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Comment: Is there a direct functional link between porin and mitochondrial anion carriers?

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Pronevich et al. published a report [1] in which they claim that the adenine nucleotide translocator and the dicarboxylate carrier of the inner membrane of rat liver mitochondria are functionally linked to the pore protein (porin) of the outer membrane. This argument is based on their observations that, in mitoplasts, promotion of state 3 by ADP and stimulation of oxygen uptake by succinate are not inhibited by carboxyatractyloside (inhibitor of adenine nucleotide translocator) and butylmalonate (inhibitor of dicarboxylate carrier), respectively. The sensitivity to both inhibitors was restored upon addition of the preparation of outer membrane or of partly purified porin.

We were unable to reproduce these results. In our hands, 'mitoplasts' obtained exactly according to the procedure of Pronevich et al. [1] were as sensitive to butylmalonate as were intact mitochondria. We made no attempt to check their sensitivity to carboxyatractyloside. We wish to express the opinion that a direct functional link between porin and anion carriers in mitochondria is unlikely for the following reasons.

(i) The preparation referred to by Pronevich et al. [1] as mitoplasts consists in fact of mitochondria only partly depleted of their outer membrane. Using rotenone-insensitive NADH-cytochrome *c* reductase as the marker for the outer membrane [2], we found that as much as 70% of the original activity was retained in the 'mitoplast' prepared following hypotonic swelling and hypertonic contraction, the procedure used by Pronevich et al. [1].

(ii) We also found that the matrix compartment (determined as the ^3H_2O-accessible and [^{14}C]sucrose-inaccessible space [3]) in both mitochondria and mitoplasts obtained by the procedure of Pronevich et al. [1] was fully accessible to [^{14}C]malonate and became practically inaccessible to this substance in the presence of 0.5 mM mersalyl, the known powerful inhibitor of the dicarboxylate carrier [4]. These experiments provide a further evidence that, in mitoplasts, the dicarboxylate carrier is functionally competent and sensitive to inhibitors.

(iii) It is well established that both the adenine nucleotide translocator [5,6] and the dicarboxylate carrier [7,8], when purified and reconstituted into phospholipid vesicles, become fully sensitive to their respective inhibitors, carboxyatractyloside and butylmalonate, without addition of porin.

In view of these arguments we wish to express our opinion that the statement that 'porin regulates the sensitivity of anion carriers to inhibitors' [1] must be taken with extreme caution.

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