Ca++ AND MITOCHONDRIAL MEMBRANES: EVIDENCE FOR SPECIFIC ENZYMIC CARRIERS

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The field of Ca++ transport in mitochondria has become rather complicated in recent times. In addition to the energy-linked transport, which has been studied intensively in the last seven or eight years (1), other Ca++ binding processes have been described. Azzone and his group (2-3) have reported the binding of rather large amounts of Ca++ by liver mitochondria in the absence of metabolism; part of the binding takes place at the surface of the mitochondrion, and is thought to reflect the reaction of Ca++ with the phospholipids of the mitochondrial membrane, another part probably occurs in the intramitochondrial space, and is linked to the opposite translocation of a stoichiometric amount of intramitochondrial K+: the efflux of K* is responsible for the uptake of Ca++. More recently, Reynafarje and Lehninger (4) have described the so called "high-affinity" binding of very small amounts of Ca++ by isolated mitochondria, and have suggested that the phenomenon reflects the existence of a carrier molecule specific for Ca++ in the mitochondrial membrane.

In this paper, the most significant properties of the various Ca++ binding processes will be briefly described; emphasis will be put on those which are relevant to the main purpose of this presentation, which is that of surveying the evidence for the existence of a Ca++ carrier, and of discussing its role in the process by which isolated mitochondrial actively translocate Ca++ from the external medium.
Figure 1 shows that the energy-linked Ca\(^{++}\) transport requires the expenditure of the energy pressure maintained in mitochondria by either respiration or ATP hydrolysis. The respiration-driven process is inhibited by respiratory chain inhibitors and not by oligomycin, whereas the opposite is true for the ATP-driven process. Both systems are inhibited by uncouplers. Although the nature of the energy-pressure is still debated, it is important to mention that it is generally accepted that there are two levels of energy conservation, only the second involving the participation of phosphate. It is also generally accepted that uncouplers discharge the non-phosphorylated high-energy level, whereas oligomycin acts at the phosphorylated level. The effects of the inhibitors clearly indicate that the energy-linked uptake of Ca\(^{++}\) does not involve the discharge of phosphorylated levels of energy conservation; it has been shown long ago that energy-linked Ca\(^{++}\) uptake can proceed in the complete absence of inorganic phosphate, up to an uptake level of about 100–150 nMoles of Ca\(^{++}\) per mg of mitochondrial protein. This amount probably represents the saturation of fixed anionic charges in the mitochondrial membranes; however, when phosphate is present, much more Ca\(^{++}\) can be taken up, since phosphate penetrates into the mitochondria and removes Ca\(^{++}\) as insoluble salt. The formation of Ca\(^{++}\)-phosphate precipitates inside the mitochondria has been documented (5).