c.1250A>G, p.N417S is a Common American TNSALP Mutation Involved in all Clinical Forms of Hypophosphatasia (HPP), Including Pseudo-HPP

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INTRODUCTION

Hypophosphatasia (HPP) is a rare autosomal or recessive inherited metabolic bone disorder caused by mutations in the tissue non-specific alkaline phosphatase (TNSALP) gene on chromosome 1p36. Three clinical presentations of HPP have been described: infantile, perinatal, and childhood. 

RESULTS AND DISCUSSION

The molecular basis of the disease is a defect in TNSALP enzyme activity or its synthesis. The most frequent mutations are found in the catalytic domain of TNSALP, which is involved in the pyrophosphate binding and catalytic sites. The TNSALP protein is a calcium-independent homodimeric enzyme that contains two complementary catalytic sites. In wild type, homodimeric TNSALP has two catalytic sites per molecule. However, many TNSALP mutations found in individuals with HPP result in loss of function, which can be explained by a decrease in the number of catalytic sites or by a decrease in the activity of the enzyme. 

The c.1250A>G, p.N417S mutation, which is a missense mutation in exon 11 that changes an arginine to glycine, is a common mutation in individuals with HPP. This mutation leads to a loss of function of the enzyme, which results in decreased TNSALP activity and decreased pyrophosphate binding. 

CONCLUSION

The c.1250A>G, p.N417S mutation is a common mutation in individuals with HPP and is involved in all clinical forms of the disease. Further studies are needed to determine the clinical significance of this mutation and to understand the pathogenesis of HPP.