Methylation Status Of *LARP2* and *IGSF4* Gene Promoter Region In Hb E/B-Thalassemia And B-Thalassemia Major Patients

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Abstract

Hypermethylation of *LARP2* and *IGSF4* in β-thalassemia have been implicated in the pathogenesis of abnormal β-globin chain production. However, methylation status has not been fully explored in Hb E/β-thalassemia which has variable clinical presentation ranging from mild to severe. This study aimed to compare DNA methylation status of *LARP2* and *IGSF4* gene promoter of Hb E/β-thalassemia and β-thalassemia major patients who have less clinical variability. DNA were extracted from nucleated red blood cells (NRBCs) from peripheral blood (PB) of 21 Hb E/β-thalassemia and 12 β-thalassemia major patients at Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II (HRPZII). Methylation status of the promoter region of *LARP2* and *IGSF4* promoter were examined by using bisulfite sequencing PCR (BSP) and methylated specific PCR (MSP) respectively. The results showed that none were fully methylated in *LARP2* promoter region of both patients. Partial methylation was detected in 9 of 21 (43%) of Hb E/β-thalassemia patients and 17% in β-thalassemia. Out of 18 CpGs analyzed, CpGs 3 and 5 were mostly partially methylated, 36% of Hb E/β-thalassemia and 17% in β-thalassemia major. In *IGSF4* promoter region, 75% of β-thalassemia patients were fully methylated while 95% Hb E/β-thalassemia patients were partially methylated. Significant difference reported between types of thalassemia and *IGSF4* methylation status (p<0.05). This study demonstrated that partially methylated *IGSF4* and *LARP2* are common in Hb E/β-thalassemia. Partial methylation may either cause down- or up-regulation expression of *LARP2* and *IGSF4* genes. We speculated that these epigenetic changes may contribute to the large clinical spectrum of Hb E/β-thalassemia. However, this has yet to be confirmed with further study to correlate the findings with clinical severity parameters.

**Keywords**: Methylation; β-thalassemia; *LARP2*; *IGSF4*

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