00524 Study of CAG Expansion in Spinocerebellar Ataxia 17 in Singapore

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Aims: Spinocerebellar ataxia 17 (SCA17) is a condition with the expansion of CAG/CAA repeats in the coding region of the TATA box binding protein leading to an abnormal expansion of polyglutamine in the corresponding protein. Affected individuals usually have more than 49 repeats. To date, limited data is available in Asians hence genetic analyses of SCA are performed routinely in Singapore. Ataxia patient underwent SCAs (1, 2, 3, 6, and 7) genetic testing for nucleotide repeat expansion. About 30% of the patient have been identified and classified while the remaining 70% SCA suspected patient were further screened for other SCAs (8, 10, 12, 17, and 36). SCA17 drew our interest as the pathologic repeat number as low as 27 overlap with the normal repeat numbers.

Methodology: This study involved 240 healthy and 284 SCA suspected individuals. Up to 80% of the subjects are Chinese. Genetic analyses of CAG expansion frequency in SCA17 gene were performed on all samples. CAG repeat region were amplified with a pair of primers, the forward primer was labeled with fluorescent dye. The number of CAG repeats was detected by capillary electrophoresis followed by GeneScan analysis based on an internal size standard.

Result: Published data has shown that healthy individuals have CAG repeat range between 25 and 40. Screening showed that majority of the samples contains CAG repeats within the normal range in both groups. However, 9 SCA suspected individuals carried 40 to 44 CAG repeats and 13 healthy individuals were also presented with 40 to 47 CAG repeats. The results suggested that normal repeats range should be higher than 40 in local populations. The CAG repeats range may be variable in different populations.

Conclusion: In conclusion, a higher definite cutoff value should be established for SCA17 patients due to higher repeat number in the healthy individuals.