ORAL PRESENTATIONS 2

OP9

MUTATION SPECTRUM OF DYSTROPHIN GENE IN MALAYSIAN PATIENTS WITH DUCHENNE/BECKER MUSCULAR DYSTROPHY

Abdulqawee M Rani¹, Teguh H Sasongko¹, David J Bunyan², Abdul R Salmi³,
Bin A Zilfalil¹, Zabidi AMH Zabidi–Hussin³

1. Human Genome Centre, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia
2. National Genetics Reference Laboratory (Wessex), Salisbury Hospital NHS Trust, Salisbury, Wiltshire, UK
3. Department of Paediatrics, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia

The gene for Duchenne/Becker Muscular Dystrophy (DMD/BMD), is the largest gene in the human genome. Data on the mutation spectrum of this gene in Malaysian patients with DMD/BMD are limited. In this study, we identified the mutation spectrum of dystrophin gene in Malaysian patients with DMD/BMD. 35 patients with symptoms and signs of DMD or BMD were screened for mutations in the 79 exons of the dystrophin gene using multiplex ligation-dependent probe amplification (MLPA) followed by direct sequencing of selected exons. 28 patients (80%) showed mutations of the Dystrophin gene; two of them were novel (c.3709A>T and c.4742delA). The MLPA technique also found 23 patients (66%) with confirmable deletions of one or more exons and one patient (3%) with a single exon duplication. Confirmatory direct sequencing on patients found by MLPA to carry an apparent one exon deletion revealed a patient with a single nucleotide deletion (c.4742delA). Further direct sequencing on selected exons detected 3 cases with nonsense mutations and one case with missense mutation. We could not find Dystrophin mutations in the rest 7 patients (20%). According to previous studies, this detection rate is reasonable since 20% of Dystrophin mutations may be occurred as small mutations beyond the studied exons. Our study showed that the majority of the mutations (61%) were in the distal hotspot. Although most of our clinical and molecular diagnoses showed compliance to the reading frame rule, we found two unrelated DMD patients with an in-frame deletion. We found the MLPA approach to be simple, rapid and reliable, although it does need to be supported by other independent methods in certain cases. This study showed the mutation spectrum of Dystrophin among Malaysian patients with DMD/BMD and conforms to other studies, which reported that the distribution of mutations were concentrated in the distal hotspot of the gene, although the frequency of the mutations along the gene may vary.