

***FCN3* and *MASPI* Gene Polymorphisms Modulate the Protein Levels in Serum and Influence the Susceptibility to Leprosy**

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Leprosy is a chronic disease caused by *Mycobacterium leprae* that affects thousands of individuals worldwide, causing severe physical deformities and social stigma. Macrophage ingestion of *M. leprae* increases with pathogen opsonization, driven by activation of the complement cascade. Ficolin 3 initiates the lectin pathway of complement through transactivation of mannan-binding lectin serine protease 1 and 2 (MASP-1 e MASP-2). Several gene variants encoding products of this pathway modulate the susceptibility to leprosy, but a possible influence of the *FCN3* and *MASPI* genes on leprosy is currently unknown. The present aimed to investigate whether *FCN3* gene polymorphisms (rs28357092, rs28362807 and rs4494157) and *MASPI* (rs7609662, rs13064994, rs72549262, rs1109452 and rs850314) as well as Ficolin 3 and the proteins encoded by *MASPI* gene (MASP-1, MASP-3 and MAp44) levels in serum are associated with development and progression of leprosy. We genotyped up to 196 Leprosy, being 150 (76%) lepromatous patients; and up to 238 controls with sequence-specific PCR and measured protein levels in up to 139 leprosy and 101 controls, using ELISA and TRIFMA. Median concentration of ficolin-3 was higher in patients than in controls (26034 vs. 18231 ng/mL; $p=0.005$), as well as higher in patients with the *FCN3* *CinsA* haplotype ($p=0.04$). In contrast, leprosy patients presented lower MASP-3 and MAp44 serum levels (4603 vs. 5606 ng/mL, $p<0.005$; 1732 vs. 2350 ng/mL, $p<0.0001$; respectively) as well as lepromatous, compared with non-lepromatous patients ($p=0.0016$ for MASP-3 and $p<0.0001$ for MAp44). There was an association between the T allele of rs1109452 with higher MASP-1 ($p=0.0081$) and lower MASP-3 ($p=0.0011$) levels in controls. The *MASPI***GCCCG* haplotype was associated with lower Map44 levels in heterozygous controls and with increased susceptibility to leprosy ($P=0.028$, $OR=1.43$ [$CI_{95\%}=1.04-1.94$]). In conclusion, *FCN3* and *MASPI* gene polymorphisms probably modulate the concentration of these proteins and may influence susceptibility to leprosy and its progression.

Keywords: Leprosy, *FCN3*, *MASPI*