MEETINGS

BIOCHEMISTRY OF MITOCHONDRIA

A COLLOQUIUM on the biochemistry of mitochondria was included as part of the third meeting of the Federation of European Biochemical Societies, which was organized in Warsaw during April 4–7, 1966. The colloquium was arranged by Prof. E. C. Slater (Amsterdam) and organized by Dr. Z. Kaniuga and Dr. L. Wojtczak (Warsaw). Seven invited addresses were included and delivered by B. Chance (Philadelphia), J. B. Chappell (Bristol), L. Ernster (Stockholm), M. Klingenberg (Marburg), H. A. Krebs (Oxford), P. Mitchell (Glynn Research Laboratories, Bodmin) and E. C. Slater (Amsterdam), together with eighty-one short communications by research workers from seventeen countries. Although almost all current problems of mitochondrial biochemistry were discussed, the invited addresses and most of the short communications were concerned with the following topics: (1) the structure and function of the respiratory chain; (2) the mechanism of energy conservation; (3) transport mechanisms in mitochondria; (4) the regulation of substrate utilization; (5) activation and oxidation of fatty acids; (6) metabolic interrelationships between mitochondria and the cytoplasm.

Immediately after the Federation's meeting a "closed" symposium was held in Warsaw during April 8–9. This was organized by the departments of biochemistry of the Universities of Amsterdam and Warsaw and of the Nencki Institute of Experimental Biology in Warsaw. The symposium, which was attended by sixty-five invited scientists from fourteen countries, was devoted to discussions of data already presented during the Federation's colloquium. The following six topics were discussed: (1) the place of ubiquinone and cytochrome *b* in the respiratory chain; (2) the chemiosmotic theory of oxidative phosphorylation; (3) uptake of cations by mitochondria; (4) the chemical coupling theory of oxidative phosphorylation; (5) regulatory mechanisms of substrate utilization; (6) oxidation and activation of fatty acids.

The present report is concerned with both meetings.

Two alternative theories dealing with the role and the position of ubiquinone in mitochondrial respiration were proposed by M. Klingenberg (Marburg) and E. R. Redfearn (Leicester), respectively. M. Klingenberg, in his invited address, presented several lines of evidence in favour of the view that ubiquinone is located on the main pathway of electron transport, and that it acts as a common pool for reducing equivalents from various flavoproteins. This was supported by data on the redox state of ubiquinone, compared with nicotinamide-adenine dinucleotide and cytochromes, for both forward and reversed electron transfer, and by studies of the kinetic of either the reduction of ubiquinone after substrates have been added to the terminally inhibited respiratory chain, or its oxidation after oxygen has been added in the anaerobic state. E. R. Redfearn postulated the existence of a branching pool of ubiquinone in the respiratory chain. Related problems concerning the place of cytochrome *b* were not discussed in detail, presumably because of the lack of sufficient new experimental data.

As E. C. Slater pointed out in his introductory address, three theories have been proposed for the energy coupling mechanism in mitochondria: (i) the chemical coupling theory; (ii) the concept of phosphorylation driven by proton transport (proposed by P. Mitchell); (iii) the concept of conformation changes in specific proteins (proposed by P. Boyer). Lively discussions of both the first two theories took place at the colloquium and the "closed" symposium. P. Mitchell presented new experimental evidence in favour of his concept. He postulated that both the *p*H changes produced by submitochondrial particles catalysing forward and reverse electron transport, and the burst of proton ejection after a rapid transition from the anaerobic to the aerobic states support the concept that adenosine triphosphate is synthesized by a mechanism involving the ejection of protons and which is intimately connected with the respiratory chain. On the other hand, B. Chance, J. B. Chappell and J. M. Tager presented evidence that proton transport is a secondary effect of the conservation of energy. The basic differences between these two theories were depicted by E. C. Slater in the following scheme:

CHEMICAL COUPLING THEORY

Respiratory chain → high-energy intermediate ⇌ ATP

⇅

cation uptake = H^+ production

CHEMIOSMOTIC THEORY

Respiratory chain → H^+ production ⇌ ATP

↓

cation uptake

A new concept of the action of arsenate on the energy-coupling mechanism was proposed by L. Ernster. He postulated the formation of a relatively stable arsenylated derivative of a high energy intermediate.

Ion transport in mitochondria was extensively discussed by J. B. Chappell, B. Chance, E. Carafoli (Modena), G. F. Azzone (Padua) and A. Azzi (Padua). The main topic in the discussion of cation transport was the stoichiometry (or its lack) between the calcium and oxygen taken up by, and the protons ejected from, mitochondria.

Of considerable importance for a better understanding of the utilization of substrate in mitochondria are the problems of anion transport. J. B. Chappell classified anions (including respiratory substrates) into four groups: (1) those which easily penetrate mitochondrial membranes, for example phosphate and arsenate; (2) those which penetrate mitochondrial membranes only in the presence of phosphate (for example, D- and L-malate, succinate and *meso*-tartrate); (3) those which penetrate mitochondrial membranes in the presence of phosphate and L-malate (for example, citrate); (4) those which are unable to penetrate the mitochondrial membrane, such as chloride ions and fumarate. He also postulated the existence of specific carriers for these different groups of penetrants, as did E. J. de Haan (Amsterdam) for α-oxoglutarate.

Another factor which controls the citric acid cycle is oxaloacetate. Its effect on the oxidation of succinate and the factors controlling the level of oxaloacetate itself were discussed by A. B. Wojtczak (Warsaw), A. M. Roberton (Oxford) and S. Papa (Bari).

New concepts on the activation and oxidation of fatty acids were discussed both at the colloquium and at the "closed" meeting. The group at the University of Bristol working under P. B. Garland was represented at the meetings by D. Shepherd and D. W. Yates. The essential point of their theory is that an intramitochondrial pool of coenzyme *A* involved in the β-oxidation of fatty acids can be acylated only by acyl-carnitine formed either extramitochondrially or intramitochondrially. On the other hand, S. G. van den Bergh presented evidence in favour of his view that carnitine is not involved in the normal pathway of fatty acid oxidation.

Sir Hans Krebs dealt with the problem of the transport of reducing equivalents between mitochondria and the cytoplasm. He showed that the reduced nicotinamide-adenine dinucleotide which is required in the cytoplasm for glucogenesis is formed primarily within the mitochondria and is transferred to the cytoplasm by way of an oxaloacetate-malate system. The same system, working in the reverse direction, transports reducing equivalents, which are produced during glycolysis, from the cytoplasm to mitochondria.

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