Association of 4874 A/G (rs4969170) polymorphism in SOCS3 gene promoter region and RNA expression with liver fibrosis progression in patients with chronic hepatitis C

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Context: Chronic hepatitis C virus infection (CHC) is one of the most important risk factor of hepatocellular carcinoma (HCC). However, the pathogenesis of Insulin Resistance (IR) in hepatitis C infection is a very intriguing problem. In fact, the HCV is now recognized responsible for direct interference with the insulin signaling pathway. In addition, HCV-related IR has been shown to have a remarkable clinical impact on the progression of hepatic fibrosis and development of HCC.

Objective: The present study aims to evaluate the association of 4874 A/G (rs4969170) polymorphism in SOCS3 gene promoter region and RNA expression with liver fibrosis progression in chronic hepatitis C infected patients.

Material & Methods: In this study 226 Moroccan patients chronically infected with HCV (95 patients with mild fibrosis and 131 patients with advanced fibrosis) were genotyped for 4874 A/G (rs4969170) variant using the real time PCR. SOCS3 mRNA expression analysis was performed by using Sybr Green. Logistic regression was used to assess the association between polymorphism and progression of HCV infection.

Results: A significant difference in genotypes distribution of rs4969170 was detected between mild and advanced fibrosis group. The AA genotype was significantly overrepresented in Ad-LD patients compared to m-LD, the AA genotype was associated with a 5-fold increase of AdLD risk when compared to mild chronic hepatitis C (OR = 5.14; 95% CI, 2.29 - 11.54; P=0.00004). A similar situation was observed with the dominance model (OR = 4.18; 95% CI, 2.19 - 7.97; P=6.374e-06). The relative expression of SOCS3 to GAPDH mRNA was increased by 2 fold in Ad-LD as compared to m-LD group with AA genotype.

Conclusion: Our results suggest that polymorphism in SOCS3 gene promoter modulates the progression of chronic hepatitis C infection toward advanced liver disease by affecting its mRNA expression.

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