CHAPTER 4

DISCUSSION

In this study we designed to explore the difference in the amount of α mRNA in the two types of Hb H disease. It is well known from previous study that the molecular basis of these two types formed in the combination of α-thalassemia$_1$ and α-thalassemia$_2$ gene (α-thal$_1$/α-thal$_2$) or α-thalassemia$_1$ and Hemoglobin Constant Spring (α-thal$_1$/Hb CS). (see in the figure 14)

Previous study by Kan et al (1982). and Orkin et al (1981) showed that the α_2 globin gene produces α mRNA more than α_1 globin gene in the ratio 75 : 25 and 60 : 40 respectively. However Paqnier et al (1979) and Kan et al (1982) noted that the final result of gene product, α globin synthesis from these two α globin are not different.

But looking again at the function of the hybrid gene no information yet that this hybrid gene behave like the α_1 or α_2 gene. If the hybrid gene function like the α_2 gene, the gene product from this hybrid gene should be 30% of the total α mRNA level as the α_2 gene behave. But if the hybrid gene function like the α_1 gene, the gene product should be 20% of total α mRNA as well. On the contrary in α-thal$_1$/Hb CS which there is two α globin gene intact : α_1 and α_2^{cs} gene we expect to have the total α mRNA level of 20% plus some α^{cs} mRNA.

The severity difference between two types of Hb H disease is well known and previously reported by Fucharoen et al (1981). Difference in pathology in these two types of Hb H disease was observed and reported by Bunyaratavej et al 1982). The explanation for these differences in R B C pathalogy and clinical profiles are not established. The in vitro protein synthesis in these two types of Hb H disease revealed the α/β ratio of 0.70 and 0.57 for α-thal$_1$/Hb CS and α-thal$_1$/ α-thal$_2$ respectivety (Wasi et al, 1980). That seems to be very difficult to draw an explanation from such in vitro study about the imbalance protein synthesis which did not mimic with the clinical observation. Furthermore the recent study by Wood et al (1984) revealed that there seems to be a degradation of β-chain in Constant Spring condition. This may interfere with the result of in vitro protein synthesis.

Investigation to solve the problem of different severity in this two types of Hb H aimed at the molecular level in term of α mRNA synthesis.

The result showed that there are more α mRNA in α-thal$_1$/α-thal$_2$ the α-thal$_1$/Hb CS at various total RNA level (table 3, figure 11). This is firmed when expressed the result as α/β mRNA ratio. Because the β mRNA ratio suppose to be constant in both types of Hb H (table 4, figure 12). In table 5 and figure 13 showed the rather constant α/β mRNA ratio in both type of Hb H at various total mRNA level. The

α/β mRNA ratio in α-thal$_1$/α-thal$_2$ is higher than α-thal$_1$/Hb CS.

Thus from this study suggest that the difference between α-thal$_1$/α-thal$_2$ and α-thal$_1$/Hb CS may result from the difference in amount of mRNA synthesis. It means that the hybrid gene should function like the α_2 gene. This is being expect from (Proudfoot et al, 1980) which show that the promotor region of eukaryotic gene is in the 5' flanking region.