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Cooperation of Mitochondrial and Cytoplasmic Protein Synthesis in the Formation of the Mitochondrial Membrane

Mitochondrial and cytoplasmic ribosomes contribute to the biogenesis of mitochondrial membranes. The two types of ribosomes have been shown to be different with respect to electron microscopic structure, sedimentation properties, protein and RNA composition and immunological properties[1-3].

Polypeptides synthesized on mitochondrial ribosomes are integrated into the inner mitochondrial membrane, thus contributing ca. 15% of the total inner membrane protein. The other proteins of the inner membrane and those of the outer mitochondrial membrane are made by cytoplasmic ribosomes[4].

On the level of individual membrane proteins, the two types of ribosomes cooperate in the formation of cytochrome *c* oxidase (EC 1.9.3.1) and of oligomycin-sensitive ATPase (EC 3.6.1.3)[5-8]. For cytochrome *b* a cooperation is also discussed[9]. The best studied example is cytochrome oxidase, for which it is shown that three polypeptide subunits of the complex enzyme are translated on mitochondrial ribosomes and four subunits on cytoplasmic ribosomes[6,10].

The application of selective inhibitors of ribosomal function, e.g. cycloheximide for cytoplasmic ribosomes and chloramphenicol for mitochondrial ribosomes, has turned out to be useful in studies on the origin of subunits and on their assembly to the complex enzyme[11,12]. Experiments with isolated mitochondria to study the formation of cytochrome oxidase in a reconstituted system are in an initial stage (A. v. Rücker, S. Werner and W. Neupert, unpublished results).

The regulation mechanisms which guarantee the coordinated synthesis of membrane components on the two types of ribosomes are for the most part unknown. Experiments with *Neurospora* have shown that in the presence of chloramphenicol cytoplasmic protein synthesis continues and gives rise to even higher cellular concentrations of several mitochondrial components (e.g. cytochrome *c*). On the other hand, in cells treated with cycloheximide, the rate of amino acid incorporation into mitochondrial membrane protein decreases in an exponential way with a $t_{1/2}$ of ca. 10 min. However, the biosynthetic activity of mitochondrial ribosomes remains at a high level for several hours, as measured by the amount of nascent peptide chains on the ribosomes and by the rate of chain elongation. This indicates that the mitochondrial membrane has a limited number of binding sites for newly formed polypeptides of mitochondrial origin provided by polypeptides of cytoplasmic origin. If the system is out of balance, polypeptides which cannot be integrated into the membrane may be subject to immediate degradation. Specific degradation of newly made polypeptides can be demonstrated in isolated mitochondria.

A mechanism for the regulation of cytoplasmic-mitochondrial cooperation is proposed, in which the nucleus controls the activity of mitochondrial protein synthesis via the synthesis (and possibly turnover) of the components of the mitochondrial transcription and translation machinery. Specific degrading enzymes may be responsible for a fine control.

The number of mitochondrially formed polypeptides which can be attributed to definite membrane components is 5 or 6. The size of the mitochondrial genome (at least in higher eucaryotes) points to a maximal number of 10 – 15 polypeptides. However, the possibility of messenger RNA import into mitochondria is not excluded. The question remains to be answered why for a few mitochondrial membrane enzymes two systems of transcription and translation have to cooperate. In this context, the following observations are important:

1. Until now, mitochondrial translation products were only found in membrane components which are involved in oxidative phosphorylation. 2. Mitochondrial translation products have a strongly hydrophobic character. For example, a mitochondrially made polypeptide with a molecular weight of ca. 8500 was isolated from the nuclear mutant *cni-1* of *Neurospora* which has an extremely high proportion of nonpolar amino acids (polarity 0.24) (R. Michel et al., unpublished results). This polypeptide is insoluble in water but soluble in chloroform/methanol. These observations led to the hypothesis that ribosomes are necessary inside the mitochondrial membrane to synthesize polypeptides which, because of their hydrophobic character, cannot be transported from the cytosol to the inner mitochondrial membrane and which are essential for oxidative phosphorylation[13].

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[1] Borst, P. & Grivell, L. A. (1971) *FEBS Lett.* **13**, 73 – 88.

[2] Kleinow, W., Neupert, W. & Miller, F. (1974) *J. Cell Biol.*, in press.

[3] Hallermayer, G. & Neupert, W. (1974) *FEBS Lett.* **41**, 264 – 268.

[4] Neupert, W. & Ludwig, G. D. (1971) *Eur. J. Biochem.* **19**, 523 – 532.

[5] Weiss, H., Sebald, W. & Bücher, Th. (1971) *Eur. J. Biochem.* **22**, 19 – 26.

[6] Mason, T. L. & Schatz, G. (1973) *J. Biol. Chem.* **248**, 1355–1360.
[7] Tzagoloff, A., Rubin, M. S. & Sierra, M. F. (1973) *Biochim. Biophys. Acta* **301**, 71–104.
[8] Jackl, G. & Sebald, W. (1974) *this J.* **355**, 1211–1212.
[9] Weiss, H. & Ziganke, B. (1974) *Eur. J. Biochem.* **41**, 63–71.
[10] Sebald, W., Machleidt, W. & Otto, J. (1973) *Eur. J. Biochem.* **38**, 311–324.
[11] Sebald, W., Weiss, H. & Jackl, G. (1972) *Eur. J. Biochem.* **30**, 413–417.
[12] Werner, S. (1974) *Eur. J. Biochem.* **43**, 39–48.
[13] Michel, R. & Neupert, W. (1973) *Eur. J. Biochem.* **36**, 53–67.

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