Name of the PhD student: Gaurav Roy

Name of the Supervisor: Dr. Mohammad Husain

Name of the Co-Supervisors: 1) Dr. Ranjana Gondal

2) Dr. Anil Agarwal

Title of the PhD Thesis: Role of Transforming Growth Factor-βI Gene Expression in Hepatitis B Virus Related Hepatocellular Carcinoma

ABSTRACT

OBJECTIVES: The objective of this study was to assess the expression profile of *TGF-β1* gene in HBV related HCC at both transcriptional and translational levels. In addition, functional polymorphisms of *TGF-β1* gene were also studied to delineate the impact of variant alleles at particular locus in developing HBV related HCC.

METHODS: Expression of tissue *TGF-β1* mRNA was determined by qRT-PCR. Serum TGF-β1 protein concentrations were assessed by 3rd generation ELISA. Functional polymorphisms in regulatory regions of *TGF-β1* gene [-800G/A (rs1800468) and -509C/T (rs1800469), codon10 (rs1800470) and codon25 (rs1800471) in exon1] were analyzed using PCR-RFLP method in the tissues. Additionally, TGF-β1 protein expression at tissue level was determined by immunohistochemistry

RESULTS: A group of 120 patients (HBV related HCC as cases; n=60, HBV related cirrhotics as disease controls; n=60) opting for living donor liver transplantation were recruited. Additionally, adjacent non-tumorous tissues (n=60) obtained from the cases were included as third group. It was observed that tissue *TGF-β1* mRNA expression levels in cases (n=30) were higher by 1.69 fold compared to disease controls (n=30) and 1.14 fold higher compared to the third group (n=30). Similarly, TGF-β1 protein concentrations in serum were higher in cases (29.51±4.10 ng/ml) compared to disease controls (18.59±5.41 ng/ml) ($p<0.001$). Analysis of tissue specific genotyping, haplotyping and linkage disequilibrium

profiles among cases (n=60), disease controls (n=60) and third group (n=60) demonstrated a significant predisposition of rs1800468A, rs1800469C, rs1800470T and rs1800471C risk alleles of *TGF-β1* gene to develop HBV related HCC. Additionally, immunohistochemical analyses revealed higher TGF-β1 tissue protein expression in cases (n=30) than third group (n=30) and disease controls (n=30).

CONCLUSIONS: Our data on expression and variations in specific *TGF-β1* gene alleles show a distinct difference between cases and disease controls as well as between cases and third group. Our comprehensive and integrated structural equation modelling may highlight the gene as a potentially diagnostic and prognostic biomarker for HBV related HCC. A novel mathematical equation derived through generalized linear modelling in this study may facilitate a better prediction of the probability of recurrence of HBV related HCC.

[Word Count: 340 words]