Código #13401

Title: COMPLEMENT POLYMORPHISMS INFLUENCE SUSCEPTIBILITY TO HIV, AIDS AND HEPATITIS COINFECTION

Authors: Caroline Grisbach Meissner[a,b]; Angelica Beate Winter Boldt[a,b]; Márcia Holsbach Beltrame[a]; André de Oliveira Marcondes[b]; Marina Cavassin Paes[b]; Sandra Jeremias dos Santos Catarino[b]; Fabiana Antunes de Andrade[b]; Renato Mitsunori Nisihara[b]; Maria Regina Pinheiro de Andrade Tizzot [b]; Iara José Taborda de Messias-Reason[b].

Institutions: [a] Laboratório de Imunopatologia Molecular, Hospital de Clínicas, Universidade Federal do Paraná, Curitiba, Brazil; [b] Laboratório de Genética Molecular Humana, Universidade Federal do Paraná, Curitiba, Brazil

Objective: To evaluate the association between functional polymorphisms of genes encoding the major proteins involved in the activation of the lectin pathway of the complement system (*FCN2, FCN3, MASP1* and *MASP2*) and serum concentrations of the ficolins (FCN-2 and FCN-3) and serine proteases associated with the mannose-binding lectin (MASP-2 and MASP-3), with the susceptibility and progression of HIV infection. **Methodology:** A retrospective analytical study was conducted in 94 controls and 126 Euro-Brazilian HIV+ patients, of which 57 were positive for past HBV infection, 13 were HBV/HCV coinfected and 4 HCV-coinfected, 71 with AIDS (CDC criteria). We genotyped 22 polymorphisms, using multiplex sequence-specific PCR, and analyzed them by logistic regression, correcting the results, if necessary, by gender and age using STATA (version 9.1) and R (version 3.3.3). The variables that presented p <0.20 were selected for the multiple analysis and the final reduced model was obtained using the level of significance of p <0.05. **Results:** Higher MASP-2 levels were associated with resistance against HIV infection (summing all patients: OR=0.02, P=0.001), independently of higher MASP-3 levels. This protein is an inhibitor of the lectin pathway and activator of the alternative pathway, and was associated with susceptibility (OR=12.6, P=0.014). In contrast, *MASP2* genotypes containing low-expression alleles were associated with protection against AIDS (OR=0.19, P=0.028), which may be explained by its pro inflammatory role. Haplotypes *MASP2*CDV* (*g.1961795C*, *p.371D* and *p.377V*) and *FCN3*CInsA* (*g.27373182C, g.27371297-27371298insTATTTGGCC* and *g.27370346C*) were associated with susceptibility to HIV alone (OR=5.1, P=0.013 and OR=2.7, P=0.016, respectively). Higher FCN-2 levels predisposed HIV-infected individuals to HBV coinfection (OR=9.8, P=0.048), in contrast to the *FCN2*AGA* (*g.680489A*, *g.680873G* and *g.681471A*) haplotype, which protected against coinfection (OR=0.11, P=0.018). Finally, *MASP1*58267T* (*rs1109452*), located in the untranslated region of exon 12 and associated with decreased serum MASP-3 levels, was found as a protective factor against any coinfection, HBV or HCV (OR=0.17, P=0.001). **Conclusion:** The results lead us to suggest an important role of the lectin pathway of complement in the susceptibility not only of HIV per se, but also of HBV/HCV coinfection and AIDS. Although activation of the lectin pathway seems to be important in getting rid of HIV/HBV/HCV infection, exacerbated inflammation may predispose infected individuals to AIDS.