INTERDEPENDENCE OF OXIDATIVE PHOSPHORYLATION COMPONENTS FOR ASSEMBLY AND STABILITY

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The mitochondrial Oxidative Phosphorylation (OXPHOS) system is composed of five multisubunit complexes (Complexes I-V) and two mobile, single molecule electron carriers (coenzyme Q10 and cytochrome *c*). In the last few years, it became clear that these components interact not only functionally, but also physically, forming "respirasomes". This supercomplex arrangement likely increases the efficiency of electron transport between complexes. To better understand the requirements for assembly and stability of OXPHOS complexes, we have studied cell lines lacking either Complex III, Complex IV or cytochrome *c* We found that cells lacking complex III due to a nonsense mutation in cytochrome *b* had very low levels of Complex I. Likewise, cells lacking Complex IV due to the conditional knockout of *COX10*, a gene participating in the synthesis of heme *a*, also had Complex I markedly reduced. Finally, cells with a conditionally deleted cytochrome *c* lacked both Complexes IV and I. Pulse-chase experiments indicate that this interdependence occurs at the level of assembly of the individual complexes. These data demonstrates that OXPHOS complex assembly is an intricate process and supports the view that respirasomes are the main functional units of OXPHOS.

Key words: oxidative phosphorylation, mitochondria, supercomplex, cytochrome c, complex I.