

# Molecular characterisation of $\beta$ -globin gene mutations in Penang and Kedah, Malaysia

## ABSTRACT

### Introduction:

Beta-thalassaemia is an autosomal recessive disorder and it is a public health problem in the Malaysian Malays and Chinese. This disorder mainly results from point mutations, small insertion or deletions in the  $\beta$ -globin gene complex. Beta-thalassaemia major patients require life-long monthly blood transfusions and iron-chelation therapies to sustain their lives. Mutation characterisation is necessary for affected couples at risk of having a  $\beta$ -thalassaemia major child.

### Objective:

1. To develop the TaqMan genotyping platform as a time- and cost-effective approach for characterisation of  $\beta$ -globin gene mutations. 2. To characterise the mutations using the developed assays in transfusion-dependent patients in Penang and Kedah.

### Methods:

Ten sets of primers and TaqMan probes were designed to identify the common mutations in Malaysian Malays and Chinese: 28 (A G), CD17 (A T), CD19 (A G), HbE (G A), IVS1-1 (G T), IVS1-5 (G C), CD 41/42 (-CTTT), CD71/72 (+A), IVS2-654 (C T) and Poly A (AATAAAHAATAGA). Another 7 sets of TaqMan genotyping assays were designed to identify the rare mutations in Malays and Chinese: 29 (A G), Cap (+1) (A C), CD8/9 (+G), CD16 (-C), CD27/28 (+C), IVS1-1 (G A) and CD43 (G T). The developed assays were used to screen 54 and 62 transfusion-dependent patients in Penang and Kedah respectively.

### Results & Discussion:

The developed assays detected 92.9% of mutations in the  $\beta$ -thalassaemia major patients. The remaining mutations were detected by ARMS, gap-PCR and DNA sequencing. The most common mutation in  $\beta$ -thalassaemia major patients in Penang is CD41/42 with a frequency of 20.9%. The most common mutation in  $\beta$ -thalassaemia major patients in Kedah is HbE with a frequency of 30.8%.

### Conclusion:

The simplicity and reproducibility of the TaqMan genotyping assays enable rapid and cost-effective analysis of the  $\beta$ -globin gene mutations in Malaysia.

**Keyword:** Molecular characterisation;  $\beta$ -globin; Gene mutation; Penang; Kedah; Malaysia