

Poster Presentation

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Structural Insights into Bak Activation and Oligomerisation

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Apoptotic stimuli activate and oligomerise the pro-apoptotic proteins Bak and Bax resulting in mitochondrial outer membrane permeabilisation and subsequent cell death. This activation can occur when certain BH3-only proteins directly interact with Bak and Bax. A recent crystal structure by Czabotar et al. (2013) revealed a novel conformational change for Bax upon activation by BH3-only peptides. Distinguishing characteristics of BH3-only proteins capable of directly activating Bax were also elucidated. Here we describe complementary studies on the related protein Bak. We identify specific BH3-only peptides capable of inducing Bak dimerisation and describe crystal structures that provide key insights into Bak activation and oligomerisation. These structures demonstrate that Bak undergoes similar conformational changes upon activation to those observed with Bax. Altogether our results confirm an analogous mechanism for activation and dimerization of Bak and Bax in response to BH3-only peptides.

[1] Czabotar, P.E., Westphal, D., Dewson, G., Ma, S., Hockings, C., Fairlie, W.D., Lee, E.F., Yao, S., Robin, A.Y., Smith, B.J., Huang, D.C.S., Kluck, R.M., Adams, J.M., and Colman, P.M., *Structural Transitions Activating Bax for Apoptosis*. *Cell*, 2013. 152 (3)

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