CHAPTER SIX

CONCLUSION

In summary, this study has optimised and employed successfully the denaturing high performance liquid chromatography (DHPLC) technique to screen the LDLR gene mutations in patients with FH. Disease-causing variants found by DHPLC in intron 3, exons 5, 9, 10 and 12 were confirmed using Sanger sequencing. Combinations of clinical diagnosis criteria with DNA-based molecular screening and confirmatory methods assist tremendously in the definitive diagnosis of FH.

Of 74 clinically-diagnosed FH patient samples, only three different types of mutations were identified. The identified C234S mutation of exon 5 affects the ligand binding domain while mutation R385W of exon 9 affects the EGF-precursor homology domain of LDLR gene. This study has also identified a mutation of an-intronic region (intron 3) affecting the splice site domain.

Disease-causing variants of exons 10 and 12 were found to have not caused amino acid change and predicted to cause no abnormality to the LDLR protein. Further studies are needed to investigate the role and effect of these genetic variations of exons 10 and 12 in the non-affected family members of recruited FH patients.

It is hoped that with the advancement of high-throughput sequencing, combined with larger number of recruited FH patients, disease-causing variants in other candidate genes of cholesterol metabolism will be able to be studied to better understand the spectrum of mutations among FH patients in Malaysia.