Type 1 and 2 Lewis antigens of *Helicobacter pylori* – a potential marker of the human geographical distribution

Lewis antigens have been found both in human gastric epithelium and in *Helicobacter pylori* isolates (Monteiro et al., 1998; Wirth et al., 1997). That *H. pylori* LPS antigens can mimic human Lewis antigens may help *H. pylori* to evade the immune response and thus enhance bacterial adherence to gastric epithelium (Monteiro et al., 2000; Sheu et al., 2003; Wirth et al., 1996). Up to now, several host Lewis antigens, such as Lewis b (Leb), Lea and even sialyl-Lea, have been shown to serve as putative adhesion receptors for bacterial blood group antigen binding adhesion (BabA), Lea and sialyl acid-binding adhesin (SahA) of *H. pylori* isolates, respectively (Monteiro et al., 2000; Sheu et al., 2006, 2007). Such interactions between the host receptors on gastric epithelium and bacterial adhesion facilitate bacterial colonization and inflammation, and may consequently enhance virulence during long-term chronicity.

A recent cell line approach confirmed that the anti-Lea antibody significantly enhanced *H. pylori* adhesion to human gastric epithelium cells, particularly in those isolates expressing high levels of Lea antigen (Sheu et al., 2007). This study supports the novel finding of Taylor et al. (1998), who showed by electron microscopy that Lea was present on both *H. pylori* and gastric epithelium in adhesion pedestal formation. These data support the proposal that bacterial Lewis antigens have an impact on *H. pylori* infection outcome. Moreover, the study raised the idea checking whether Lewis antigens of *H. pylori*, other than the common type 2 Leb, could serve certain pathogenic roles.

*H. pylori* isolated from North American and European hosts predominantly expresses type 2 Lewis antigens (Le and Leb epitopes) (Monteiro et al., 1998). A recent study from Chile showed that South American *H. pylori* isolates had a higher prevalence rate (24%) of type 1 Lewis antigen (Altman et al., 2008). More strikingly, only the Lea epitope could be traced in their series. These data disproved the theory that only LPSs from Asian strains have the capacity to express Leb structures. Furthermore, the study suggested that it would be interesting to check whether type 1 antigens, especially the Lea epitopes, were more prevalent in Asian isolates.

We checked this by studying 100 isolates in Taiwan, a nearly 100% cytotoxin-associated antigen (CagA)-positive Eastern Asian country. Our isolates carried 25% and 35% prevalence rates for type 1 Lea and Leb epitopes, respectively. In North America or Europe, type 1 expression is relatively rare, and in Latin America, the type 1 (but only Leb) prevalence rate is up to 24%. However, in Asia, the prevalence rate of type 1 can be up to 35%, and both Lea and Leb can exist. Accordingly, type 1 or 2 Lewis antigens of the *H. pylori* isolates should be a potential marker for identifying the geographical distribution in the worldwide human population.

Wirth et al. (1996) showed that the Lea and Leb antigens of *H. pylori* are closely correlated with CagA in *H. pylori* isolates, and thus contributed to a more severe inflammation and bacterial persistence. In the study in Chile, the majority of *H. pylori* strains examined were CagA-positive (83.3%). Maybe due to the high CagA-positive rate, there was no significant correlation between CagA and bacterial Lewis antigens (Altman et al., 2008). Nevertheless, it is interesting that their CagA-negative isolates were uniformly shown to have no Lea antigen (Altman et al., 2008). The implication of such a finding deserves further study.

The disease outcomes of such type 1 Lewis antigen *H. pylori* infections in Chile were also studied, but maybe due to the relatively small-scale design, there was a nonsignificant equivocal correlation between type 1 infection and various clinical outcomes (Altman et al., 2008). The other weakness of the study is the lack of comparison of the histological features of patients to illustrate whether those with type 1 isolates had a heavier bacterial colonization or more severe inflammation. Based on our preliminary analysis, the isolates with coexisting type 1 and type 2 epitopes showed significantly denser *H. pylori* colonization and polymorphonuclear infiltrations than the isolates expressing type 2 epitopes only (data not shown). Thus more longitudinal data or interventional treatment trials are needed to determine the exact clinical significance of such type 1 *H. pylori* infections.

The reasons why Asian or Latin American people can harbour *H. pylori* isolates with more type 1 Lewis epitopes remain uncertain. The adaptation of *H. pylori* isolates to the host Lewis phenotype may be a good explanation. We have studied the host gastric Lewis antigen expression in 35 patients with type 1 infection in Taiwan, and significantly revealed that Lea and Leb of the infected host could concordantly match up to 90% of the type 1 Lewis epitopes of the isolates (data not shown). Accordingly, the host should have the possibility of selecting or adapting the Lewis types of *H. pylori*. It would thus be interesting to investigate whether the host Lewis antigens of the human population worldwide could show different prevalences of Lea and Leb. Moreover, if Lewis antigens of *H. pylori* could serve as a virulence factor facilitating colonization or inflammation, the selection of vaccine targeting the Lewis antigens will be different for patients from different geographical populations.

Overall, the work by Altman et al. (2008) adds to previous evidence indicating the need for further study of the clinical impact of type 1 and 2 Lewis antigen *H. pylori* infections. Currently, we see that at least...
type 1 or 2 Lewis antigens of *H. pylori* could be a potential marker of the geographical distribution in the human population.

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