This Week's Citation Classic®

Lyons J M & Raison J K. A temperature-induced transition in mitochondrial oxidation: contrasts between cold and warm-blooded animals.
Comp. Biochem. Physiol. 37:405-11, 1970.
[Department of Vegetable Crops, University of California, Riverside, CA]

A comparison was made of the effect of temperature on succinate oxidase activity of liver mitochondria from homeotherms and poikilotherms. For the poikilotherms, Arrhenius-type plots were linear over the temperature range 4° to 30° C. In contrast, for the homeotherms, the plots were biphasic with a "break" or "discontinuity" at about 23° C and an increase in Arrhenius activation energy in the temperature range below the "break." The results suggest that a phase change occurs in membrane lipids of mitochondria from homeotherms, at about 23° C, that alters the thermal properties of the membrane and limits survival of the animal below this temperature. The lack of a phase change in the mitochondria from poikilotherms is consistent with their ability to survive body temperatures near 0° C. [The *SCI*® indicates that this paper has been cited in over 135 publications.]

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This study was initiated because Jim Lyons and I had just completed a similar comparison of the effect of chilling temperatures (nonfreezing temperatures below about 12° C) on succinate oxidase activity of mitochondria from chilling-sensitive and chilling-insensitive plants. This work was carried out in Australia while Jim Lyons was on sabbatical leave and was designed to shed some light on the molecular basis of chilling injury in crop plants. We found marked differences in the two groups of plants in that Arrhenius plots of the membrane-associated enzyme system, from the sensitive plants, were biphasic, with a "break" at about 12° C, a temperature coincident with the critical temperature for the plant. With mitochondria from insensitive plants, the plots were linear. These findings were published in *Plant Physiology*,[1] and the paper was recognized as a *Citation Classic* in 1981. The work described in that paper was selected by the American Institute of Biological Sciences for the Campbell Award for "distinguished research on a vegetable crop."

From the results of the work on plants we reasoned that the thermal response of mitochondria from homeotherms might resemble that of mitochondria from chilling-sensitive plants, while that of mitochondria from poikilotherms might resemble mitochondria from chilling-insensitive plants. Chilling-sensitive plants have adapted to lowland, tropical regions where temperature fluctuations are comparatively small and the minimum temperature is rarely below 10° C. For mammalian homeotherms the tissue is maintained within an even narrower temperature range: 40° to 35° C. In contrast, the tissue of chilling-insensitive plants derived from temperate regions, and the tissue of poikilotherms, fluctuate over the range of ambient temperature. The results of the study confirmed our reasoning. Arrhenius plots of the enzyme from homeotherms showed a "break" at about 23° C and thus resembled the response of enzymes of chilling-sensitive plants. Those of poikilotherms were linear, resembling chilling-insensitive plants.

With the advantage of "hindsight" a number of reasons can be advanced that might explain why this paper became a *Citation Classic*. It provided new data on the role of membranes in hypothermia in that the temperature for the "break" in enzyme activity, at 23° C, is only a few degrees above the minimum critical temperature for the animal. Thus it appears that the phase change, or change in molecular ordering in the membrane lipids, is critical for metabolism and survival. It follows that for mammalian homeotherms to undergo hypothermic hibernation it would be necessary to lower or abolish the phase change. Thus, the paper opened up a new area of research relative to understanding the molecular aspects of hypothermia and mammalian hibernation.[2,3]

The paper also provided a remarkable example of the unity concept in biochemistry. Animals and plants have evolved separately for about 200 million years. However, the lipid components of their membranes are similar, and from the data in this paper it appears that when presented with a relatively thermostable environment the membranes develop the same type of thermal response. Added to these features, the paper also contained Arrhenius-type plots. Much controversy has developed regarding the analysis and interpretation of these plots and it is likely that the paper has been much quoted in this context.

1. **Lyons J M & Raison J K.** Oxidative activity of mitochondria isolated from plant tissues sensitive and resistant to chilling injury. *Plant Physiol.* 45:386-9, 1970. (Cited 230 times.) [See also: **Lyons J M.** Citation Classic. (Barrett J T, comp.) *Contemporary classics in plant, animal, and environmental sciences.* Philadelphia: ISI Press, 1986. p. 98.]
2. **Raison J K & Lyons J M.** Hibernation: alteration of mitochondrial membranes as a requisite for metabolism at low temperature. *Proc. Nat. Acad. Sci. USA* 68:2092-4, 1971. (Cited 85 times.)
3. **Aloia R C, Augee M L, Orr G R & Raison J K.** A critical role for membranes in hibernation. (Heller H C, Musacchia X J & Wang L H C, eds.) *Living in the cold: physiological and biochemical adaptations.* New York: Elsevier, 1986. p. 19-26.

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