Modulation of Bax by Protein Kinase C in yeast

Rui D. Silva[1], Stephén Manon[2], Jorge Gonçalves [3a], Lucília Saraiva [3b] and Manuela Côrte-Real[1]

[1]Molecular and Environmental Biology Centre, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal; [2]CNRS, UMR5095, Université de Bordeaux 2, 1 Rue Camille Saint-Saëns, 33077 Bordeaux, France; [3]REQUIMTE/CEQUP, Laboratório de Farmacologia[a] e Microbiologia[b], Faculdade de Farmácia, Universidade do Porto, Rua Aníbal Cunha, 4050-030 Porto, Portugal.

A crucial feature of mammalian apoptosis is the permeabilization of mitochondria, and the release of apoptogenic factors that leads to activation of proteases responsible for cell death. This permeabilization is regulated by the Bcl-2 protein family, namely the pro-apoptotic members Bax and Bak. Despite the importance of these proteins, the mechanisms by which they are regulated are not fully understood. Protein kinase C (PKC) is a family of serine/threonine kinases with at least 12 isoforms that have been implicated in the regulation of members of the Bcl-2 family proteins. It is now clear that the different PKC isoforms have different roles in mammalian apoptosis regulation. However, the study of the role of each isoform has been hampered by the co-existence of several isoforms in the same cell. Yeast has been used as a model to study the role Bcl-2 family proteins in apoptosis and to screen for new PKC modulators. Recently, we showed in yeast that distinct PKC isoforms can differently modulate Bcl-xL anti-apoptotic effect and that PKCα enhances translocation and insertion of Bax c-myc into the outer mitochondrial membrane. Following these results we set out to exploit this model system to study the regulation of Baxα by different PKC isoforms, namely PKCα, δ, ε and ζ.

We found that PKC isoforms regulate differently Baxα phosphorylation, activation and translocation to the outer mitochondrial membrane. Together, our results give a mechanistic insight on apoptosis regulation by PKC isoforms and provide a proof of principle of yeast as an important tool for this study.

This work was supported by the FCT project PTDC/BIA-BCM/69448/2006.