Thesis Title: Identification of β^{O}-thalassemia/HbE gene in Thai population using synthetic oligonucleotide probes.

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ABSTRACT

β^{O}-Thalassemia is a genetic disorder causing a complete absence of β-globin chain in hemoglobin. In Thai population, β^{O}-thalassemia associated with HbE (β^{26} GAG--->AAG) is found in high frequency. More than 50 types of molecular mutations in β-thalassemic gene have been reported, including large sequence deletion, short sequence deletion or insertion, and single base substitution. The presence of large sequence deletion (619 b and 3.4 kb) were screened in 60 Thai patients with β^{O}-thalassemia/HbE using fragment length analysis, but none were detected. Single base substitution or insertion and short sequence deletion in β-globin gene of 30 Thai patients with β^{O}-thalassemia/HbE were screened by direct gel hybridization of BamH I fragmented DNA and by dot-blot hybridization of amplified DNA with a set of

allele specific oligodeoxyribonucleotide probes. Frequency of mutations detected were as follows : 17 cases of a 4 base-pair deletion at codons 41-42, 5 cases of amber mutation (TAG) at codon 17, one case each of a single base substitution (G--->C) at position 5 of IVS-I, a single base substitution (C--->T) at position 654 of IVS-II, and an ochre mutation (TAA) at codon 35. However, no mutations of single nucleotide (A) insertion at codons 71-72 were found. These data provide a basis for future application of prenatal diagnosis by DNA hybridization.