UNIVERSITI TEKNOLOGI MARA

PCR AMPLIFICATION OF EXON 7 OF *MET* GENE IN AUTISM SPECTRUM DISORDER

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ABSTRACT

Autism is a complex neurodevelopmental disorder in which genetic factor strongly influences the risk of developing autism among children worldwide. The *MET* gene which located in a common autism linkage region, chromosome 7q31 has been identified as the major genetic determinant for the development of autism. *MET* gene is responsible for the development of brain system such as cerebral cortex and cerebellum. It also has contribution to gastrointestinal and immune system functions. As children with autism often exhibit disruption in all these functions, *MET* gene was chosen as one of the vulnerability-conferring genes in this research project. The objective of this research is to design a set of primers for the amplification of exon 7 of *MET* gene using polymerase chain reaction (PCR). A set of specific primers was designed using NCBI Primer BLAST tool. Successfully amplified amplicons were sent for DNA sequencing, followed by analysis of SNPs. Pairwise comparison showed that only one SNP (rs13223756) was found at A2146G for this exon; and it was a synonymous SNP as the substitution of A>G did not change the resultant amino acid that is glutamine, for both CAA and CAG codons. In conclusion, the newly designed primer set was able to amplify exon 7 of *MET* gene successfully. However, the SNP found was not reported as clinically significant for the development of autism spectrum disorder. Synonymous change is not always silent as it may have implication on transcription, translation, splicing, as well as for mRNA transport. Therefore, further protein expression studies are required.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND OF STUDY

Nowadays, autism is one of the disabilities that commonly affect children worldwide. Autism can be defined as a complex neurodevelopmental disorder and usually children with autism can be recognised by three features. Firstly, the children lack social interaction; meaning that they have problems with their non-verbal communication during interaction with people surrounding them. Secondly, autistic children also have impairment in their communication skill in which they cannot develop a proper spoken language and they have difficulty in initiating any conversation with others. Thirdly, the children also have repetitive and stereotyped behaviors as well as restricted interests and activities (Ting, Neik, & Lee, 2014).

Autism term is often used to represent a person with autism spectrum disorder (ASD) (Campbell et al., 2006). ASD broadly refers to a collection of behaviorally and socially concerned condition which includes autistic disorder (classical or atypical autism), pervasive developmental disorder and Asperger disorder (Sana Nasir Zaidi, 2016). It is highly capable of being inherited from one generation to the next through the numerous genes which are responsible for this disorder with a heritability of 70% to 90% (Zhou et al., 2011). It commonly affects male population rather than female population in which its sex ratio is 4:1 and its symptoms usually start to appear before 3 years of age (Sousa et al., 2009).

The population prevalence of autism in Malaysia was last updated by Ministry of Health Malaysia in 2014, since thence, there was no further local epidemiological study regarding ASD prevalence rate in Malaysia. An earlier study on the prevalence of autism using Modified Checklist for Autism in Toddlers (M-CHAT) was conducted on autistic children aged 18 to 36 months, and it was estimated that there were approximately 1.6 autistic children in 1000 children population (1:625) (Balakrishnan et al., 2013). The prevalence rate is increasing in Malaysia. This may be due to increased awareness regarding this illness and because of the advancement of diagnostic tools.