IgA 신증의 진행에 관련된 Soluble Epoxide Hydrolase의 유전자적 다양성

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Sequence Variations of the Soluble Epoxide Hydrolase (EPHX2) Associated with the Progression of IgA Nephropathy

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Purpose : Epoxyeicosatrienoic acids (EETs) are endothelium-derived hyperpolarizing factors and play a important role preventing endothelial dysfunction via profibrinolytic effect, anti-inflammatory actions and inhibition of smooth vascular muscle cell migration. The genetic variations of soluble epoxide hydrolase (EPHX2), which inactivates EETs through hydrolysis, may alter levels of expression of EPHX2 contributing biological activity of EETs. Here, we examined the association of EPHX2 genetic variation and progression of IgA nephropathy, which is the most common glomerulonephritis worldwide.

Methods : Progression of kidney disease was defined as reduction of GFR by 50% or ESRD. Three single nucleotide polymorphisms (SNPs) spanning EPHX2 (K55R, R287Q, rs1042032) were genotyped in 349 patients (male:female 198:151) who were histologically confirmed as primary IgA nephropathy in Seoul National University Hospital. Clinical data was reviewed retrospectively.

Results : The mean age at kidney biopsy was 34.0±13.6 years old. The mean follow-up duration was 5.6±5.1 years. There was no variant allele K55R among our study population. Progression of IgA nephropathy was significantly lower in the patients with R287Q polymorphism variant allele (28.2% vs. 17.5%, respectively, p=0.021). On multivariate binary logistic regression, patients with R287Q variant allele had significant lower risk for progression (p=0.034; Odds Ratio (OR)=0.55; 95% Confidential Interval (CI) 0.32-0.96). Although the rs1042032 polymorphism variant allele (A/G) in 3' UTR was not associated with the progression of IgA nephropathy (p>0.05) by itself, the haplotype analysis of R287Q and rs1042032 improved the predictive power of disease progression (Haplotype with both of minor alleles was significantly lower risk for the progression of IgA nephropathy. p = 0.021; OR = 0.52; 95% CI 0.30-0.91).

Conclusion : These findings suggest that genetic variations of EPHX2 are associated with progression of IgA nephropathy and EPHX2 could be a potential therapeutic target for chronic glomerulonephritis.