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SHORT COMMUNICATION

GDF15 as a Marker of Ineffective Erythropoiesis and Erythroid Expansion in Thalassemia: a Clinical Perspective

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SUMMARY

Background: **Ineffective erythropoiesis is a hallmark of thalassemia syndromes. Growth differentiation factors, such as GDF15, play a crucial yet not fully understood role.**
Methods: **Serum GDF15 levels were measured by ELISA in 486 individuals (362 thalassemia patients, 53 β-trait carriers, and 71 healthy subjects) and analyzed alongside biochemical and clinical parameters.**
Results: **GDF15 levels were elevated in transfusion-dependent (TD) β-thalassemia (26-fold), non-transfusion-dependent (NTD) β-thalassemia (6-fold), and β-thalassemia carriers (2-fold) compared to healthy controls. Moreover, GDF15 levels were elevated in α-thalassemia patients (2-fold) compared to carriers. In TD β-thalassemia, GDF15 correlated inversely with hemoglobin and positively with erythropoietin. GDF15 also correlated with iron metabolism markers. Longitudinal analysis in a TD patient subgroup showed dynamic GDF15 changes post-transfusion, reflecting erythropoietic activity. Furthermore, GDF15 levels correlated with transfusion intervals, particularly in splenectomized patients.**
Conclusions: **GDF15 represents a promising biomarker for assessing thalassemia severity, monitoring treatment responses, and guiding therapies.**
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Supplementary Data

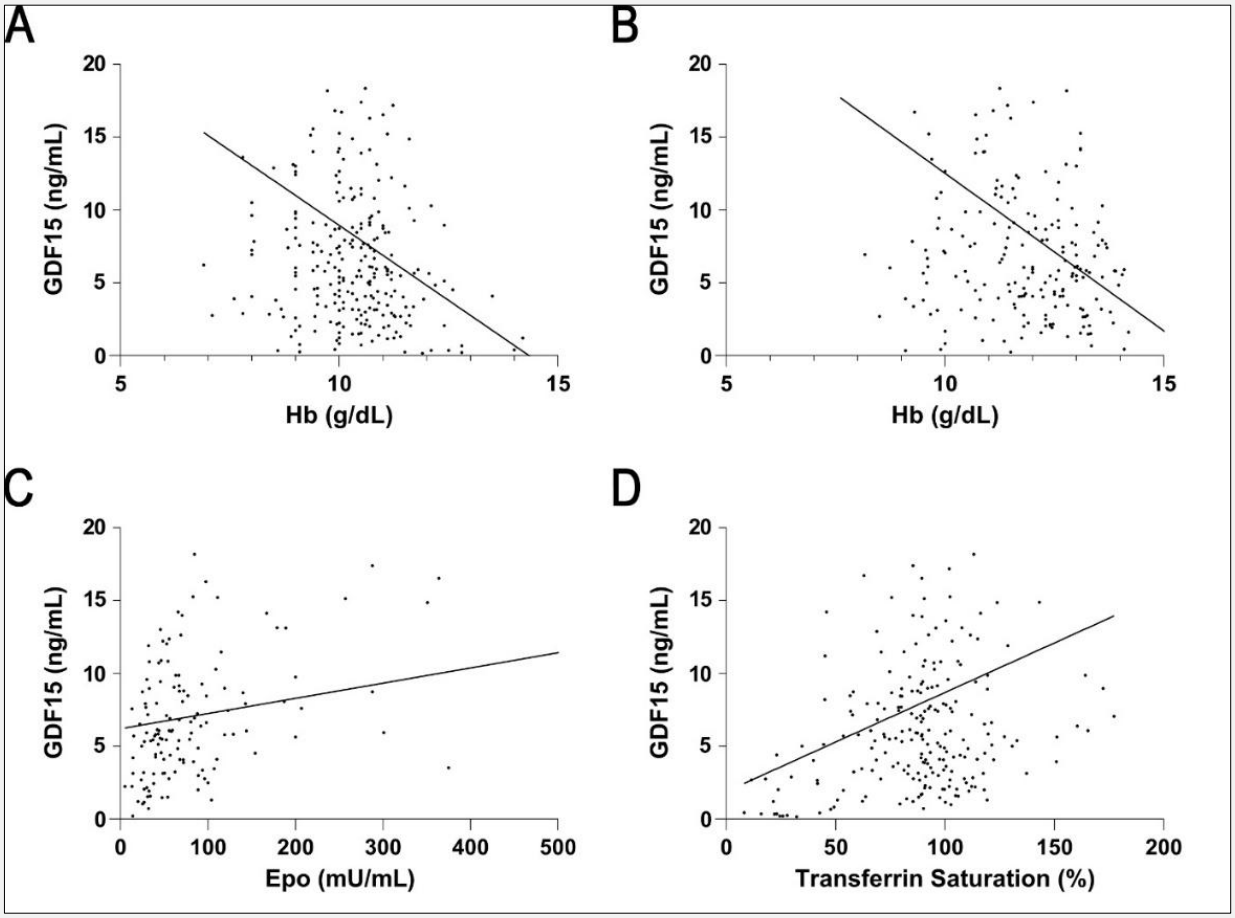

Figure S1. Linear correlations between GDF15 and A) single-point Hb, B) previous year mean Hb, C) EPO, and D) transferrin saturation in TDT patients. Only parameters that reached a statistically significant correlation are shown.

