

Format for ANSWERING REVIEWERS

March 30, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 16685-review.doc).

Title: Is erythroferrone finally the long sought-after systemic erythroid regulator of iron?

Author: Alfons Lawen

Name of Journal: *World Journal of Biological Chemistry*

ESPS Manuscript NO: 16685

The manuscript has been improved according to the suggestions of reviewers:

reviewer 00227526:

However, the explanation is too brief to have general readers understand the function of this molecule. Therefore author should add some figures explaining the functional relationship between erythroferrone and other molecules such as hepcidin to illustrate clearer this review.

In addition, the Core tip is a mere repetition of the Abstract. The author should summarize the Core tip more briefly.

The core tip has been shortened.

reviewer 00227418:

Specific remarks The paper by Pigeon C 2001 J Biol Chem should be included among those first describing hepcidin.

A sentence referring to the above paper has been included (Murine hepcidin was found to be over-expressed during iron overload (Pigeon *et al.*, 2001).).

The sentence beginning at line 96, page 6 is not clear. Indeed, CTRP15 belongs to the C1q/TNF-related proteins family.

I believe the reviewer missed the difference between erythroferrone (CTRP15) and "myonectin" (C1QTNF5). To make it clear that both are different, I inserted a "the related, but not identical" into the sentence.

reviewer 00253956:

Manuscript fine for publication as is - my only suggestion is that it would benefit from an image or two to better illustrate the text to the reader.

Two figures have now been included.

reviewer 00609371:

It is better to focus only on the functions of erythroferrone and give a fairly complete review of available literatures and explain why erythroferrone might be the long sought-after systemic erythroid regulator of iron, otherwise, the article will be too shallow and the title too misleading.

To the best of my knowledge, all literature on erythroferrone has been covered. As this is a relatively recently discovered molecule, research into erythroferrone is still in its infancy.

The author should list the potential criteria of systemic erythroid regulator of iron.

These have now been included.

Based on the criteria, the author should explain why Growth Differentiation Factor 15 (GDF15), Twisted Gastrulation (TWSG1) and transferrin receptor 1 are not the long sought-after systemic erythroid regulator of iron.

This has now been included.

The author should provide a schematic working model to reconcile the two functions of erythroferrone.

This has been done (Figure 2).

In addition, the reference Nai *et al.*, 2014b, which is now published, was updated to Nai *et al.*, 2015 and Nai *et al.*, 2014a was changed to Nai *et al.*, 2014.

I hope you find the manuscript now suitable for publication in World Journal of Biological Chemistry

Sincerely Yours

Alfons Lawen