Schizophrenia is a severe psychiatric disorder that affects 1% of the population worldwide. It impairs an individual’s perception, thought, and behaviour that results from complex genetic interactions with environmental factors. The aetiology of schizophrenia remains enigmatic. There is strong evidence indicating that both genetic inheritance and environmental factors may provoke the disorder. Family-based and twin-based studies showed that there is indeed a genetic risk for family members of schizophrenic patients to develop the syndrome.

Significant technological advances for identification of single nucleotide polymorphism (SNPs) have further strengthened research methodologies for genetic analysis of this disease. Thus, SNPs in genes of the neurotransmission systems are hypothesized to be associated with schizophrenia. Recently, large genome-wide association studies had shown that v-akt-murine thymoma viral oncogene homolog 1 (AKT1), transcription factor 4 (TCF4), and microRNA 137 (MIR137) gene are among the most prominent susceptibility genes for schizophrenia. The role of these genes in schizophrenia has been hypothesized to affect normal brain development and related to different forms of neurodevelopmental disorders. Thus, the objective of this study is: (1) to investigate three susceptible genes (AKT1, TCF4 and MIR137) associated with schizophrenia among Malaysians on the aspects of gender, ethnic, subtype and co-morbidity; (2) to test SNP haplotypes of the genes in order to further conclude the genetic evidence; (3) to study the interaction between the SNPs and different phenotypes; and (4) to predict schizophrenia using Artificial Neural Network (ANN).

A total of 417 schizophrenic patients will be recruited from Hospital Besar Ulu Kinta.
and 429 control subjects without family history of schizophrenia or related disease will be included in this study. Peripheral whole blood will be collected for DNA extraction. SNPs within the intron and untranslated regions of the three genes will be selected by means of ‘NCBI-GENBANK’. Taqman® Assays-by-Design SM SNP Genotyping based assays will be employed for allelic discrimination of the SNPs. Thermal cycling and end-point PCR analysis will be performed on an ABI PRISM® 7900 Sequence Detection System and analysed with SDS software.

The sample population will be divided into subgroups based on different phenotypes such as schizophrenia severity, subtype, co-morbidity, and age of onset. The interaction between the selected SNPs with different phenotypes will be tested. Linkage disequilibrium and haplotype frequencies, as well as association between a haplotype and schizophrenia, will be analysed using the Haploview software program. Meta-analysis will be done for global association of the genes to schizophrenia. Then, the results collected will be converted and analysed using the right types of neural network and model. The neural network will be fed with the processed samples for training and analysis. Performance evaluation and error analysis will be conducted to fine-tune the models until an acceptable performance is achieved.