Treatment for alkaptonuria by gene therapy

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Background

Alkaptonuria (AKU), the prototypic inborn error of metabolism, was the first human disease to be interpreted as a mendelian trait. Alkaptonuria is a disorder caused by deficiency of recessive homogentisate 1,2 dioxygenase, an enzyme required for the catabolism of phenylalanine and tyrosine in liver and kidney.

Objective

The defect is caused by mutation in HGD gene that maps to human chromosome 3q21-q23. CCC sequence motif is a mutational hot spot in homogentisate-1,2-dioxygenase gene.

Methodology

A total of 43 single residue substitutions impairing HGO enzyme activity have been identified in AKU patients and model organisms. For mutation analysis, 10 ml EDTA blood samples were obtained from two different group of subjects, one unaffected and the other affected. Genomic DNA was isolated from leukocyte nuclei and the sequence differences were analyzed by single stranded conformational analysis (SSCA). Since, a substitution of the amino acid valine for methionine at position 368 (Met368Val) is the most common HGD mutation. Mutations in the HGD gene probably inactivate the enzyme by changing its structure. Therefore gene therapy has to be implemented by changing the amino acid sequence.

Conclusion

If being diagnosed earlier in foetus, the gene therapy method can easily be implemented. In adults , reduction in intake of phenylalanine rich food can help in reducing the

Accumulation of HGA and thus will reduce the symptoms of alkaptonuria.