CHAPTER I
INTRODUCTION

1.1 Statement and significance of the problem

In 1994, the patient is a 8 year-old northern thai girl who was a β-thalassemia. The percentages of elevated level of Hb A_2 synthesis in father, mother, elder sister, younger sister, younger brother and the patient are 3.9, 4.4, 5.2, 5.4, 5.3 and 5.0 respectively, indicated the β-thalassemia trait phenotype except the father(Figure 1). The blood samples were sent for hemoglobin typing according to a HPLC and cellulose acetate gel electrophoresis (pH8.5) (Figure 2 and 3). The abnormal hemoglobin was identified as a separated band that moved to the anode slower than the normal Hb A and Hb F in cellulose acetate gel electrophoresis at pH8.5 indicating the change of a total negative charge of its globin chains. That kind of abnormal hemoglobin has not been identified by any molecular level technology before. The knowledge in protein synthesis indicated that the abnormal hemoglobin was resulted from the abnormal genes. Thus the DNA sequencing as used as a tool to detect the abnormal genes.

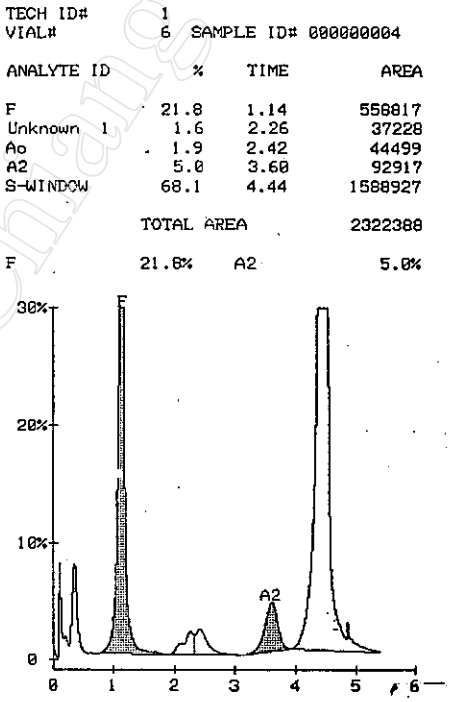

Figure 1. HPLC elution profile for abnormal hemoglobin using the Bio-Rad Variant™.

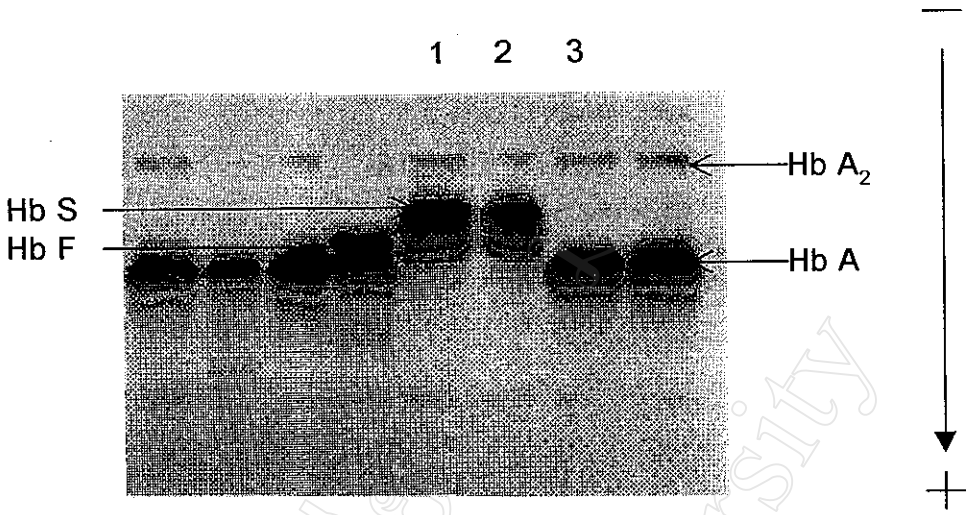

Figure 2. The cellulose acetate electrophoresis of the blood hemolysates from the patient's family. Abnormal hemoglobin moved slower to the cathode than the normal hemoglobin (lane 1= patient, lane 2= sister and lane 3= brother).

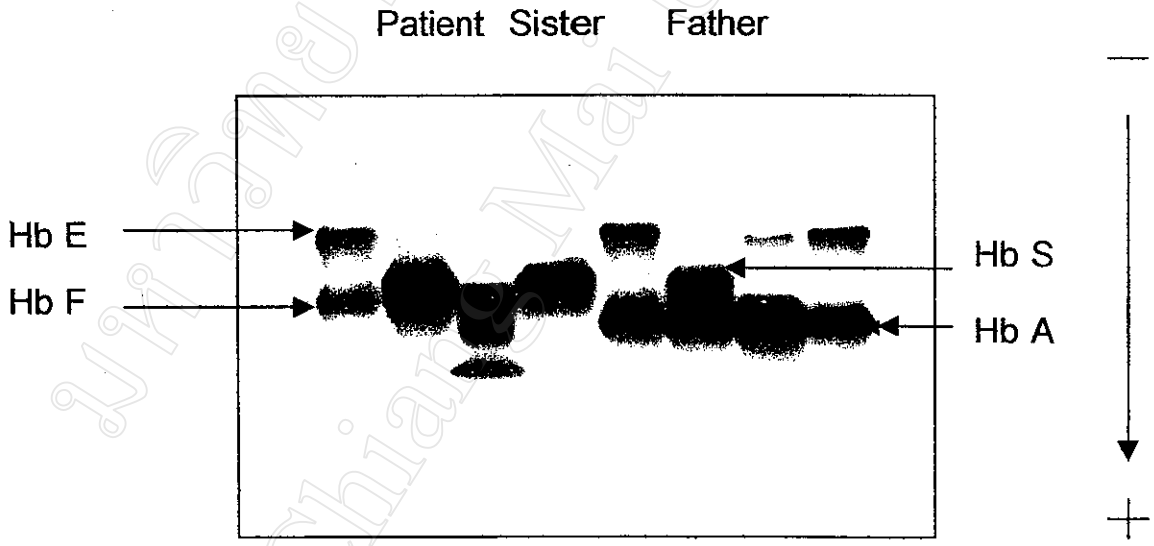

Figure 3. The cellulose acetate electrophoresis of the blood hemolysates from the patient's family. Abnormal hemoglobin moved slower to the cathode than the normal hemoglobin.

1.2 Objective of this study

Sequencing of the β–globin gene exons to detect a putative point mutation in an unknown hemoglobin variant.