

RFLP Report

**MET 235 THR POLYMORPHISM OF
ANGIOTENSINOGEN
IN INDONESIANS**

M. Mansyur ROMI,* Suryono Yudha PATRIA, and Masafumi MATSUO**

*Division of Genetics, International Center for Medical Research,
Kobe University School of Medicine, Kobe 650, Japan*

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The renin-angiotensin system is closely involved in the physiological regulation of blood pressure. Angiotensinogen is a key component of this system, and its plasma level is correlated with blood pressure. One variant of angiotensinogen encoding threonine instead of methionine at position 235 (Met 235 Thr) (T235) has been reported to correlate with development of hypertension in Caucasians (Jeunemaitre *et al.*, 1992). Among Asians, Japanese have been shown to have a higher frequency of the T235 allele than Caucasians (Hata *et al.*, 1994). In the previous report, we have also disclosed the high incidence of T235 allele in population based material of Japanese (Nishiuma *et al.*, 1996).

Pregnancy-induced hypertension (PIH) is one of serious complications of pregnancy and is characterized by high blood pressure. A significant association of preeclampsia with a variant of angiotensinogen (T235) has been reported in some studies (Argrimsson *et al.*, 1993; Ward *et al.*, 1993), but other study failed to obtain evidence of the association (Morgan *et al.*, 1995). Though high incidence of preeclampsia has been noted in Indonesia, no study on the genetic factor predisposing to hypertension has been conducted. We first analyzed the T235 in the Indonesian population.

T235 variant of angiotensinogen is induced by a single nucleotide change from T to C at 704th nucleotide near the 3' end of exon 2 of the angiotensinogen gene. This nucleotide change can be investigated by Tth 111-I restriction fragment polymorphism as described before (Nishiuma *et al.*, 1996; Russ *et al.*, 1993). DNA samples obtained at Dr. Sardjito Hospital, a teaching hospital of Gadjah Mada

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*On leave Department of Anatomy, Embryology and Anthropology, Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia

**To whom correspondence should be addressed.

Table 1. Angiotensinogen genotypes and gene frequencies in Indonesians.

		Indonesian		Japanese* (n=213)
		Eclampsia (n=20)	Non-eclampsia (n=100)	
Genotype	AA	2	14	20
	Aa	10	48	114
	aa	8	38	79
Allele	A	0.35	0.38	0.36
	a	0.65	0.62	0.64

Values are expressed as absolute numbers of each genotype and gene frequency. Alleles are designated A (M235) and a (T235), respectively.

* From our previous report (Nishiuma *et al.*, 1996).

University, Yogyakarta, Central Jawa, Indonesia were analyzed for its polymorphism at nt 704. One hundred patients, who visited the outpatient clinic with some complaints for blood examination, and 20 preeclampsia patients, who were diagnosed in accordance with the defined criteria and showed hypertension and proteinuria, were enrolled in this study after obtaining the informed consent. Statistical analysis was done using X²-analysis.

The frequency of T235 among 100 non-eclampsia patients was 0.62 (Table 1), and was found to correspond closely to that previously reported for a Japanese population (0.64) (Nishiuma *et al.*, 1996). And the distribution of genotype was the same among Indonesians and Japanese. These suggested that both Japanese and Indonesian have the same genetic background as far as T235 of angiotensinogen concerns.

In the group of preeclampsia patients, frequencies of T235 was 0.65, while it was 0.62 in non-eclampsia (Table 1). There found no significant difference in the frequency of T235 of angiotensinogen between preeclampsia and non-preeclampsia patients. This suggested that T235 of angiotensinogen seems not a major contributing factor for preeclampsia in Indonesian people. Although incidence of several genetic diseases such as thalassemia, glucose-6-phosphate dehydrogenase deficiency and ovalocytosis has been reported to be high in Indonesians due to tropical environmental pressure (Takeshima *et al.*, 1994) our results suggested that pressure on the angiotensinogen gene in Indonesians remains the same as Japanese.

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