

Histo-Blood Group Carbohydrates and *Helicobacter pylori* Infection

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The ABO, Secretor and Lewis histo-blood group systems are characterized by the expression of carbohydrates (glycoproteins, glycolipids and free oligosaccharides) in different tissues as result of epistatic interactions between the *FUT2* (Secretor; 19q13.3), *FUT3* (Lewis; 19p13.3) and *ABO* (*ABO*; 9q34.1) genes which code the FUTII, FUTIII and GTA/GTB glycosyltransferases, respectively. These enzymes act in sequential steps modifying precursor oligosaccharides and creating new antigenic specificities. Therefore, the qualitative and quantitative variations in these carbohydrates depend on the presence, absence, combinations and activities of these glycosyltransferases [1].

The biological significance resulting from these carbohydrates is not totally understood but their expression in high levels in mucosa tissue and in exocrine secretion suggests an important role in interactions with pathogenic and non pathogenic microorganisms. The expression of histo-blood group carbohydrates in the gastrointestinal tract and exocrine secretions is complex. The FUTII enzyme allows the expression of carbohydrate antigens (e.g. H, A and/or B) derived from type 1 oligosaccharide precursor (Gala1→3GlcNAcβ→R) in combination with GTA and/or GTB glycosyltransferases. The FUTIII enzyme diversifies the structure of these carbohydrates creating new antigenic structures (e.g. Le^b, ALe^b, BLe^b). Therefore, individuals carrying both FUTII and FUTIII enzymes are classified as Secretors. Non Secretors did not carry the FUTII being unable to synthesize these carbohydrate antigens but when carrying the FUTIII enzyme they express high levels of Le^a antigen [2]. These biochemical events affect the susceptibility and resistance to microorganisms like *H. pylori*.

The experimental demonstration that the Le^b glycolipid acts as an important receptor for *H. pylori* [3] and the subsequent characterization of its BabA adhesin (Blood group antigen binding Adhesin) [4] filled a gap opened with the old report that individuals belonging to O blood group are more prone to suffer from peptic ulcers [5]. These studies clearly established a functional relationship between histo-blood group carbohydrates and a microorganism infecting thousands of people around the globe. It reached its peak with the observation that *H. pylori* strains isolated from Amerindians are strongly adapted to infect those belonging to O blood group. This adaptability is coincident with the high prevalence of blood group O in South America natives [6].

The expression of Le^b carbohydrate is higher in O and Secretor individuals and increases the availability of Le^b carbohydrate in comparison to other ABO blood groups (A, B and AB). Also, it favors the development of a host genetic profile which can be exploited as a marker of susceptibility to *H. pylori* infection and the diseases related to this microorganism [7]. However it is important to take in account that *H. pylori* has marked genetic variability what results in great diversity of strains and it able uses other carbohydrate than Le^b as potential receptors facilitating the infection in individuals of non-O blood groups (A, B and AB) [8].

Epidemiological studies carried out aiming to prove these experimentally obtained data presented conflicting results. Some of them reported prevalence of O blood group among those infected but others were unable to confirm the expected results. Therefore the discordances remain unsolved. Our group showed that infection by *H. pylori* is prevalent among patients belonging to O blood group and the infection

by CagA strains is strongly associated with this blood group, especially in adult patients with chronic active gastritis and peptic ulcers [9,10].

Recently it was shown that the Secretor phenotype plays an important role in intrinsic resistance to infection by this organism. The high concentration of mucus in carriers of this phenotype appears to be crucial in preventing the adhesion of BabA strains to histo-blood group carbohydrates expressed in the gastrointestinal tract. Additionally, carriers of the weak secretor phenotype (weak secretor) have partial protection against mucosal inflammation and proliferation of this microorganism, thus confirming the importance of the FUT2 gene in resistance to infection by some *H. pylori* strains [11].

Although most studies show that the presence of Le^b carbohydrate increase the susceptibility of O blood group for infection by *H. pylori* some questions concerning the contribution of histo-blood group carbohydrates still need to be answered. Carriers of chronic gastritis, peptic ulcer and gastric cancer did not present necessarily evidence of infection by this microorganism. Are these carbohydrates acting only as ligands for *H. pylori* adhesion or playing additional roles in the manifestation of these diseases? The gastric cancer related to *H. pylori* is more frequent in A blood group. What is the influence of histo-blood group carbohydrates in this differential susceptibility when compared with O blood groups? The presence of FUTII glycosyltransferase diversifies and reduces the extension of histo-blood group carbohydrate chains. What is the contribution of these short histo-blood group carbohydrate chains in infection by this organism?

Understanding the biological and clinical importance of histo-blood group carbohydrates in the diseases resulting from *H. pylori* infection may provide a better basis for potential therapeutic applications. Would be possible to identify adhesins other than BabA and use them in the production of vaccines capable of inducing localized humoral immune responses with the expression of high affinity specific IgA antibodies. Moreover, these carbohydrates could be useful in anti-adhesion therapy which apart from deterring colonization by this microorganism may contribute to the treatment of infection by strains resistant to conventional antibiotics [1].

Studies aimed to clarify the relationships between histo-blood group carbohydrates and *H. pylori* may contribute to understanding the selective forces that created and maintain the high polymorphism of ABO, Secretor and Lewis histo-blood group carbohydrates in man.

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