CHAPTER 4

DISCUSSION

Most studies on the *TaqI* A polymorphism were done in Caucasian populations. The publications that studies in Asian population were conducted in Chinese and Japanese. No study in Thai population were published. The aim of this study was to investigate the genotypes and allele frequency of the *TaqI* A site in Thai population between moderate dependence, severe dependence and controls (non-alcohol dependence). The proportion of T and C allele were calculated to determine the association of polymorphism and severity of dependence.

Reliable *TaqI* A genotype data of the participating subjects are of utmost importance for this study. Using an restriction enzyme for genotyping always bears the risk of false genotyping. For example in the case of the T allele the amplicon will not be cleaved by the enzyme. On the other hand if the amplicon is not cleaved by restriction enzyme can one be sure that this outcome is not an experimental artifact? This problem was addressed by the inclusion of a CC genotype positive control in all restriction enzyme assays and the preparation of a mastermix containing the TaqI restriction enzyme for all tested samples. A second independent *TaqI* A site within the amplicon sequence would have been a nice restriction internal control, but unfortunately no natural *TaqI* restriction site exists in proximity to rs 1800497. Grandy *et al.,* 1993 overcame this shortcoming in an elegant way by using modified forward and reverse with built-in *TaqI* sites (TCGA). All of their amplicons were

therefore shortened by restriction enzyme by eight basepairs independently from a rs 1800497 C allele.

We did not find the significant difference in percentage of C/T SNP alleles among 3 groups (p = 0.224). This data was conformed to Arinami *et al.,* 1993 that the percentage of A1 allele in the moderate alcoholic was resembled to controls.

In Table 4, the percentage of A1+ allele carriers in severe dependence was higher than another two groups. As Blum *et al.,* 1996 have suggested that the association between A1+ allele and alcoholic was distinct only in severe type. However, we found no significant difference when we compared the percentage of TT genotype between severe dependence against control or moderate dependence. Also, the % TT genotype in severe group was slightly different compared to moderate group (χ^2 = 3.354, p = 0.067).

In Table 5 also showed no significant difference of the odds ratio (OR) of A1+/A1- allele between 3 groups. However, we found that the OR of moderate/ control was the same (OR = 1.0). This may show that the frequency of A1+ carriers in moderate dependence and control was similar and genetic may not effect the dependence in moderate groups. On the other hand, severe dependence may associated with genetic background.

When we compared the positive family history in all groups, we found that there was a significant difference among groups (p = 0.00). The percentage of positive family history in moderate dependence or severe dependence was different from controls (p = 0.00). However, when we compared the family history between moderate and severe dependence there was a bit difference (p = 0.071). Moreover, when we pooled the dependence groups together and compared to control group there

was significantly different at $p = 0.00$. This data show that the severity of dependence may be associated with genetic heritability especially in severe alcoholics.

In summary, the *TaqI* A polymorphism may not affect the susceptibility in alcohol dependence in Thai population but somehow the severity of dependence especially in severe type. Moreover, environmental factors may affect the individual's susceptibility to alcohol due to parent's imitation in childhood especially from the first degree relative (Andreasen *et al.,* 2006). Therefore, the different social culture may influence the drinking susceptibility in population.

Japan and Korea have cultures and tradition that differ from Thailand. In Korea for example, young people must accompany drinking with the elderly one (Kim and Baik, 2004). Moreover, Japanese accept that drinking and drunkness afterwork with co-workers and bosses is a social norm (Wada, Price and Fukui, 1998). The drinking culture in these countries may make people more susceptible to alcohol. In addition, living in developed countries with high expenses is inevitable stressful. That is a major factor leading alcohol abuse.

The number of subjects in each group was calculated based on the study of Blum *et al.,*1991 on Caucasians. The C/T allele frequency at *Taq*I A however may differ between Caucasian and Asian population. Secondly, the control group comprised of Faculty staff members may not represent all ethnic groups of Thailand. A larger and more random population sample should therefore be used in further studies.

In conclusion, the result revealed that the allele and genotype at the study site did not significantly differ between three group subjects. The *Taq*I A1+ allele may

therefore contribute just a little, environmental factors however much to the susceptibility and severity of alcohol dependence.