

4036149 MBMG/M : MAJOR: MOLECULAR GENETICS-GENETIC
ENGINEERING; M.SC. (MOLECULAR GENETICS-
GENETIC ENGINEERING)

KEY WORDS : HEMOPHILIA B / FACTOR IX / MUTATION
DETECTION / SINGLE STRAND CONFORMATION
POLYMORPHISM / SOUTHERN BLOT ANALYSIS

THEERAWIT TASANEEYAPAN : MOLECULAR BASIS OF HEMOPHILIA B
IN THAILAND. THESIS ADVISORS: VARAPORN AKKARAPATUMWONG,
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171 p. ISBN 974-663-317-1

Hemophilia B is an X-linked recessive hemorrhagic disorder caused by mutations of the coagulation factor IX (*FIX*) gene, leading either to quantitative deficiency or functional abnormality of FIX. The *FIX* gene spans about 34 kb of DNA and is located on the long arm of the X-chromosome at the region Xq27.1. It consists of eight exons encoding seven functionally important domains. The molecular defects of *FIX* gene are heterogeneous and have been studied in many ethnic groups. The mutations included single base substitutions, insertions, and gene deletions. To characterize the molecular defects of hemophilia B, which have never been described in Thai patients, genomic DNA samples from the patients were analyzed for abnormalities of *FIX* gene by polymerase chain reaction and single strand conformation polymorphism (PCR-SSCP), followed by DNA sequencing. Of 10 DNA samples from unrelated hemophilia B families were analyzed and, 9 mutations were identified. They were five missense mutations (G12E, C99S, M348I, C350Y and G352V), a nonsense mutation (S174X), two frameshift mutations due to 1-bp deletion (17,775 del C) and a 2-bp deletion (6,377-6,378 del AT), and an in-frame mutation due to a 6-bp deletion (30,942-30,947 del AACTGG). One DNA sample from a patient failed to give any amplified products. Southern-blot analysis using probes corresponding to coding sequences in exon I and exon VIII indicated that the entire *FIX* gene was deleted in this patient. The data obtained from this study provides the understanding of molecular defects of *FIX* gene in Thai hemophilia B patients and, are useful for carrier detection and molecular diagnosis of this disease by direct mutation analysis.