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Effect of Mycophenolate Mofetil on Expression of MicroRNA-155 in Patients with IgA Nephropathy
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Objective: This dissertation would investigate the urinary, serum and intra-renal expressions of miR-155 of patients with IgAN, and try to elucidate whether MMF could regulate miR-155 expression in IgAN patients.

Methods: 33 patients with biopsy-proven IgAN were designated as IgAN group. 47 IgAN patients who received MMF treatment for 3 months were matched with IgAN group as MMF group. 15 healthy volunteers were recruited as members of healthy control group, while 15 patients with renal cell carcinoma were recruited as members of control group. Serum and urine samples from all three groups as well as normal renal tissues from the nephrectomy specimen of control group and renal biopsy tissues from IgAN group were analyzed through real-time PCR to explore the effect of MMF on expression of urinary and serum miR-155.

Results: In IgAN group, as compared with control group, the urinary, serum and intra-renal expressions of miR-155 were increased ($p < 0.05$). Intra-renal and serum expressions of miR-155 were positively correlated with proteinuria ($r = 0.402, P = 0.028$; $r = 0.347, P = 0.046$) and inversely correlated with evaluated glomerular filtration rate (eGFR) ($r = -0.488, P = 0.008$; $r = -0.343, P = 0.048$) in IgAN group. Urinary expression of miR-155 was positively correlated with serum expression of miR-155 ($r = 0.639, P < 0.001$) in IgAN group. The serum level of miR-155 in MMF group was significantly lower than that of IgAN group ($P = 0.045$).

Conclusion: The urinary, serum and intra-renal expressions of miR-155 were significantly increased in patients with IgAN. Intra-renal and serum miR-155 levels were closely related to the progress and severity of IgAN. MMF could down-regulate the serum level of miR-155 in IgAN. Serum miR-155 might be considered as biological marker, reflecting the effect of MMF in the treatment of IgAN.
Objectives: To replicate the association of 7 single nucleotide polymorphisms (SNPs; which were identified as strong association with IgAN in a genome-wide association study) and investigate whether the 7 SNPs influence the clinical manifestation and prognostic for IgAN patients, a case-control genetic study from an independent western Han cohort was conducted.

Methods: Genomic DNA was extracted from 521 patients with IgAN and 535 healthy controls, and TaqMan allelic discrimination assay was used to type SNP polymorphism. Traditional linear logistic regression analyses were used to detect 7 SNP associations in dominant, recessive and additive genetic models. Bonferroni correction was used to adjust the P-values for multiple testing. A total of 459 IgAN patients with integrated clinical data were investigated the relationship between the genotype and phenotype of IgAN. 315 IgAN patients were followed-up. Then, a retrospective cohort study of 191 patients with IgAN with crescent less than 50% glomeruli in Chinese population was conducted to explore the relationship between genotype and the progression of renal disease over a mean period of 44.49 ± 19.94 months.

Results: After Bonferroni correction, no significant SNP association was observed between IgAN patients and controls (P > 0.05). For genotype-phenotype correlation studies, marginally significant association of rs2856717 T/C recessive model for the T allele was significantly associated with eGFR (< 60 ml/min) of IgAN patients (P = 0.008, Pc = 0.056, OR = 1.527). T allele at position of rs9275596 was significantly associated with macroscopic hematuria of IgAN patients under the dominant and additive models of inheritance (P < 0.001, P = 0.007, OR = 2.983) and (P < 0.001, P = 0.007, OR = 2.17), respectively. Results from Kaplan-Meier analysis showed that patients carrying the TT+TC genotype for rs2856717 had reduce renal survival rate than patients carrying the CC genotype (85.1% vs. 92.7%, P = 0.046).

Conclusion: Rs 2856717 may influence the clinical manifestations and poor outcome of IgAN. Further studies are required to definition of the mechanistic effects of genetic variants on clinicaltraits.

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