Biointeractomic scaffold hovering over apoptotic cytochrome c

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The role of cytochrome c in apoptosis is well-established, but its participation in signaling pathways in vivo remains still poorly understood due to its essential role in mitochondrial respiration. Upon an apoptotic stimulus, cytochrome c is released from the mitochondria into the cytosol, where it interacts with APAF1 and leads to apoptosome formation and caspases activation [1]. Other unexplored functions of cytochrome c in apoptosis have been proposed based on the resistance that cytochrome c knockout mutants exhibit to agents that activate the cytochrome c-independent apoptotic pathway [2]. To gain further insight into the involvement of cytochrome c in apoptosis, here we have used human cytochrome c as bait in an affinity chromatography-based proteomic approach aimed at identifying new putative cytochrome c partners.

The in vivo interaction and localization of the complexes formed during apoptosis by cytochrome c with its novel partners identified by proteomics have been further afforded by Bimolecular Fluorescence Complementation. Our results suggest that cytochrome c interacts with an ample set of pro-survival and anti-apoptotic proteins, thereby interfering with cell survival signaling pathways and unlocking apoptosis. Thus, extra-mitochondrial cytochrome c seems to be responsible for avoiding the spatial and temporal co-existence of pro- and anti-apoptotic signals in cells, so letting the appropriate progress of the apoptotic program.
