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 (Le^b), Le^x and even sialyl-Le^x, have been shown to serve as putative adhesion receptors for bacterial blood group antigen binding adhesion (BabA), Le^x and sialyl acid-binding adhesin (SabA) 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-Le^x antibody significantly enhanced *H. pylori* adhesion to human gastric epithelium cells, particularly in those isolates expressing high levels of Le^x antigen (Sheu *et al.*, 2007). This study supports the novel finding of Taylor *et al.* (1998), who showed by electron microscopy that Le^x 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 Le^x, could serve certain pathogenic roles.

H. pylori isolated from North American and European hosts predominantly expresses type 2 Lewis antigens (Le^x and Le^y 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 Le^b epitope could be traced in their series. These data disproved the theory that only LPSs from Asian strains have the capacity to express Le^b structures. Furthermore, the study suggested that it would be interesting to check whether type 1 antigens, especially the Le^a 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 Le^a and Le^b epitopes, respectively. In North America or Europe, type 1 expression is relatively rare, and in Latin America, the type 1 (but only Le^b) prevalence rate is up to 24%. However, in Asia, the prevalence rate of type 1 can be up to 35%, and both Le^a and Le^b 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 Le^x and Le^y 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 Le^x 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 Le^a and Le^b 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 Le^a and Le^b. 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.

Bor-Shyang Sheu^{1,2} and Jiunn-Jong Wu³

¹Department of Internal Medicine, National Cheng Kung University Medical Center, Tainan, Taiwan, ROC

²Institute of Clinical Medicine, National Cheng Kung University Medical Center, Tainan, Taiwan, ROC

³Institute of Basic Medical Sciences, National Cheng Kung University Medical Center, Tainan, Taiwan, ROC

Correspondence: Bor-Shyang Sheu (sheubs@mail.ncku.edu.tw)

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