Letter to the editor: Usage of U7 snRNA in gene therapy of hemoglobin J Iran disorder: why it is not applicable?

Viroj Wiwanitkit

Wiwanitkit House, Bangkhae, Bangkok Thailand 10160
Email: wviroj@yahoo.com
Phone: 662-4132436


Editor

Hemoglobinopathy is an important genetic problem affecting millions of world population. The new alternative treatment is the use of gene therapy. The repair based on small nuclear RNAs (SnRNAs) is a widely discussed method. It is proved and validated for many hemoglobinopathies with underlying beta globin gene defects [1]. Many recent publications indicate the feasibility of using U7.623 gene therapy for several beta hemoglobinopathies such as hemoglobin (Hb) C [2] and S disorders [3]. However, this approach has never been tested for the Hb J Iran (beta 77 His----Asp), which is a problematic hemoglobinopathy in Middle East [4]. For a brief assessment, the author uses the previously published in silico method by Wiwanitkit for assessment of recovery of function and biological process of hemoglobin Iran after application of U7.623 gene therapy [2-3]. The validity and reliability of the used method is approved [2-3]. Based on the gene ontology study, the complete recovery cannot be determined. The question is why this technique is not applicable for treatment of hemoglobin J Iran. Basically, the rationale of using U7.62 is that it contains a sequence antisense to a region between the aberrant splice sites, therefore it reduces the incorrect splicing of pre-mRNA and leads to increased levels of the correctly spliced b-globin mRNA and protein. Therefore, it is justified to use U7 in certain mutated Hbs (such as mutations at 654, 705 or 745 in intron 2 of the Hb) because these mutations can activate aberrant 3’ and 5’ splice sites within the intron, prevent correct splicing of beta-globin pre-mRNA and result in inhibition of beta-globin synthesis [5]. Hence, this is the reason that using U7 snRNA in hemoglobin J Iran where His77 is substituted by Asp is not applicable. Although this article did not report on any novel but negative finding, the report in this work is different from the previous reports by the authors in the serial study of gene therapy for hemoglobin disorders that highlighted the efficacy of U7.623 gene therapy in several beta hemoglobinopathies [2-3]. It is interesting that U7.623 gene therapy cannot be applicable for treatment of hemoglobin J Iran and it is required to find and test other alternative gene therapeutic approaches.

References