OP 03 - Design and Implementation of an assay for genetic variants associated with Non deletion Alpha Thalassaemia in a cohort of Sri Lankan population

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Introduction: Non-deletional variants of the α-globin gene are rare cause of alpha thalassaemia, Haemoglobin Quong Sze (HbQS) is a common non-deletion variant in Southeast Asian population. The etiology of HbQS is with a high risk of life-threatening anemia. This study was undertaken to design and implement a genotyping assay for Genetic variants associated with non-deletion alpha thalassaemia in a cohort of Sri Lankan patients.

Methods: A descriptive cross sectional study was carried out on a cohort of selected non – deletion alpha thalassaemic patients. Significant SNP for HBA2:c.377 T>C, (rs41397847) was selected for this study. Novel single variant tetra-amplification refractory mutation system (T-ARMS) polymerase chain reaction (PCR) assays was designed. The assay was optimized by genotyping the SNPs in an existing sample resource obtained from a cohort of non-deletion alpha thalassaemic patients who had given prior consent. A total of 100 samples were genotyped for (HbQs) HBA2:c.377 T>C variant.

Results: The expected results were obtained by T-ARMS-PCR and confirmed by Sanger sequencing. Genotype frequencies for HBA2:c.377 T>C rs41397847, were: (homozygotes – 8.0%), (heterozygotes- 4.0%) and (benign variant -88%). The ancestral allele frequency was (0.08%) for HBA2:c.377 T>C.

Conclusion: Total of four individuals were found to be heterozygotes and eight cases were homozygote for Hb Quong Sze. Ancestral allele for the variant was identified in heterozygous form in the genotyped cohort. This genotypic assay can be used as an efficient, sensitive and specific molecular diagnostic screening test for non-deletion alpha thalassaemia in Sri Lankan population.

Keywords: T-ARMS PCR, non-deletion variant, Hb Quong Sze

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