Usage of U7 snRNA in gene therapy of hemoglobin S disorder - is it feasible?

Hemoglobin S hastalığının gen tedavisinde U7 snRNA kullanımı uygun mu?

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Letter to the Editor

Of several hemoglobinopathies, hemoglobin (Hb) S disorder [beta6(A3)Glu-->Val, GAG-->GTG] is one of the most common forms [1]. Similar to a thalassemia carrier, heterozygous Hb S without concomitant thalassemia is usually asymptomatic. For treatment of hemoglobinopathies, the new alternative is the usage of gene therapy. Recently, repair of defective splicing by small nuclear RNAs (SnRNAs), as a therapeutic agent, was proposed. This process involves replacement of the natural antisense sequence with that tackles to the desired RNA [2] and becomes a new modality in advanced gene therapy for hemoglobinopathies. This process allows for possible long-term expression of RNA antisense to its targets such as the aberrant thalassemic splice sites in beta globin RNA [2].

Here, the author performs a basic bioinformatic analysis to assess the effect of co-expression between nucleic acid sequence for human Hb S beta globin chain and U7.623. To answer the raised question, a gene ontology technique was applied. The database PubMed was used for data mining of the nucleic acid sequence for human beta globin chain, and then the mutation beta 6 was experimentally done to obtain the primary sequence in Hb S disorder. In addition, the modified U7 snRNA (U7.623) was also searched and used for further study. Later, the author performed prediction of molecular function and biological process for the combination between nucleic acid sequence for human Hb S beta globin chain and U7.623 using a novel gene ontology prediction tool, GoFigure, which accepts an input DNA or protein sequence, and uses BLAST to identify homologous sequences in gene ontology databases [3]. As a result, the molecular function and biological process in the co-expression between nucleic acid sequence for human Hb S beta globin chain and U7.623 was predicted as oxygen transporter activity for molecular function and oxygen transport for biological process, indicating complete recovery.

Gene therapy is a new therapeutic focus in modern medicine for many genetic diseases including hemoglobinopathy [2]. Concerning thalassemia, modified U7 snRNA [4] is a widely documented SnRNA for therapy for beta globin gene defect. Here, the author assessed the effect of co-expression between nucleic acid sequence for human Hb S beta globin chain and U7.623 by the standard published technique by Wiwanitkit [5]. According to this study, the gene ontological results showed that full recovery of hemoglobin in both molecular function and biological process can be achieved. Indeed, U7.623 antisense is already confirmed for its effectiveness in repairing gene therapy for several beta-thalassemia mutations [5-8]. However, there is a limited knowledge on Hb S disorder. This work is intended to extend our knowledge, and it implies the usefulness of this antisense approach to correct splicing defects in Hb S disorder. However, this is only a prediction that needs to be confirmed by in vitro analysis**.**

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