Genetic polymorphisms of *Interleukin 17A*, *Interleukin 17F* and *Interleukin 17RA* and their relationship to ocular toxoplasmosis

Danilo Donizete da Silva[1], Fábio Batista Frederico[2], Alexsandra Passarelli Giabardo Marques[3], Mariana Previato[1], Rubens Camargo Siqueira[1], Cinara de Cássia Brandão[1], Luiz Carlos de Mattos[1], Christiane Maria Ayo[1]

[1] Faculdade de Medicina de São José do Rio Preto (FAMERP), SP, Brasil.

[2] Hospital de Base de São José do Rio Preto, Fundação Faculdade Regional de Medicina de São José do Rio Preto (HB-FUNFARME), SP, Brasil.

[3] Universidade Federal do Mato Grosso do Sul (UFMS), MS, Brasil.

Ocular toxoplasmosis (OT) is an inflammation that affects the retina and choroid regions, resulting in asymptomatic, temporary, or severe lesions due to the action of the immune response to the parasite *Toxoplasma gondii*. Cytokines act on the immune system in response to fighting infectious agents. *IL17A* and *IL17F* have an inflammatory role and there is an overexpression of *IL17A* during an active OT condition. The production of certain cytokines is genetically mediated, therefore polymorphisms can lead to interferences in gene transcription processes, especially SNPs or microsatellites. The aim of this study was to search for relationships between rs2275913 (*IL17A*) and rs763780 (*IL17F*) polymorphisms and OT in 260 individuals serologically diagnosed for *T. gondii* and to verify the frequency of genotypes and alleles related to rs4819554 (*IL17RA*) polymorphism in 321 individuals of the same population. In the analysis of *IL17A* and *IL17F* genotype and allele frequency, participants with positive serology were classified into two groups after funduscopic exams according to the presence (n=84) or absence (n=91) of presumed toxoplasmic eye scars/lesions. The control group consisted of individuals without *T. gondii* infection (n=85). Three groups were formed for *IL17RA*: presence (n=110) or absence (n=104) of presumed toxoplasmic eye scars/lesions; and a control group consisting of individuals without *T. gondii* infection (n=107). The PCR-RFLP technique was applied. The TT genotype, of the rs763780 (*IL17F*) polymorphism, was associated with OT susceptibility: the frequency was higher in individuals with OT than in individuals without OT (11.9 vs 0.0%; P=0.002, OR=24.46; CI=1.40-425.7) and controls (11.9 vs 0.0%; P=0.003, OR=22.87; CI=1.31-397.2). Statistically significant difference was seen in the TC genotype, related as a protective factor to OT, when the group of individuals with OT was compared with the group of individuals without OT (86.9 vs 98.9%; P=0.003; OR=0.07; CI=0.009-0.58) and with the control group (86.9 vs 98.8%; P=0.004; OR=0.07; CI=0.009-0.52). The rs4819554 (*IL17RA*) polymorphism showed a higher frequency of the GA genotype in patients with OT than in the control group (40.0 vs 26.2%; P=0.04; OR=1.87; CI=1.05-3.36). There were no relationships involving the rs2275913 (*IL17A*) polymorphism. Polymorphisms in cytokine genes may result in interferences to the gene transcription process and that may cause interindividual variations. The literature shows evidence that the variant form (C allele) of the F protein of IL-17 (His121Arg) can cause a suppression of the expression and activity of the wild type (T allele) and is related to protection against inflammatory diseases, such as OT. The study indicates susceptibility to OT related to the rs763780 (*IL17F*) polymorphism.

Funding: CAPES