

## SHORT COMMUNICATION

### ORO-DENTAL FEATURES IN HYPOPHOSPHATASIA : A VALUABLE PHENOTYPE FOR DISEASE DIAGNOSIS AND EVALUATION OF FUTURE TREATMENT OUTCOMES

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Hypophosphatasia (HP) is a rare inherited disorder characterized by a wide spectrum of defects in mineralized tissues and caused by deficiency in the tissue non-specific alkaline phosphatase gene (ALPL). The mode of inheritance is autosomal recessive or dominant with variable expressivity and incomplete penetrance.

The prevalence is estimated at 1/300 000 for severe forms and 1/6370 for moderate ones. The symptoms are highly variable in their clinical expression, relating to numerous mutations in the gene and ranging from stillbirth without mineralized bone to rickets and to pathologic fractures developing only late in adulthood. The first diagnostic sign of the disease, mostly in the moderate forms, is often a premature loss of primary teeth.

Dental anomalies however cover also a large spectrum of defects from abnormal tooth shape (small bulbous crown, cervical constrictions, enlarged pulp spaces), abnormal tooth structure (enamel, dentin, and cementum malformation), colour, eruption/exfoliation with premature loss of predominantly the primary,

but also the permanent dentition. Delayed eruption of teeth and primary teeth impaction (ankylosis) are also recorded.

These anomalies are linked to the presence and roles of the alkaline phosphatase protein during odontogenesis.

The mouse model *Akp2*<sup>-/-</sup> of hypophosphatasia recapitulates the phenotype of the disease with severe skeletal and dental hypomineralization. Delay and defect in dentin mineralization, together with a deficiency in acellular cementum, are characteristic. Enzyme replacement therapy with daily administration of sALP-FcD10 prevents dentin hypomineralization and restores acellular cement formation. ENB-0040 (human recombinant tissue non-specific alkaline phosphatase) is a subcutaneous bone-targeted enzyme replacement therapy for hypophosphatasia and is currently in Phase II clinical studies. Besides improvement of bone phenotype in children with hypophosphatasia, it will be important to gather information about the evolution of dental symptoms as they may constitute early markers of treatment efficacy.