Identification of Single Nucleotide Polymorphisms in Myxovirus Resistance-1 (MxA) Gene Promoters (G/T at nt -88 and C/A at nt-123) Correlated With the Response of Hepatitis C Patients to Interferon

Thesis
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SUMMARY AND CONCLUSION

Hepatitis C Virus is recognized as a major threat to global public health. An estimated 170 million people worldwide are infected, and at risk for liver cirrhosis and hepatocellular carcinoma. In addition to viral and environmental behavioral factors, host genetic diversity is believed to contribute to the spectrum of clinical outcomes of patients chronically infected with HCV.

Human MxA is an interferon-induced cytoplasmic protein with anti-viral activity against a number of RNA viruses. MxA proteins target the nucleoprotein complex of MxA-sensitive viruses, forming oligomeric rings around tubular nucleocapsid structures, thereby blocking their transport into the nucleus; the site of viral transcription and replication.

The current study included 160 individuals classified into two groups: one hundred HCV patients selected from both sexes came from different governorates of Egypt and admitted to the Tropical Medicine Department of Kasr El-Aini Hospital. For all HCV patients, thorough history was taken and clinical data were recorded. Sixty normal, apparently healthy individuals were included in the work as control group.

Genomic DNA was extracted from whole blood. Polymorphisms of MxA gene (at positions –88 and –123) were determined by PCR amplification followed by

restriction endonucleases. HCV-RNA levels, as well as, stages of liver fibrosis were also determined in all participants.

The current study showed that the pretreatment laboratory data including the mean serum levels of ALT, AST, total and direct bilirubin, ALP, AFP and PT were significantly higher in the group of HCV patients as compared to the control group, while the mean serum level of albumin was significantly lower.

In the present work, the response of patients to treatment with IFN-α was significantly associated with less pretreatment fibrosis on liver biopsy (stages 0-2) and a low level of viremia.

The frequency of G/G genotype at position –88 in the promoter region of the MxA gene was significantly lower in sustained responders to IFN-α therapy than in non-responders, while G/T genotype was more likely to have sustained response with high significance. Carriage of the T allele was significantly correlated with sustained response to IFN-α therapy.

Moreover, the frequency of heterozygous C/A genotype at position –123 of the MxA gene, as well as the frequency of the A allele were significantly higher in sustained responders in comparison with non-responders.

Data from the current study concluded that heterozygosity for both –88 and –123 polymorphisms of the MxA gene may be important predictors of sustained response to IFN-α therapy.