Role of Interleukin-10 polymorphism in determining the outcome of interferon therapy on Hepatitis C patients infected with genotype 3a

By

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2008-NUST-BS-V&I-03

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We hereby recommend that the thesis prepared by Mr. **Talha Shafi** Titled: **Role of Interleukin-10 polymorphism in determining the outcome of interferon therapy on Hepatitis C patients infected with genotype 3a**, be accepted in its present form to satisfy the thesis requirement of BS (Hons) degree.

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Dedication

I dedicate my work to

My parents,

My brothers

And

All those who supported me

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LIST OF ABBREVIATIONS

~	Approximate
%	Percentage
GT	Genotype
ARMS	Amplification Refractory Mutation System
CD	Cluster of differentiation
DNA	Deoxyribonucleic acid
HCV	Hepatitis C virus
IFN-α	Interferon - α
IFN-γ	Interferon - γ
IL-2	Interleukine-2
IL-4	Interleukine-4
IL-5	Interleukine-5
IL-6	Interleukine-6
IL-10	Interleukine-10
IL-13	Interleukine-13
NFκB	Nuclear factor kappa beta

kDa	Kilo Dalton
LPS	Lipopolysaccharide
PBMC	Peripheral blood mononuclear cell
PCR	Polymerase chain reaction
SNP	Single nucleotide polymorphism
SOCS	Suppressor of cytokine signaling
STAT	Signal Transducers and Activators of Transcription
Th 1	T helper 1
Th 2	T helper 2
TNF	Tumor necrosis factor
SVR	Sustain virological response
NSR	Non sustained virological response

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ABSTRACT

Pakistan is a low socio economic country having more than 10 million people infected with hepatitis C Virus (HCV) with a major genotype of 3a (GT 3a). Due to high rate of resistance to standard interferon plus ribavirin therapy, it is highly needed to identify new marker for response prediction to therapy. Interleukin 10 (IL-10) is a key member of cytokine, which regulates Th1/Th2 cytokine balance, a major part of immune system against infection. As IL-10 production varies interindividually based on some functional polymorphism in its promoter region. We studied the impact of functionally important polymorphism (-1082 G/A, -819 C/T and -592 C/A) on HCV infection susceptibility and on outcomes of standard interferon plus ribavirin therapy. 90 healthy subjects and 140 HCV patients (95 were responder and 45 were non-responder to therapy) were included in this study. Amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) method was used for IL-10 polymorphism genotyping. High IL-10 producing -1082 GG genotype (p= 0.02; OR= 0.4; 95% CI= 0.2-0.8) and GTA haplotype (p=0.03; OR= 0.55; 95% CI= 0.3-1) were significantly higher in HCV patients as compared to healthy subjects. IL-10 -1082 GA genotype (p=0.03; OR= 1.95; 95% CI= 1.1-3.4) showed protective effect against HCV infection while other allelic, genotypic and haplotypic variants were nonsignificant among HCV patients compared with healthy controls. The current data failed to show any significant co relation between IL-10 polymorphism inheritance and therapy response in HCV patients. Our data showed a significant effect of IL-10 promoter gene polymorphisms and HCV infection susceptibility or protection but fail to demonstrate the influence of IL-10 promoter gene polymorphisms on the

response to combination therapy in Pakistani chronic hepatitis C patients infected with 3a genotype. The impact of genetic variations in IL-10 polymorphic variants on the response to anti-HCV treatment among different ethnic populations deserves further examination.