



UNIVERZITA KARLOVA 3. lékařská fakulta

Re: Master Thesis of Lawrence Rudy Cadena III. BSc.

I have read with great interest the submitted theses for the degree of Master of Science.
Below is my evaluation.

The introduction covers very well the related topics of mitochondrial structure, function and origin, the MICOS complex and related proteins, ATP synthase as both an essential OXPHOS enzyme and part of the cristae scaffolding, Trypanosoma as a model organism phylogenetically fairly distant from opisthokonts such as us and finally the association between components of the MICOS and ATP synthase.

After the introduction there follows the fulltext of a published paper describing the association of T. brucei Mic10 paralog with ATP synthase and the identification of ATPb8 as homolog to yeast subunit e. A third hypothetical model for the role of these interactions is proposed.

The conclusion then brings further hypotheses about the biophysical mode of action of Mic10-ATP synthase interaction and suggestions for further experiments.

The thesis is submitted as an introduction to the field followed by a published paper and conclusions. While I found a few typographical errors, which can at times slow down the reader, overall the language and structure of the text are clear and comprehensible. There is no doubt the submitted work shows a thorough grasp of the research topic and methods and together with an original approach brings new and important scientific data. The submitted work fulfils, in my view, more than sufficiently the requirements for the degree of Master of Science.

I recommend that this Thesis be admitted for the degree and my proposed grade is 1.

Question:

1. You mention the range of observed cristae morphology types seen in various organisms. Are there any hints that these may serve a functional purpose/adaptation or are they more likely the results of evolutionary divergence without functional impacts?
2. You mention a hypothesis that soluble proteins tend to be more conserved than membrane-bound ones. Could you elaborate on this hypothesis?
3. Is there any data showing a functional effect (or lack thereof) of Mic10 association with ATP synthase dimers, ie. on ATP synthesis?

Sincerely,

Jan Trnka, MD, PhD.