Thesis Title Combined Analysis of Molecular Variant of the Renin-Angiotensin System Component Genes in Thai IgA Nephropathy

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ABSTRACT

Since the renin angiotensin system (RAS) is established as an important factor in renal disease progression, this study determined whether RAS alleles affect severity of IgA nephropathy. These genetic variants include angiotensin I converting enzyme deletion polymorphism in intron 16 (ACE I/D), a point mutation in the angiotensinogen (AGT) gene resulting in a methionine to threonine substitution at residue 235 (M235T) and an angiotensin receptor type 1 (ATR) A to C transition at bp 1166 (A1166C). A total of 53 patients with biopsy-proven IgA nephropathy and 80 normal control subjects were recruited in this study. The patients were divided into two groups : group 1 patients had normal renal function with serum creatinine at biopsy $\leq$ 1.5 mg/dl (N=40) and group 2 patients had renal insufficiency with serum creatinine at biopsy $>$ 1.5

mg/dl (N=13). We studied the I/D polymorphism of the ACE in relation to serum ACE activity in total IgA patients and normal control subjects. The results indicated a potentially important variation in genetic regulation of the serum ACE activity. We also determined three gene polymorphisms in the RAS and the effect of these polymorphisms in subgroups of IgA nephropathy. Most of the Thai patients comprised of ID (47%) genotype, followed by II (45%) and DD (8%) genotype of ACE gene. Genotype distributions and allele frequencies were not significantly different between controls and patients with IgA nephropathy, although trends for higher frequency of the ACE-DD genotype and the AGT-TT genotype were noted in IgA nephropathy group 2. The combined analysis of the ACE-DD and AGT-TT genotypes did not show any genetic influence on the risk of the disease susceptibility. To extend further knowledge from this pilot study of whether the genetic of the ACE will indicate the risk of the disease progression, a larger sample size is needed.