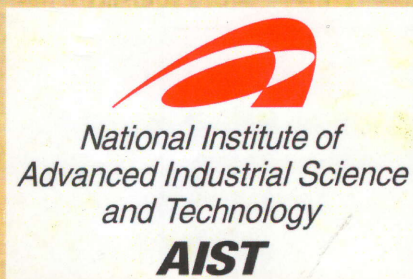
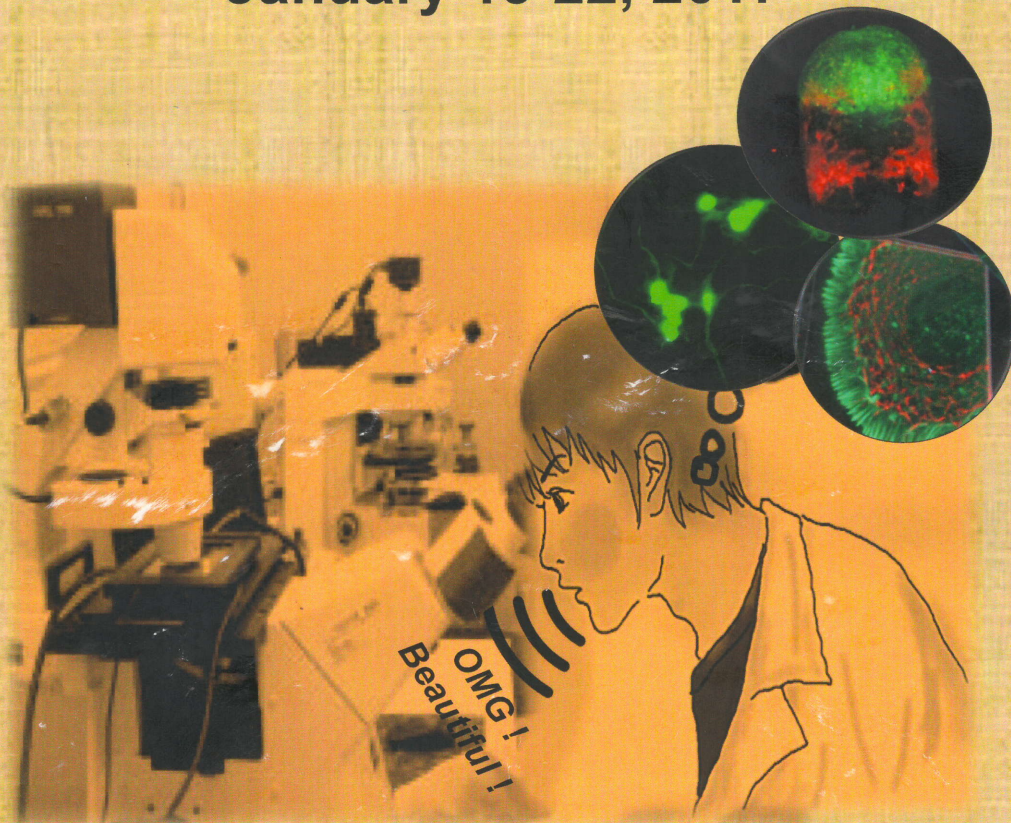


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Analysis of Mutation Pattern of Duchenne Muscular Dystrophy (DMD) in Sri Lanka: A Cohort Study

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Background: DMD is characterized by muscle degeneration, developmental, behavioural abnormalities with interpatient variability due to disparities in mutation patterns.

Objective: To ascertain variability in age of onset, development delay, behavioural abnormalities (Irritability) in respect to distal, proximal mutation patterns of dystrophin gene.

Method: Mutation detection comprised of Multiplex PCR (20 primers), and/or Multiple Ligation Dependent Probe Amplification (MLPA) of 75 clinically diagnosed DMD patients; aged 3.8-13yrs (mean age, 8.6±2.6yrs). Clinical data were recorded via a standard questionnaire.

Results: Genomic aberrations: intragenic deletions; n=54(72%); distal deletions n=47(89%) of which n=42(89%) localized in the distal hotspot (45-53). Proximal deletions n=7(11%). Mean Age of Onset (MAO) (*p= 0.004); Distal deletions = 4.7±1.8yrs, Proximal deletions= 6.4±1.4yrs.

Gross motor development delay- in distal deleted patients n=16(34%), proximal n=3(42%). Behavioural abnormalities (Irritability)-in distal deleted patients n=21(45%), proximal n=1(14%).

Exons 49, 46, 47 were frequent distal mutations of patients with Gross motor development delay and behavioural abnormalities.

Discussion and Conclusion:

As highlighted in literature, differential effects of different mutation sites on the expression of dystrophin isoforms in brain remain to be clarified. Brain specific dystrophin transcripts (dp140, dp71), which are involved in cellular synaptogenesis, neural development, are disrupted due to mutations in distal hotspot region. Thereby intellectual and development delay in toddlers may be considered as an early identification of the risk for DMD. Muscle specific isoform (dp427m) is disrupted by both distal and proximal mutations. This warrants an immunohistochemical analysis of dystrophin isoform levels in muscle (mutations not accordance with reading frame hypothesis) and brain tissue in respect to mutation patterns.