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Not a single comment to the MIG on my MitoAlmanac review of condensed versus orthodox mitochondria and request for ideas and discussion. Why? There are several possibilities. First nobody reads the MitoAlmanac. Second, people read it but have nothing to say about volume changes of mitochondria. Third, people read it, care, but are far too busy to write e-mails OR….?
O.K. which is it?

To try and stimulate discussion this month I am going to provide you with a hypothesis and see if it triggers a response.

The proposal is as follows;

THE BROAD ACETYLATION OF METABOLIC PROTEINS IN MITOCHONDRIA CHANGES THE ACTIVITY OF SOME ENZYMES UP OR DOWN BUT

THIS IS NOT THE PRIMARY ROLE OF THIS GLOBAL MODIFICATION. THE KEY FUNCTION OF ACETYLATION IS TO STABILIZE A POOL OF INACTIVE ENZYMES THAT IS NOT YET INCORPORATED INTO A COMPLEX OR OTHER TYPE OF ASSOCIATION IMPORTANT FOR CONFORMATION AND FUNCTIONING. DEACETYLATION ACTIVATES THIS FRACTION THEREBY ADDING EXTRA ENZYME WITHOUT THE NEED FOR NEW PROTEIN SYNTHESIS TO RE-ADJUST METABOLIC PATHWAYS AND MAINTAIN HOMEOSTASIS IN RESPONSE TO CELL EVENTS.
Remember that acetylation occurs at lysine residues, that there are multiple modifications on many proteins, and when acetylated, lysines are unavailable for ubiquitinylation, and thereby protected from degradation. In this model, sirtuins measure cellular metabolic flux and act accordingly to ensure that metabolism remains optimal for the substrates available and metabolic need overall of the cell.

Far fetched? No evidence? You think I've lost my marbles! O.K. what is the role of acetylation?

Acetylation and de-acetylation of fatty acid oxidation enzymes.

HIRSCHEY et al. SIRT 3 regulates mitochondrial fatty acid oxidation by reversible enzyme deacetylation. Nature 464. 121-5 (2010)

SHIMAZU et al. SIRT3 deacetylates mitochondrial 3-hydroxy-3-methylglutaryl CoA synthase 2 and regulates ketone body production.
Cell Metabolism 12. 654-61 (2010)

Acetylation and de-acetylation of urea cycle enzymes.

HALLOWS WC. et al. Sirt 3 promotes the urea cycle and fatty acid oxidation during dietary restriction.
Mol Cell 41. 139-49 (2011)

Acetylation and de-acetylation in relation to oxidative stress.

SOMEYA S. et al. Sirt 3 mediates reduction of oxidative damage and prevention of age-related hearing loss under caloric restriction.
Cell 143. 802-12 (2010)

Bell EL & Guarente L. The Sirt3 divining rod points to oxidative stress.
Mol Cell 42. 561-8 (2011)

Ozden O et al. Acetylation of MnSOD directs enzymatic activity responding to cellular nutrient status or oxidative stress.
Cancer Cell 19. 416-28 (2011)

AND MODULATION OF OTHER MITOCHONDRIAL PROTEINS

FINLEY LW.et al. SIRT3 opposes reprogramming of cancer cell metabolism through HIF1α destabilization Cancer Cell.19. 416-28 (2011)

HAFNER AV et al. Regulation of the mPTP by SIRT3-mediated de-acetylation of CypD at lysine 166 suppresses age-related cardiac hypertrophy. Aging 2. 914-23. (2010)

FINLEY LW. et al. Succinate dehydrogenase is a direct target of sirtuin 3 deacetylase activity. PLoS One. 6:e23295. (2011)

YANG Y. et al. NAD+-dependent deacetylase SIRT3 regulates mitochondrial protein synthesis by de-acetylation of the ribosomal protein MRPL10. J Biol Chem. 285. 7417-29. (2010)

THE PIONEERS OF MITOCHONDRIAL RESEARCH REMEMBERED. PAUL BOYER.

Paul Boyer won the Nobel Prize for Chemistry in 1997 for his contributions to the understanding of the mechanism of ATP synthesis by the F1F0ATP synthase (ATP synthase). The work that led him to the alternating site mechanism of this enzyme is well documented in a biography by the Nobel Foundation.
http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1997/boyer-autobio.html

But there is much more to this man that is not fully documented. I first met Paul in Madison Wisconsin when I was a post doc as he regularly visited to spend time with his good friend Henry Lardy. Later we met at Conferences where Paul would inevitably be carrying a tennis racket and looking for a game. It is important to realize that the alternating site hypothesis preceded any evidence of the rotary mechanism of the ATP synthase. Paul was quick to marry the two ideas and this was followed relatively quickly by the X Ray structure of the F1 part of the complex, which confirmed the differences in the 3 catalytic sites that had been long championed by Boyer.

Our field of bioenergetics has been blessed in that it has attracted many gentlemen and few sharks. Paul is the very model of a modern gentleman. He has time for everyone, actually listens and provides feedback in discussions of science, and gives credit where credit is due and sometimes when not.

In reviewing materials for this note I read a number of articles and looked up several websites that I did not know existed.

For example I was surprised to learn that Paul said “I remember such things as picnics in Provo Canyon, and the anticipation that I might get to lick the dasher after cranking the ice-cream freezer." I know of this quote because I looked it up at www.bellaonline quotations.com. It is listed under ice cream quotations. Another quote from Boyer I did not know about is “Most of our accomplishments [in science] are the coal we mine while looking for diamonds.” I found this

in an article written in 2002 and published in the J. of the History of Biology by Douglas Allchin and entitled "To err and win a Nobel Prize: Paul Boyer, ATP Synthase and the emergence of bioenergetics".
I encourage young scientists, particularly the more timid of you, to read this article.

Paul Boyer is now in his 90s, further establishing how healthy it is to study bioenergetics (Bill Slater and Britt Chance are other examples; see earlier MitoAlmanacs), or is it the passion for tennis that equates with long life?