*Question 1- The studies of cellular iron supplementation should be done more carefully. The iron concentration and time of incubation should be stated. Moreover the quantification of cellular iron uptake by counting the Perl’s positive cells is not straightforward.* *Perl’s stains mainly hemosiderin iron which is only a fraction of total iron and that is deposited only when iron is in excess. Moreover, I do not see the blue cells in the strong red background in fig 3 and 4. More direct methods would be more convincing, such as measurement of total cellular iron, or of ferritin protein, ferritin-iron or also transferrin receptor mRNA.*

Answer: Thanks for the question and suggestion. In our study, iron supplementation changed to ferric ammonium citrate (FAC) in the presence of ascorbate. The concentration of ascorbate and FAC was 500 μM and 10 μM which was suggested by Sinead Healy et al (Prog Neurobiol. 2017 Nov;158:1-14) and the time of incubation was 48h in Ferrozine assay, Perl’s stains, Western blot. In order to quantify cellular iron, we use the ferrozine assay (Anal Biochem. 2004 Aug 15;331(2):370-5.) and the protein level of Ferritin by western blot. In addition, the intracellular accumulation after FAC treatment was also confirmed by Perl’s staining (supplementary figure). The conclusion was in accord with previous research.

*Question 2- The differential uptake of Fe(II) and Fe(III) cannot be used as an evidence of hepcidin-dependent iron uptake. Fe(III) at neutral pH readily forms polynuclear insoluble complexes the absorption of which is not studied. Fe(II) is supposed to be taken up mainly by ZIP14, which is unrelated to hepcidin activity. Most studies of iron supplementation use ferric ammonium citrate in the presence of ascorbate to maintain it in a mononuclear and soluble form.*

Answer: We completely agree with reviewer’s suggestion. FAC and ascorbate applied to iron incubation experiments.

*Question 3- The finding that FGF6 overexpression induces hepcidin mRNA is rather convincing, less clear is the effect of the three mutants. The claim that M2 (D174V) differs from M1 (E172X) and M3 (R188Q) is supported only by fig 4B and 4D, and not by fig 4E-G.*

Answer: Thanks for the comments. M2 (D174V) differs from M1 (E172X) and M3 (R188Q) was supported by Ferrozine assay, Western blot, Perl’s stains.

*Question 4- A list of abbreviations would help the reader.*

Answer: Thanks for the suggestion. We added a list of abbreviations to help the reader understand the paper.