Mitochondrial alterations in apoptosis at the single molecule level

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A.J. Garcia Saez[I]

[I]University of Tübingen, Tübingen, Germany

The permeabilization of the mitochondrial outer membrane (MOM) is a key step in the regulation of apoptosis, a form of programmed cell death. Bax is a proapoptotic member of the Bcl-2 family that, during apoptosis, accumulates at discrete sites in the MOM, called apoptotic foci, to mediate its permeabilization. We showed that this process requires a conformational change in Bax, which partially opens its pore-forming hairpin, and is accompanied by self-assembly into multiple oligomeric species based on dimer units. This results in the opening of membrane pores, which can be fully or partially delineated by Bax molecules. Based on this, we proposed a new models for the molecular mechanism of Bax in MOM permeabilization. We also provide new insight into the interplay between Bax and other components of the apoptotic foci, which form complex macromolecular assemblies to orchestrate this key apoptotic event.