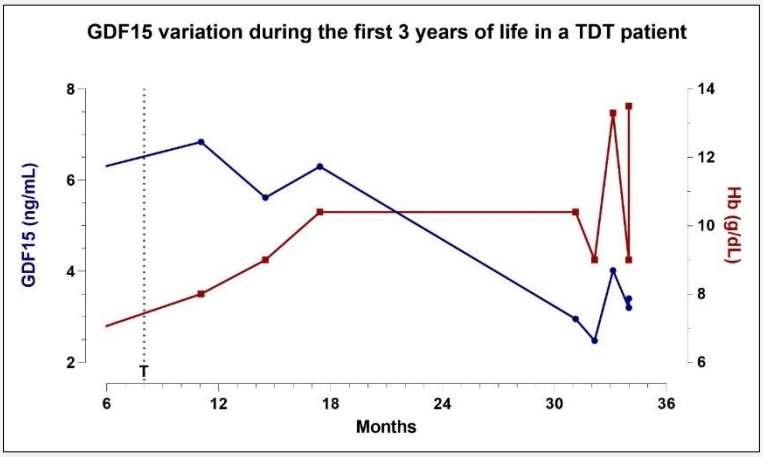

Figure S2. GDF15 (blue line, left axis) and Hb (red line, right axis) variations during months after birth in a single patient prenatally diagnosed (homozygous for HBB c.93-21G>A, previously known as IVS I:110 mutation).

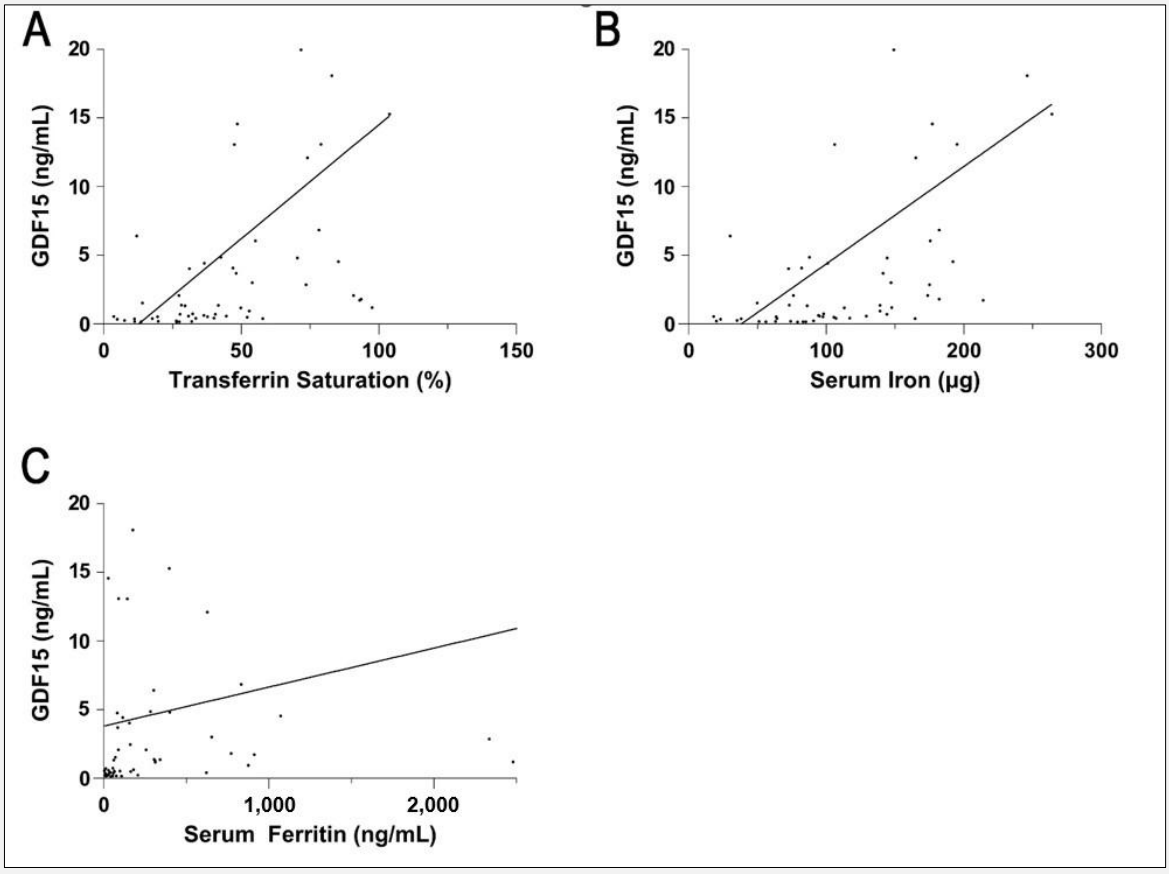

Figure S3. Linear correlations between GDF15 and A) transferrin saturation, B) serum iron, and C) serum ferritin in NTDT patients. Only parameters that reached a statistically significant correlation are shown.

