

Reviewer #1:

**Specific Comments to Authors:** In my opinion, the introduction of the article could have been written more professionally, however, the manuscript is accepted.

Answer: Suggested modifications have been incorporated in the manuscript

Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade C (A great deal of language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:**

- ✓ Especially interesting is the connection to erythropoiesis and iron metabolism. I would appreciate an enlargement on this in the discussion section which is too thin at the moment.

Reply: Suggested modifications have been incorporated in the discussion sections of manuscript.

- ✓ If I would summarize, as it is, this review looks at existing studies on GDF-15 and lists their results, confirming what is already known. The only therapeutic advice deriving from the review is the potential use of iron chelating agents. There are no speculations on how GDF-15 impacts the pathogenesis of COVID-19, connections to erythropoiesis, inflammation, hepcidin and iron metabolism.

Reply: Suggested modifications have been incorporated in the discussion sections of manuscript.

- ✓ The few sentences: from “Hyperactivity of the immune response in the pathogenesis.... to the end” are in my opinion too convoluted, and thin without making much sense either.

Reply: Paragraph has been reframed and incorporated in the manuscript.

- ✓ How does the “imbalance” between immune response activation and cytokine response lead to all those conditions? Most of it is borrowed and rephrased, not much novel thinking?

Reply: Suggested modifications have been incorporated in the discussion sections of manuscript..

- ✓ The associations between GDF-15 and FGF23 in kidney diseases could be discussed.

Reply: As such, we did not find any relationship between the variable and disease phenotype.

- ✓ The interactions between metformin and GDF-15 are interesting as GDF-15 mediates metformin effects and metformin is supposedly protective in SARS?! How is all this reconciled? Even if it is not, it is a worthwhile and stimulating discussion that will keep the reader interested in similar ways it did for me, but rather than looking for it myself I would have liked to see it served right there.

Reply: Suggested modifications have been incorporated in the discussion sections of manuscript.

- ✓ 2. Language is not captivating. At times, boring and incorrect. Needs the touch of a native speaker.

Reply: Language has been modified to meet the requirements.