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Experimental evidence for a ββα-Me-finger nuclease motif to represent the active site of the caspase-activated DNase

Scholz S., Korn C., Bujnicki J., Gimadutdinow O., Pingoud A., Meiss G.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

The caspase-activated DNase (CAD) is an important nuclease involved in apoptotic DNA degradation. Results of a sequence comparison of CAD proteins with ββα-Me-finger nucleases in conjunction with a mutational and chemical modification analysis suggest that CAD proteins constitute a new family of ββα-Me-finger nucleases. Nucleases of this family have widely different functions but are characterized by a common active-site fold and similar catalytic mechanisms. According to our results and comparisons with related nucleases, the active site of CAD displays features that partly resemble those of the colicin E9 and partly those of the T4 endonuclease VII active sites. We suggest that the catalytic mechanism of CAD involves a conserved histidine residue, acting as a general base, and another histidine as well as an aspartic acid residue required for cofactor binding. Our findings provide a first insight into the likely active-site structure and catalytic mechanism of a nuclease involved in the degradation of chromosomal DNA during programmed cell death.

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