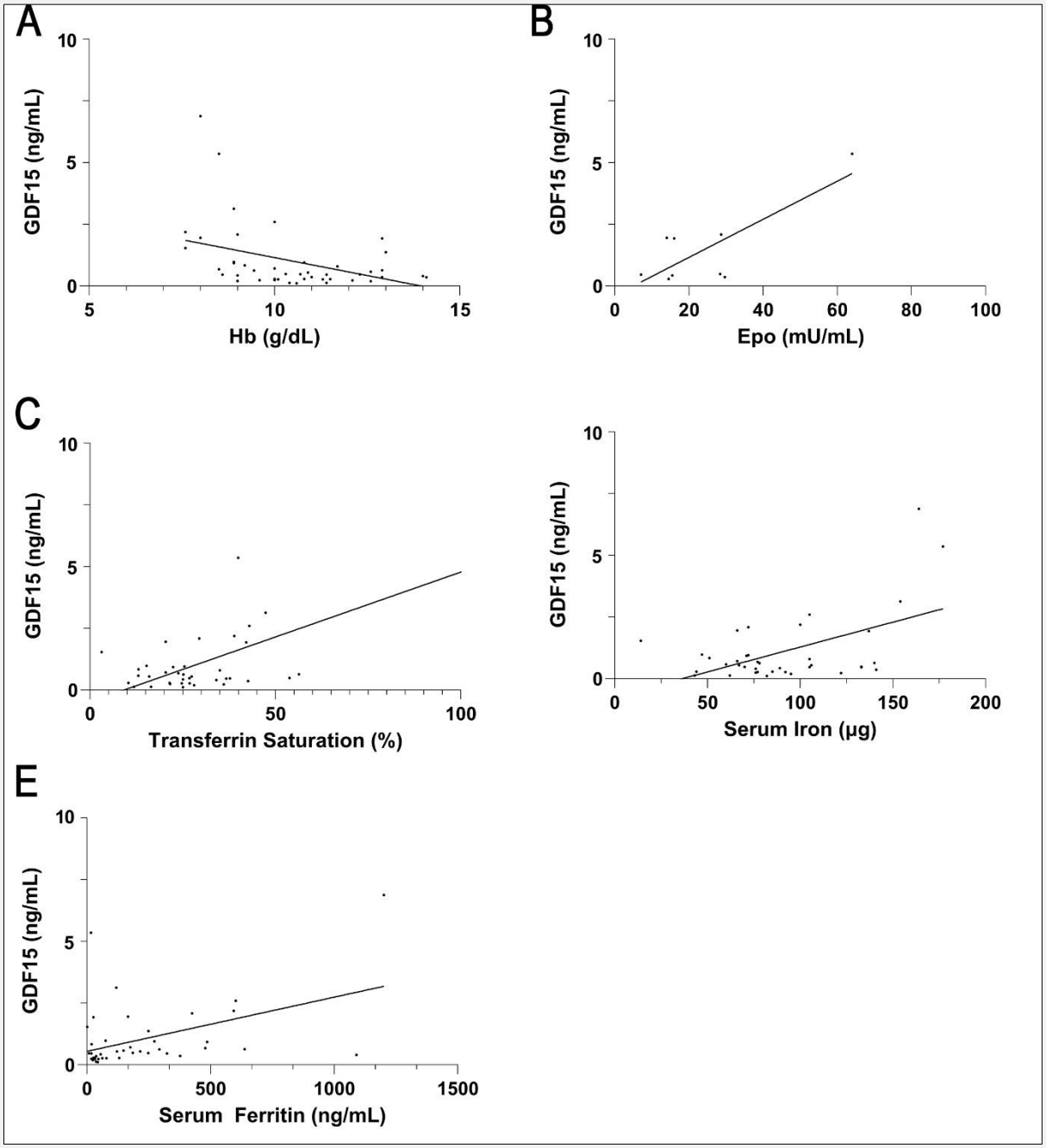

Figure 4. Linear correlations between GDF15 and A) single-point Hb, B) EPO, C) transferrin saturation, D) serum iron, and E) serum ferritin in β-Thal carriers. Only parameters that reached a statistically significant correlation are shown.