

(P64) REVERSING THE EFFECT OF THE IDUA GENE W402X MUTATION?

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Introduction: Mucopolysaccharidosis type I (MPS I; OMIM #252800) is an autosomal recessive disorder, which results from the defective activity of the lysosomal enzyme α -L-iduronidase (IDUA, EC 3.2.1.76). The gene encoding α -L-iduronidase (IDUA; OMIM #252800) maps to chromosome 4p16.3 and contains 14 exons.

The W402X mutation is the most common in patients of European Caucasian origin, appearing in over 45% of alleles in unrelated patients of various western European origins. In addition, this mutation has been considered to play an important role in terms of the pathophysiology of MPS I.

The main objective of this work was to functionally evaluate the susceptibility of the nonsense mutation W402X of the IDUA gene to mechanisms of nonsense suppression with two individual compounds.

Methods: Nonsense suppression therapy experiments were carried out in fibroblast cell lines from individuals homozygous and heterozygous for the nonsense mutation W402X of the IDUA gene, as well as in normal control cell lines, by using variable concentrations of distinct substances and different incubation times.

Results: The results obtained with the different treatments in a W402X homozygous cell line showed that it was possible to obtain an increase in the levels of expression. It was found that the increase of the IDUA gene expression led to levels of expression comparable to those of the control cell line without treatment.

Discussion: The IDUA gene mutation W402X not only results in nonsense mediated decay, but is also susceptible to suppression of nonsense with different compounds. Further experiments are underway in order to determine the possible implications of this type of approach in the recovery of protein function.

Additional information:

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