

Thesis Title	Characterization of Hemoglobin C in Thailand
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ABSTRACT

An abnormal hemoglobin, Hb C, was found in a twenty-nine year old male of Thai origin. A normal hematological profile was observed except that the MCV was somewhat lower (77 fl). Hemoglobin typing by cellulose acetate electrophoresis under native conditions showed Hb A together with an abnormal hemoglobin co-migrating with Hb E / Hb A₂. However, the concentration of this abnormal hemoglobin (42%) was higher than that expected for heterozygous Hb E (25-30%). This abnormal hemoglobin, was successfully separated from Hb E on citrate agar gel electrophoresis under acid conditions. Globin separation by Triton-acid-urea polyacrylamide gels under denaturing conditions indicated that the abnormal β chain moves towards the cathode faster than the β^E chain. The abnormal hemoglobin was further isolated by DEAE-cellulose column chromatography and the abnormal β chain was purified by CM-cellulose column chromatography. Protein sequence analysis (ABI Model 473A) and tryptic peptide mapping of the β globin chain indicated that the abnormal hemoglobin was Hb C since there was a replacement of Glu ----> Lys at position 6. Direct DNA sequencing of the propositus showed the

substitution of A to G at codon 6 (GAG----> AAG) of the β globin gene, which is in agreement with protein sequencing results. Haplotype analysis of the β -globin gene cluster was also performed. The 5' haplotype and 3' framework was different from the common haplotypes for Hb C found among Blacks, suggesting that the mutation occurred independently. Since Hb C and Hb E have the same Glu ----> Lys mutation (but at different positions), and move at the same position on routine hemoglobin electrophoresis, it would be interesting to see whether any other cases in Thais previously reported as Hb E are actually Hb C.