Discussion

Reply to David Nicholls’ response

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Abstract

All evidence presently available shows that there is no metabolically dependent electric potential (ΔΨ) across the mitochondrial inner membrane. The data supporting this statement are documented in our review article and in the present communication. The evidence purported to show a ΔΨ results from a miscalculation or the mistaken assumption that the distribution of lipophilic cations is in response to a ΔΨ.

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1. Discussion

My recent review article [1] on the electric potential across the mitochondrial inner membrane (ΔΨ) has demonstrated that the so-called protonmotive gradient (μH+) does not exist in native metabolizing mitochondria as indicated by a variety of results.

(1) The data purported to support the conventional chemiosmotic model using the distribution of K+ or Rb+ in the presence of valinomycin to measure ΔΨ have been misinterpreted (see [1]). The calculated potentials depend exclusively on the external K+ concentration. Therefore, they correspond to a K+ diffusion potential and do not depend on metabolism. The calculations used to show that the calculated ΔΨ is dependent on metabolism are in error [2]. They report a partial decrease in electric potential in the presence of a metabolic block and an uncoupler and its increase produced by the addition of ATP. The assumption was made erroneously that the decrease in internal K+ accompanying the block in K+ transport or its reversal with the addition of ATP is not accompanied by osmotic volume changes. These osmotic responses would maintain the concentration constant and result in an unchanged calculated ΔΨ. Furthermore, the maintenance of a metabolically dependent ΔΨ would be impossible in the presence of an uncoupler (which acts as a H+ uniport) and valinomycin (which increases the permeability to K+).

(2) The H+ efflux needed to produce the required ΔΨ (or a ΔpH) when metabolism is activated doesn’t take place.

(3) The lipophilic cations used to estimate ΔΨ in mitochondria do not distribute as the consequence of a ΔΨ since interfering with metabolism affects only the influx but not the efflux of the probes.

(4) Microelectrode studies in giant mitochondria do not detect a ΔΨ even while mitochondria are phosphorylating ADP or accumulating Ca2+. The location of the microelectrode inside the inner mitochondrial space was demonstrated using dyes.

References