New Method Developed to Identify Genetic Determinants of Alzheimer’s Disease

A rapid and accurate denaturing high-performance liquid chromatography (DHPLC) assay for the determination of apolipoprotein E genotypes has been developed by researchers from the Department of Medical Genetics, School of Basic Medical Sciences, Southern Medical University, Guangzhou, China. This assay combines polymerase chain reaction (PCR) and DHPLC and can be used to conduct efficient genotyping of the human population, which will help in the diagnosis and treatment of Alzheimer’s disease.

Apolipoprotein E (APOE) is a predisposing gene of Alzheimer’s disease and many other diseases. APOE has three major alleles: $\alpha_2$, $\alpha_3$, and $\alpha_4$. The combinations of these three common alleles result in six genotypes that exist within the population: $\alpha_2\alpha_2$, $\alpha_3\alpha_3$, $\alpha_4\alpha_4$, $\alpha_2\alpha_3$, $\alpha_3\alpha_4$, and $\alpha_2\alpha_4$. Many studies indicate that people who have the $\alpha_4$ allele are at greater risk of developing Alzheimer’s disease than those with the $\alpha_3$ allele, and that the $\alpha_2$ allele may help resist Alzheimer’s disease. As a result, the rapid and accurate determination of APOE genotypes and the assessment of disease predisposition will be extremely valuable in augmenting the clinical diagnosis and treatment of the disease.

The medical genetics team, led by Professor Xiang-Min Xu of Southern Medical University, developed the assay during research funded by the National Science Fund for Distinguished Young Scholars of China. PCR was designed to generate the 191-bp amplicons containing two common polymorphisms within codons 112 and 158 in exon 4 of the APOE gene. The PCR amplicons for each sample were then subjected to DHPLC analysis, which was performed under partially denaturing conditions as determined by profiling the mixture of a tested sample and a homozygous standard control amplicon at the given ratio. In almost 300 samples detected, the accuracy of the assay reached 100%.

Dr Tian-Ming Gao, head of the Neurobiology Department, School of Basic Medical Sciences, Southern Medical University, said, “As China has a huge population that is stepping into old age, the number of victims of Alzheimer’s disease is on the rise. Therefore, we felt that the development of a rapid and accurate assay that can determine individuals predisposed to Alzheimer’s disease would have great utility.”

Dr Wei-Ping Liao, head of the Institute of Neuroscience, Guangzhou Medical College, said, “This method can be applied to a vast range of diseases and has created a new approach for the molecular diagnosis of genetic diseases. Based on the results from this method, neurologists can know more about the genetic background of a patient. It will help in further diagnosis and treatment.”