GDF15, a Marker and Cause of Morbidity in Thalassemia

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Technology description

Summary

The invention includes methods for the measurement of Growth Differentiation Factor 15 (GDF15, also known as MIC-1 or NAG-1) levels in order to diagnose or predict disease severity in patients with thalassemia and with related complications, as well as methods for treating thalassemia by administration of a GDF15 antagonist. Also disclosed is a method to reduce hepcidin levels by administration of GDF15, a GDF15 substitute, or GDF15 agonist.
GDF15 is a member of the TGF-Beta superfamily of proteins, which are known to control cell proliferation, differentiation, and apoptosis in numerous cell types. The inventors are additionally interested in investigating the role of GDF15 in other disorders characterized by ineffective erythropoiesis, as well as the role of GDF15 in the regulation of iron metabolism.
Thalassemia consists of a group of inherited diseases of the red blood cells, arising from deficient or absent production of globin chains. In beta-thalassemia, also known as Cooley's anemia or Mediterranean anemia, defective globin production reduces the number and viability of red blood cells, causing anemia and subsequent expansion of bone marrow. As a result of marrow expansion distorted bone formation ensues. Beta thalassemia, the most severe form of thalassemia, also results in iron overload, which is the major cause of beta-thalassemia mortality worldwide. As a result of iron overload, the patient may develop hypropituitarism, hypothyroidism, hypoparathyrodism, diabetes, arthropathy, cirrhosis and cardiopulmonary disease. Treatment of beta-thalassemia involves frequent blood transfusions and chelation therapy to remove excess iron from the blood.
In thalassemia, the patient's hepcidin expression is pathologically suppressed. Hepcidin is a protein synthesized in the liver, which reduces iron absorption in the body. The inventors have identified GDF-15 as a hepcidin-suppressing cytokine that is overexpressed in thalassemia. GDF15 levels in blood plasma have been found to be dramatically elevated in beta-thalassemia patients compared to healthy donors and patients with hereditary hemochromatosis, another form of iron overload disease.
Market:
Thalassemia is a growing global public health problem. It is estimated that seven percent of the world's population are carriers, with about 400,000 affected babies born each year. Approximately 1,000 people in the United States currently have beta-thalassemia; however, the number of patients is expected to grow. Prevalence of the disease is higher in those of Mediterranean descent and those from China,

India and other Asian countries. The U.S. Food and Drug Administration classifies thalassemia as a rare or orphan disease.

Application area

Diagnostic test to detect increased risk for thalassemia-related complications.
Treatment of thalassemia by administration of a GDF15 antagonist.
Treatment of iron-dysregulated diseases.
Treatment of ineffective erythropoiesis.
Treatment of anemia of chronic disease.

Institution

NIH - National Institutes of Health

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