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**Building a complex complex: assembly of mitochondrial respiratory chain complex I**

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**Abstract**

Mitochondrial complex I is the primary entry point for electrons into the electron transport chain, required for the bulk of cellular ATP production via oxidative phosphorylation.

Complex I consists of 45 subunits, which are encoded by both nuclear and mitochondrial DNA. Currently, at least 15 assembly factors are known to be required for the complete maturation of complex I. Mutations in the genes encoding subunits and assembly factors leads to complex I deficiency, which can manifest as mitochondrial disease. The current model of complex I assembly suggests that the enzyme is built by the association of a set of smaller intermediate modules containing specific conserved core subunits and additional accessory subunits. Each module must converge in a spatially and temporally orchestrated fashion to allow assembly of the mature holoenzyme to occur. This review outlines the current understanding of complex I biogenesis, with an emphasis on the assembly factors that facilitate the building of this architectural giant.

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