Review of: "The dual energy supply of eukaryotic cells"

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In the revised version of his article the author has made considerable changes and completed extensive editing. This effort by the author did improve the narrative of the article. However, we feel that prior to submitting this article for publication, this article must be further revised to address the comments we made below. Please note that the underlined sentences are original sentences of the article, and non-underlined sentences are our comments.

The legend to Illustration 1 should clarify the stages of symbiotic fusion. We suggest the following legend to the author to consider: “The procaryotic cell, which developed features of an early mitochondrion (defense system against reactive oxidative species and aerobic energy production), fuses with pre-eukaryote to give rise to early aerobic eukaryotic cell.”

The Evidence Supporting the Endosymbiotic Conception:

References are needed to support the conception.

The iron's nature influences iron's binding affinity to oxygen and sulphur. In the case of Fe III, it binds the oxygen, while in the case of Fe II, the sulphur bind is fevered.

It is better to write the iron’s oxidation state instead of “iron’s nature”. The word “fevered” should be changed to “preferred”. Please note that in ferrous oxide, FeO, oxidation state of iron is 2+. Does author state here that FeS is a more common compound than FeO? This contradicts to the fact that oxygen is more electronegative than sulfur. Therefore, the assertion about FeS should be supported by proper references.

In Illustration 2 the five bonds made by the S atom seem to be uncommon bonding arrangement for S. The Fe-S structure in Illustration 2 should be supported by references.

Finally, the active site cycles to the loose state (red) and will be ready for the next cycle of ATP production.

In the illustration 5 the binding site in red is not loose but has ADP linked to phosphate moiety. The Illustration 5 has a title but does not have a legend. The legend should clearly explain the work of binding sites in Complex V. Also, we feel that it will make it easier for readers to follow the narrative of this paper if Complex V is called ATP synthase.

The binding change mechanism of Complex V involves the active site of a β subunit's cycling between three states

We believe this sentence should read: “The binding change mechanism of ATP synthase facilitates the cycling of enzyme’s β subunits between three conformational states in the active center.”

The Illustration 4 provides important information. To make this information easier for readers to understand the author needs to denote each type of atoms in the adenosine diphosphate producing unit.

The SET-OP consists of three SET-AG - (3x3) ADP-PUs. It also contains one pyruvate dehydrogenase complex (PDC) and three high molecular weight cytochromes (Hmc).

The reference should be given here to support the above statement.

Austin et al. suggested that Complex 1 is in the mitochondrial membrane hanging in the mitochondrial matrix [1 5].

It is not clear if Complex 1 is in IMM or in matrix. Reference 15 does not answer to this question.

while SET-OP is in the intermembrane space hanging in the mitochondrial matrix (Illustration 6).

If the SET-OP is in intermembrane space, it cannot be exposed (hang) in the matrix. The author is probably trying to say that SET-OP is in the IMM and that some protein surface areas of SET-OP are exposed to matrix. This point should be clarified.

SET-AG consists of three ADP-Pus (ADP-PU-A, ADP-PU-B, and ADP-PU-C) and three Complex V.

The author needs to explain what the ADP-PU-A, ADP-PU-B, and ADP-PU-C units are? The author is probably implying to the three conformation states of ATP-synthase’s active center. The author needs to clearly explain this.

PO3 – the formula of phosphate group is PO_4^-

In Illustration 4 the author needs to give the color code for each type of atoms in the adenosine diphosphate producing unit. The space scales are different for the different groups of atoms: the phosphate groups are very small and could not be seen easily. The space scales for all atoms should be the same. Also, the structure for the adenosine diphosphate producing unit suggested in Illustration 4 should be supported by the references.

Cytomembrane – should be written cytoplasmic membrane.

In contrast, cells use aerobic glycolysis offered by the SET-AG in a hypoxic environment (Illustration 7). [13][14]

We believe the author wants to say anaerobic glycolysis here, not aerobic.