

## Association of the Macrophage Migration Inhibitory Factor Single Nucleotide Polymorphism with Idiopathic Membranous Nephropathy

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Idiopathic membranous nephropathy (IMN) is one of the most common forms of autoimmune nephritic syndrome in adults. Several genes that encode inflammatory cytokines have been reported to associate with IMN. Macrophage migration inhibitory factor (MIF), a proinflammatory cytokine, has been implicated in the pathogenesis of glomerular inflammation. However, the association between MIF and IMN needs to be further investigated. The purpose of this study is to evaluate whether polymorphism of *MIF* affects the development of IMN. A case-control study including 129 patients with IMN and 196 healthy volunteers from Taiwan Chinese population, were enrolled. Two functionally relevant single nucleotide polymorphisms (SNPs), -173G/C and -794(CATT)<sub>5-8</sub> in *MIF* promoter, were genotyped by polymerase chain reaction-restriction fragment length polymorphism followed by gel electrophoresis, and polymerase chain reaction followed by capillary electrophoresis, respectively. The results showed that the frequency of *MIF* -173 C/C genotype carriers was higher in patients with IMN (17.1%) than in controls (4.1%) [odds ratio (OR) = 5.6,  $p = 1.2 \times 10^{-4}$ ]. No association with -794(CATT)<sub>5-8</sub> was found. In addition, the *MIF* -173 C/C genotype carriers did not show significant association toward disease progression and probability of end-stage renal disease as compared with *MIF* -173 G/G genotype patients within 25 years from onset, suggesting that the screening of *MIF* genotype should be done at routine rather than disease onset. Moreover, luciferase reporter assays showing that the C/C genotype has the higher level of basal *MIF* promoter activity *in vitro* as compared to the G/G genotype (1.4-fold,  $p = 0.002$ ). Our results provide new evidence that genetic polymorphism of MIF may be the underlying cause of IMN which warrants further investigation.