

Regulation of cytochrome *c* peroxidase activity by nitric oxide and laser irradiation

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It is well known that apoptosis can be induced by activation of so-called “death receptors” or multiple apoptotic factors, that leads to release of cytochrome *c* from mitochondria [1-2]. This event is considered to be a “point of no return” in apoptosis. One of the most important events in the development of apoptosis is the enhancement of cytochrome *c* peroxidase activity upon its interaction with cardiolipin, which modifies the active center of cytochrome *c* [3-5]. In the present work, the effects of nitric oxide on the cytochrome *c* peroxidase activity when cytochrome *c* is bound to cardiolipin have been investigated. It was observed that cytochrome *c* peroxidase activity, distinctly increased due to the presence of anionic lipids, can be completely suppressed by nitric oxide. At the same time, nitrosyl complexes of cytochrome *c*, produced in the interaction with nitric oxide, demonstrated sensitivity to He-Cd laser radiation (441 nm), and were photolyzed during irradiation. This decomposition led to restoration of cytochrome *c* peroxidase activity. Finally, it can be concluded that nitric oxide and laser irradiation may serve as effective instruments for regulating the peroxidase activity of cytochrome *c*, and, probably, apoptosis.

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- [1] Tyurin VA, Tyurina YY, Osipov AN, Belikova NA, Basova LV, Kapralov AA, Bayir H, Kagan VE. Interactions of cardiolipin and lyso-cardiolipins with cytochrome *c* and tBid: conflict or assistance in apoptosis// *Cell Death Differ.* 14, 4 (2007). Pp. :872-875
- [2] Osipov AN, Stepanov GO, Vladimirov YA, Kozlov AV, Kagan VE. Regulation of cytochrome C peroxidase activity by nitric oxide and laser irradiation// *Biochemistry (Mosc)* 71, 10 (2006). Pp. 1128-32.
- [3] Belikova NA, Vladimirov YA, Osipov AN, Kapralov AA, Tyurin VA, Potapovich MV, Basova LV, Peterson J, Kurnikov IV, Kagan VE. Peroxidase activity and structural transitions of cytochrome *c* bound to cardiolipin-containing membranes// *Biochemistry.* 45, 15 (2006). Pp. 4998-5009.
- [4] Vlasova II, Tyurin VA, Kapralov AA, Kurnikov IV, Osipov AN, Potapovich MV, Stoyanovsky DA, Kagan VE. Nitric oxide inhibits peroxidase activity of cytochrome *c*.cardiolipin complex and blocks cardiolipin oxidation// *J Biol Chem.* 281, 21 (2006). Pp. 14554-62.
- [5] Kagan VE, Tyurin VA, Jiang J, Tyurina YY, Ritov VB, Amoscato AA, Osipov AN, Belikova NA, Kapralov AA, Kini V, Vlasova II, Zhao Q, Zou M, Di P., Svistunenko DA, Kurnikov IV, Borisenko GG. Cytochrome *c* acts as a cardiolipin oxygenase required for release of proapoptotic factors// *Nat Chem Biol.* 1, 4 (2005). Pp. 223-32.