Gene Ther Mol Biol Vol 9, 325-326, 2005

Identification of putative genes for hereditary persistence of fetal hemoglobin (HPFH)

Short Communication

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Key words: Hereditary persistence of fetal hemoglobin, putative, gene

Abbreviations: Hereditary persistence of fetal hemoglobin, (HPFH); kilobases, (kb)

Received: 3 March 2005; Revised: 7 April 2005
Accepted: 14 April 2005; electronically published: 1 November 2005

Summary

Hereditary persistence of fetal hemoglobin (HPFH) is an important hemoglobin disorder. It is noted that that the 3'-juxtaposed region (3'JR) position exerted a positional effect associated with activation of fetal gene in HPFH. In this study, computer prediction and gene homology programs was used to reveal gene homologues to this area. The identified gene can be a considerable point in gene therapy. The results of in silico analysis of the breakpoint revealed 3 most highly homologuegenes (alignment score between 50 and 80) including a) Homo sapiens G-γ globin and A-γ globin genes, b) Homo sapiens β globin region (HBB@) on chromosome 11 and c) Homo sapiens chromosome 11, clone CTD-2643I7.

I. Introduction

Hereditary persistence of fetal hemoglobin (HPFH) is an important hemoglobin disorder. Poncz et al said that the region of DNA brought into close proximity to the fetal γ-globin genes on chromosome 11 in deletional forms of HPFH were selectively hypomethylated and presumably activein normal erythroid tissue (Poncz et al, 1987). They noted that this region was normally located approximately 100 kilobases (kb) 3' (5,226078 K) to the fetal genes and the continued expression of fetal hemoglobin in adult life in these forms of HPFH had been ascribed to the effect of this erythroid-specific region in altering local chromosomal structure and allowing transcription (Poncz et al, 1987). They found that that the 3'-juxtaposed region (3'JR) position exerted a positional effect associated with activation of fetal gene in HPFH (Poncz et al, 1987). In this study, computer prediction and gene homology programs were used to reveal gene homologues to this area. The identified gene might be considered a target in gene therapy.

II. Materials and methods

In this study, computer search for the sequence in the breakpoint area was performed using the National Center for Biotechnology Information (NCBI) MapViewer. Then, exons prediction was performed by First Exon Finder (First EF) program.

The derived exon was then submitted for BLAST (basic local alignment search tool) analysis, either at the National Center for Biotechnology Information NCBI and National Library of Medicine in the USA. BLAST2 N (nucleotide versus nucleotide database) was used.

III. Results and discussion

The results from exon prediction are presented in **Figure 1**. The results of BLAST analysis of the breakpoint revealed 3 most highly homologuegenes (alignment score between 50 and 80) including a) Homo sapiens G-γ globin and A-γ globin genes, b) Homo sapiens β globin region (HBB@) on chromosome 11 and c) Homo sapiens chromosome 11, clone CTD-2643I7. Of interest, these three identified genes could be targets for diseases, such as thalassemia or sickle cell disease, that would benefit from increased production of fetal hemoglobin. Genetic factors affecting postnatal γ-globin expression, a major modifier of the severity of both β-thalassemia and sickle cell anemia have been reported (Lin et al, 2000). Lin et al proposed for the finding that the β-cluster contained a HPFH γ allele, resulting in postnatal expression of human γ-globin in transgenic mice (Lin et al, 2000).

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>TTTCCCATCTCTTCCAAAACATCTGTTTCTGAGAAGTCCTGTCCTATAGAGGTCTTTCTTCCCACCGGAT_1
 Predictions on the direct strand

No.     Promoter     P(promoter)     Exon          P(exon) P(donor)  CpG Window


>TTTCCCATCTCTTCCAAAACATCTGTTTCTGAGAAGTCCTGTCCTATAGAGGTCTTTCTTCCCACCGGAT_1
 Predictions on the complementary strand

No.     Promoter     P(promoter)     Exon          P(exon) P(donor)  CpG Window
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Figure 1. Results from exon prediction

IV. Conclusions

HPFH is an important hemoglobin disorder. It is noted that that the 3'-juxtaposed region (3'JR) position exerted a positional effect associated with activation of fetal gene in HPFH. In this study, computer prediction and gene homology programs was used to reveal gene homologues to this area. The identified gene can be a considerable point in gene therapy. The results of in silico analysis of the breakpoint revealed 3 most highly homologuegenes (alignment score between 50 and 80) including a) Homo sapiens G-γ globin and A-γ globin genes, b) Homo sapiens β globin region (HBB@) on chromosome 11 and c) Homo sapiens chromosome 11, clone CTD-2643I7.

References

Poncz M, Sutton M, Delgrosso K, Schwartz E, Surrey S (**1987**) DNA methylation in hereditary persistence of fetal hemoglobin (HPFH-2). **Nucleic Acids Res** 15, 5169-79

Lin SD, Cooper P, Fung J, Weier HU, Rubin EM (**2000**) Genome scan identifies a locus affecting γ-globin level in human β-cluster YAC transgenic mice. **Mamm Genome** 11, 1024-9