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Letter to the Editor

Sequence as well as functional similarity for DIABLO/Smac and Grim, Reaper and Hid?

Dear Editor,

DIABLO/Smac is a mammalian protein that promotes apoptosis by binding to inhibitor of apoptosis (IAP) proteins.[1,2] Chai *et al*.[3] and Srinivasula *et al*.[4] have shown that the N-terminal 4 amino acids or processed DIABLO/Smac are necessary, and the first 7 amino acids are sufficient, for this interaction, just as the N-terminal residues of the insect pro-apoptotic proteins Grim, Reaper and Hid are required for the interaction with insect IAPs.[5,6]

Sequence similarity among Grim, Reaper and Hid is restricted to their N-terminal 14 amino acids.[7] Comparison of their N-terminal sequences with those of processed DIABLO/Smac reveals it also bears similar residues and these residues are conserved in both the bovine and porcine proteins (Figure 1).

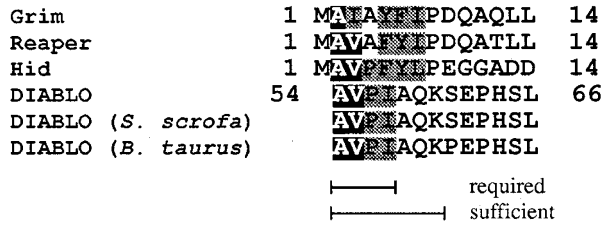

Figure 1 Comparison of the N-terminal sequences of pro-apoptotic mammalian and insect IAP binding proteins. Identical residues are highlighted in black, conserved residues in grey. Residues of DIABLO/Smac that are: (a) required for the full-length protein to antagonise XIAP inhibition of caspases; and (b) sufficient as a peptide to antagonise XIAP function are indicated.[3,4]

The sequences and functions of DIABLO/Smac and the insect apoptosis inducing proteins suggests they are structural as well as functional homologues. It will be interesting to determine whether they interact with analogous sites on mammalian and insect IAPs, and whether, for example, they can compete for binding sites.

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