroli* 接着阻害効果 (In vitro)




マウスによる IgY 効果試験方法



マウスによる IgY 効果試結果

| Treatment | Log10 CFU/100mg gastric tissue/ mouse | Mouse negativity rate |
|---|---|---|
| Negative | 0.00±0.00 | 6/6 |
| Positive | 3.64±0.39 | 0/10 |
| 0.25% in feed | 3.08±0.79 | 0/10 |
| 2.5% in feed | | 5/10 |
| 25% in feed | | 7/10 |