

Treating X-Linked Hypophosphatemia (XLH), Bone Deformity and Other Renal Phosphate Wasting Disorders

Published date: March 14, 2017

Technology description

X-linked hypophosphatemia (XLH) is a genetic type of rickets/osteomalacia marked by progressively severe skeletal abnormalities and growth retardation. It is a renal phosphate wasting disorder, which involves defective phosphate transport due primarily to elevated circulating concentrations of FGF-23. Mutations in the PHEX gene underlie the genesis of XLH, which occurs in about 1:20,000 live births and can result in bone deformities, growth retardation and tooth abscesses. Therapy currently is limited to combination drug regimens, including calcitriol and phosphate supplements, which are largely ineffective and associated with multifactorial complications, including vitamin D toxicity.

Abnormal bone mineralization and the resultant rickets and osteomalacia are present in other renal phosphate wasting disorders, such as autosomal dominant hypophosphatemic rickets and tumor-induced osteomalacia (TIO). Affected patients show elevated serum levels of the protein FGF-23 along with the renal abnormalities that result in hypophosphatemia. Elevated FGF-23 levels also are a risk-factor in kidney failure. Identifying effective gene targets could lead to new cures and prolonged life for patients. UW-Madison researchers have developed methods to treat XLH, and potentially other renal phosphate wasting disorders, using polyarginine peptides. The peptides stimulate the 7B2-SPC2 protein complex, overcoming a primary abnormality resulting from the PHEX gene mutation responsible for the cascade of abnormal protein functions that lead to the XLH phenotype.

Administered alone or with other pharmaceutical agents, the arginine peptides work by enhancing FGF-23 degradation into inactive fragments and suppressing FGF-23 production. The resultant normalized levels of FGF-23 and other proteins completely rescue the HYP phenotype, including the abnormalities in the serum phosphate and bone mineralization.

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing treatments using arginine peptides to combat renal phosphate wasting disorders that can cause bone structural abnormalities (bowing) and stunt growth.

Application area

Novel treatment for XLH and related renal phosphate wasting disorders

Advantages

Cures or arrests bone demineralization symptoms

Enhances bone growth

Restores phosphate serum levels

Pharmaceutical compositions could be flexibly administered.

Institution

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