00519 Association Between PDE10A Mutation and Huntington Disease in Singapore

Sim Weiying[1], Ong Lisa Helen[1], Law Hai Yang[2], Tan Eng King[3], Zhao Yi[1]

[1]Singapore General Hospital, [2]KK Women's & Children's Hospital, [3]National Neuroscience Institute

Aims: Huntington disease (HD) is a rare neurodegenerative disorder, characterized by choreatic movements. It is caused by CAG trinucleotide repeat expansion in the huntingtin (HTT) gene. The clinical diagnosis of HD is based on clinical presentation, family history and genetic testing of the expansion with >36 CAG repeats in HTT gene. Unfortunately, genetic testing for CAG expansion may not account for all HD patients. For instance, there are patients who are clinically presented but do not carry pathogenic CAG repeats. Recently, there were evidences suggesting that PDE10A mutation was associated with HD in which HD patients including pre-symptomatic had significant loss of PDE10A expression. As such, we aim to determine whether our local suspected HD patients with normal CAG repeats would have PDE10A mutation to confirm their diagnosis.

Methodology: Since 1995 to 2017, a total of 200 patients were suspected with HD and underwent genetic testing for CAG repeats in HTT gene. Out of 200 patients, 87 had CAG expansion in HTT gene and confirmed as HD positive. We selected 40 suspected HD patients for this study. Next, we performed DNA sequencing on the reported hotspot areas of PDE10A gene (exon 4, 11 and 12).

Result: No mutation in PDE10A was found in the 40 subjects, indicating that there was no correlation between PDE10A mutation and HD. The result obtained was inconsistent with other reported studies and could be due to low sample size in our study. The other possible reason could be HD is associated with different genotypes in different geographical regions.

Conclusion: Our study did not have the same finding as other reported studies that had demonstrated the association between PDE10A mutation and HD. As a result, we had yet to determine the diagnosis of those HD suspected patients as they neither carry pathogenic CAG repeats nor mutations in PDE10A