The Mitochondrial Transcription Factor and the Interaction on Cell Aging

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Mitochondrial DNA:

- The mitochondria are not completely autonomous and require nuclear encoded proteins for their optimal function.

- 37 genes

- 16,569 base pairs (3.3 billion in nucleus)

- 13 genes encode protein subunits of mitochondrial respiratory complex

- 22 tRNA

- 2 rRNA


<table>
<thead>
<tr>
<th>Complex I</th>
<th>Complex III</th>
<th>Complex II</th>
<th>Complex IV</th>
<th>Complex V</th>
</tr>
</thead>
<tbody>
<tr>
<td>mtDNA</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>10</td>
<td>4</td>
<td>10</td>
</tr>
</tbody>
</table>

Diagram showing the electron transport chain and ATP synthesis:
- NADH
- Succinate
- $\text{H}_2\text{O}$
- $1/2\text{O}_2$
- ADP + $\text{P}_i$
- ATP
- $\text{H}^+$
- Cyt. c
- (Fe-S)
- b
- $\text{C}_1$
- Q
- $\text{H}^+$
- $\text{F}_0$
- $\text{F}_1$
- $\text{H}^+$

Physiol Rev. 2008 Apr;88(2):611-38. doi: 10.1152.
Metabolic Syndrome

A major health challenge of the twenty-first century.

Molecular Understanding Aging

How it is regulated by diet

Many authors say that ageing-related diseases are linked to mitochondrial disturbance; for example:

- Mitochondrial dysfunction
- High ROS and damage mtDNA

Many authors say that ageing-related diseases are linked to mitochondrial disturbance; for example:

- Alterations of mitochondrial functionality

Many authors say that ageing-related diseases are linked to mitochondrial disturbance; for example:

- Alteration of the energy capacities of the cell
- Alteration on OXPHO and mtDNA mutation.

Mitochondria as therapeutic targets for cancer stem cells.
Song IS, Jeong JY, Jeong SH, Kim HK, Ko KS, Rhee BD, Kim N, Han J
Many authors say that ageing-related diseases are linked to mitochondrial disturbance; for example:

- Diminished energy supply
- ATP synthase capacity reduced

Congestive heart failure

Regulation of mitochondrial ATP synthase in cardiac pathophysiology
Qinqiang Long Kevin Yang, Qinglin Yang
Mitochondrial Transcription Factor:

- PGC-1α
- TFAM
- NRF-1
- PPAR-α
- ERR-α
Physiol Rev. 2008 Apr; 88(2): 611-38. doi: 10.1152.
Previous studies show that PQQ influences PGC-1α activity, which is a major mechanism for the regulation of mitochondrial biogenesis in mouse hepatocytes.
A

Relative activation

PQQ uM 0 15 30
NRF-1

NRF-2

B

Relative expression

PQQ uM 0 30
Tfam

TFB1M

TFB2M

Supplementation with nicotinamide riboside 400mg/kg/day significantly increased mitochondrial biogenesis in muscle and brown tissue and prevented ultrastructural abnormalities in mitochondrial proteins and mtDNA deletion.

Effective treatment of mitochondrial myopathy by nicotinamide riboside, a vitamin B3.
Khan NA, Auranen M, Paetau I, Pirinen E, Euro L, Forsstron S, Pasila L, Velagapudi V, Carrol CJ, Auwex J, Soumalainen A
Nutritional Supplement on Mitochondrial Biogenesis

Ubiquinol

Ubiquinol may enhance mitochondrial activity by increasing levels of SIRT1, PGC-1α, and SIRT3 in mouse livers.
Other factors that influence mitochondrial biogenesis

- Caloric restriction
- Physical activity
- Resveratrol
- Quercetin
- Alpha Lipoic Acid
- Acetyl L-carnitine
Thank you!

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