Genetic Background of ÃfÂŽÃ,Â² Thalassemia Modifier: Recent Update

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Author Order	of
Accreditation	2
Abstract	Thalassemia has become major health problem among developing countries. Genetic background which contain enormous mutations and variations have lead in clinical problem differences. The genetic basis of thalassemia, beta specifically, is mutations of the gene encoding the $\tilde{A}f \hat{A} \check{Z} \hat{A}, \hat{A}^2$ chain of the hemoglobin (Beta-Globin, HBB). However, today it is known that abnormalities in this gene do not necessarily determine the clinical appearance of $\tilde{A}f \hat{A} \check{Z} \tilde{A}, \hat{A}^2$ thalassemia patients. A set of genes has been found that can modify the primary $\tilde{A}f \hat{A} \check{Z} \tilde{A}, \hat{A}^2$ thalassemia disorder. Secondary modifier contains genes that have been associated with elevated levels of HbF and improvement ratio of $\tilde{A}f \hat{A} \check{Z} \tilde{A}, \hat{A}^2$ globin chain. The genes involved are HBA, HBG, BCL11A, HBS1L-MYB and other cofactor genes regulating erythropoiesis. Tertiary genetic modifier comes from other genes related to the disease severity including iron metabolism, redox activity, and clinical complications. The review aims to provide the latest updates regarding the known $\tilde{A}f \hat{A} \check{Z} \tilde{A}, \hat{A}^2$ Thalassemia modifier genes and some other genes involved in the changes of the clinical manifestations.
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