Le(a-b-) phenotype: potential risk factor for infection by the RH strain of *Toxoplasma gondii* in pregnancy

F. Nakashima

2010. Programa de Pós-Graduação em Genética, Departamento de Biologia, Universidade Estadual Paulista “Julio de Mesquita Filho”, São José do Rio Preto, SP, Brasil. Master’s thesis. Supervising Prof.: Dr. Luiz Carlos de Mattos

The Lewis histo-blood group system is characterized by the expression of the Le^a^ and Le^b^ antigens in the gastrointestinal tract, whose synthesis results in interactions between α2-L-fucosyltransferase (FUTII) and α3/4-L-fucosyltransferase (FUTIII) enzymes coded by the *FUT2* (19q.13.3) and *FUT3* (19p13.3) genes. FUTII and FUTIII fucosylate the type 1 oligosaccharide precursor (Galβ1→3NAcGlcβ1→3-R) at distinct positions to form H type 1 (Fucα1→2Galβ1→3NAcGlcβ1→3-R) and Le^a^ (Galβ1→3(Fucα1→4)NAcGlcβ1→3-R) antigens, respectively. The fucosylation of H type 1 antigens by FUTIII results in the Le^b^ antigen (Fucα1→2Galβ1→3(Fucα1→4)NAcGlcβ1→3-R). Thus, the presence of the FUTII and FUTIII enzymes leads to the expression of the Le(a+b+) phenotype, while the presence of only FUTIII allows the expression of the Le(a+b-) phenotype. The absence of the FUTIII enzyme leads to the expression of the Le(a-b-) phenotype. Independent events may be related. The aim of this study was to test the hypothesis that there is an association between the Lewis histo-blood group system and infection by *T. gondii*. Two hundred and nine serum samples collected from pregnant women were submitted to screening tests to detect anti-*T. gondii* antibodies, employing the indirect hemagglutination method. ELISA was utilized to identify IgG class anti-*T. gondii* antibodies specific for the RH strain. A hundred and ninety-five samples with concordant results for both methods were selected to form two groups: seropositive (G1) and seronegative (G2). The *G428A* mutation of the *FUT2* gene, and *T202C* and *C314T* of the *FUT3* gene, which allow inference of the gastrointestinal tract Lewis phenotypes, were identified using PCR-RFLP and PCR-SSP methods, respectively. Among the 195 samples selected, 116 (59.5%) were seropositive and 79 (40.5%) were seronegative. In G1, 68 (58.6%) were classified as Le(a+b+),
30 (25.9%) as Le(a+b-), and 18 (15.5%) as Le(a-b-), and in G2, 67 (84.8%) were classified as Le(a+b+), 12 (15.2%) as Le(a+b-), and 0 (0%) as Le(a-b-) (P < 0.0001). The Le(a-b-) phenotype is associated with a high risk of RH strain *T. gondii* infection when compared with the Le(a+b+) phenotype [P = 0.0001; OR = 36,460; 95%CI = 2.152-617,680] and Le(a+b-) phenotypes [P = 0.0118; OR = 15,165; 95%CI = 0.8463-271,710]. The Le(a+b-) phenotype showed a higher risk compared to the Le(a+b+) phenotype [P = 0.0206; OR = 2463; 95%CI = 2463-5214]. The results suggest that the Le(a-b-) phenotype is strongly associated with a greater risk of infection by the RH strain of *T. gondii* compared to the other phenotypes. It is possible that the absence of fucosylation of the type 1 oligosaccharide precursor as well as the variations in the structures of the Le\(a\) and Le\(b\) antigens influence susceptibility to infection by this parasite.

**Key words:** Toxoplasmosis; *FUT2, FUT3, Toxoplasma gondii,*

High-risk pregnancy; Lewis histo-blood group system

Research supported by CAPES, BAP-FAMERP 2007-2008, and CNPq.