Methods To Normalize FGF23 Levels

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Technology description

Short Description

A new method to normalize FGF23 levels in the treatment of diseases

Background

Elevated plasma levels of Fibroblast Growth Factor 23 (FGF23) are present in a variety of human diseases and conditions including chronic kidney disease, left ventricular hypertrophy and congestive heart failure, autosomal dominant hypophosphatemic ricketts, osteomalacia, Vitamin D deficiency, fibrous dysplasia, and aging. Since physiological processes such as phosphate homeostasis and maintaining active Vitamin D levels require FGF23, a method for modulating levels of FGF23 over complete neutralization is highly desirable.

Abstract

FGF23 is synthesized in bone by osteogenic cells and is secreted into the circulation where it primarily functions in the kidneys to control phosphate homeostasis and active Vitamin D levels. In plasma, FGF23 can be cleaved between R179 and S180, yielding inactive N- and C-terminal fragments. It is speculated that a subtilisin-like proprotein convertase mediates the inactivating proteolysis of FGF23, but the specific protease(s) involved have not been identified until now. We have recently discovered that two previously described proteases can cleave FGF23, and methods that increase the activity of one or both of these proteases can reduce or normalize FGF23 levels in plasma. This strategy is attractive for the therapy of diseases that display elevated FGF23 levels since dosing can be modulated to maintain physiological levels of FGF23.

Application area

Normalization of FGF23 for the treatment of diseases that display elevated FGF23 levels and/or signaling.

Advantages

There are no therapeutic interventions approved to date that effectively normalize FGF23 levels to physiological levels in diseases where FGF23 levels are increased.

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