rs199508964Deletion in exon 6 of IRF5 gene is correlated with IL28B gene SNP rs12980275 and predicts sustained virological response in patients with recurrent hepatitis C following liver transplantation

Deletiars199508964 din exonul 6 al genei IRF5 se coreleaza cu polimorfismulgenei IL28B rs12980275siprezicerаspunsulvirusologicsustinut la pacientii cu hepatitarecurenta C post-transplant hepatic

Speranta Iacob, Razvan Iacob, CodrutaVagu, Simona Ruta, Cristian Gheorghe, Liliana Paslaru,IrinelPopescu and Liana Gheorghe

Institutul Clinic Fundeni, Bucuresti, Romania

Background: In patients with recurrent HCV infection after liver transplantation (LT), analyses of single nucleotide polymorphisms of IL28B in recipient and donor tissues allows prediction of sustained virological response (SVR) to PEG-Interferon and ribavirin therapy. IRF-5, a member of Interferon Regulatory Factors, a transcription factor, functions as a key regulator in TLR4 cascade, and is capable of inducing inflammatory cytokines. IRF1 and IRF5 have antiviral roles that are IFN-independent and cell-type specific.
Aim: To investigate IL28B polymorphism and IRF5 mutations in Romanian LT recipients with recurrent hepatitis C in order to establish a possible functional explanation for the already proven association of IL28B gene polymorphism to SVR following double antiviral therapy in patients with recurrent hepatitis C following liver transplantation.
Methods: Fourty-five LT recipient DNA samples were screened for rs12980275 single nucleotide polymorphism near the IL28B gene and for rs199508964 deletion of 30 bases in IRF5- exon 6, using Sanger sequencing technique.
Results: There were analyzed 23 females and 22 males with a mean age of 52.5±6.9 years and a mean time since LT of 16.3±11.6 months. In our study group no other mutations than rs199508964 were identified in exon 6 of IRF5 gene. IRF genotypes were: wild type (WT) – 14%, heterozygous for the deletion – 44.2%, and homozygous for the deletion – 41.9%. Minor allele frequency (MAF) for rs199508964 in our study group was 64%, higher than - MAF according to Pubmed (48.4%). Distribution of IL28B genotypes were: C/C – 14%, C/T - 58.1%, T/T - 27.9%. There was an association between IRF5- non-WT and IL28B non-C/C genotypes (p=0.01). A significant association was found between SVR and WT genotype of IRF5 (p=0.01), however mutations in IRF5 gene were not associated to advanced fibrosis after LT.
Conclusions: There is a link between recipient IL28B and IRF5 genotypesthat could explain correlation to SVR following double antiviral therapy.