Suggestions:

Mitochondria: line 10: We suggest using "apoptosis-regulating proteins" instead of "apoptotic proteins" as there are –pro-apototic proteins and pro-survival proteins!

Mitochondria: line 11: We suggest using "over" instead of "more than"

Mitochondria: Please consider mentioning the "endosymbiotic theory". We think that this is more valuable to the readership than to define the term "bioblast" which is anyway outdated.

Introduction, page 7, lines 4,5,6: We suggest the following wording:.., <u>the MitoEAGLE network's mission</u> <u>is to generate</u> the necessary scale, type, and quality of consistent data sets and conditions to address this intrinsic complexity. <u>The MitoEAGLE network aims at developing</u> harmonized experimental protocols...

Introduction, page 7, lines 10,11: We suggest the following wording: With an emphasis on quality of research, <u>collected data</u> can be used far beyond the specific question of a <u>specific</u> experiment.

Introduction, page 7, lines 12, 13: We suggest the following wording: Reliability and comparability of quantitative results depends on the accuracy of <u>measurements...</u>

Introduction, page 8, line 1: The focus on coupling states in mitochondrial preparations is the first step...

Page 11, 2nd paragraph, line 6: "...lack of response to ADP does not exclude phosphorylation <u>from</u> having some degree of control."

Page 12, line 2: "As such, it is necessary to be specific as to which output is under consideration."

Page 15, line 1: Replace "in a range of" by "ranging from".

Page 16, OXPHOS state, line 7: Replace "zero uncoupler" by "absence of uncoupler".

Page 16, last sentence requires citations to support the claim.

Page 17, ETS state, line 12: Replace "missing" by "absent".

Page 19, uncoupling protein: You may want to expand this or entirely skip.

Page 21, third paragraph, line 2: Replace "by measurement of LEAK respiration" by "by measuring LEAK respiration".

Page 22: What is exactly a pseudo-steady state? How about "near-steady" state instead of "pseudo-steady" state?

Page 26, Eq. 6 to 9, line 3: "The unit of the force is Newton,.."

Page 28, second paragraph, line 2: "mechanisms of coupling"

Page 29, second paragraph: Consider the following change in wording: "...is often used to <u>indicate</u> <u>'divided by amount of substance'</u>..."

Page 34, line 3: "is the change in the amount..."

Page 36 and 37: You use three times the word "crucial". I recommend to use synonyms such as "essential" or "important".

Page 37, line 3: Suggest replacing "at hand" by "under investigation"

Conclusions, page 41 and 42: The conclusions should NOT contain references to tables. Also, I would recommend shortening the text to a few "key take home" messages.