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## Forward

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Rumble JM, Duckett CS. 2008. Cell Science At A Glance: Diverse functions within the IAP family. *J Cell Sci*, 121:3505-3507.

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## List of Abbreviations

AICD, activation-induced cell death  
Apaf, apoptotic protease-activating factor  
APC, antigen presenting cell  
ASK, apoptosis signal-regulating kinase 1  
BAL, broncho-alveolar lavage  
BIR, baculovirus IAP repeat  
*c*, cytochrome *c*  
C-1, caspase-1  
C-3, caspase-3  
C-8, caspase-8  
C-9, caspase-9  
c-FLIP, cellular FLICE-inhibitory protein  
c-IAP, cellular IAP  
CARD, caspase-associated recruitment domain  
CHX, cycloheximide  
COMMD1, copper metabolism (Murr1) domain-containing 1  
CYLD, cylindromatosis  
DD, death domain  
DISC, death-inducing signaling complex  
DN, double negative  
DP, double positive  
EBV, Epstein-Barr Virus  
ELISA, enzyme-linked immunosorbent assay  
FADD, Fas-associated death domain protein  
GAPDH,  
IAP, inhibitor of apoptosis  
IBM, IAP binding motif  
I $\kappa$ B $\alpha$ , inhibitor of  $\kappa$ B  
IKK, I $\kappa$ B kinase  
ILP-2, IAP-like protein 2  
INCENP, inner centromere protein  
JNK, Jun N-terminal kinase  
KO, knockout  
LPS, lipopolysaccharide  
LRR, leucine-rich repeat  
MAD1, mitotic arrest deficient 1  
MAX, myc-associated factor X  
MAP3K, mitogen-activated kinase kinase kinase  
MEF, murine embryonic fibroblast



MHC, major histocompatibility complex  
MKK, mitogen-activated kinase kinase  
ML-IAP, melanoma IAP  
MYC, avian myelocytomatosis viral oncogene homolog  
NAIP, neuronal apoptosis inhibitory protein  
NF- $\kappa$ B, nuclear factor- $\kappa$ B  
NIK, NF- $\kappa$ B inducing kinase  
NKT, natural killer T (cell)  
NOD, nucleotide oligomerization domain  
PAI-1, plasminogen activator inhibitor 1  
PNA, peanut agglutinin  
RING, really interesting new gene  
RIP1, receptor interacting protein 1  
RT-PCR, reverse transcription polymerase chain reaction  
SAP, SLAM-associated protein  
SLAM, second lymphocytic activation molecule  
Smac, second mitochondrial activator of caspases  
SRBC, sheep red blood cell  
TAB, TAK1-binding protein  
TAK1, TGF- $\beta$  activated kinase 1  
TCR, T cell receptor  
TGF- $\beta$ , transforming growth factor- $\beta$   
TNF, tumor-necrosis factor  
TNFR, TNF receptor  
TRADD, TNFR1-associated death domain protein  
TRAF2, TNFR associated factor 2  
TRAIL, TNF-related apoptosis-inducing ligand  
UBC, ubiquitin conjugation  
WT, wild type  
XIAP, X-linked IAP  
XLP, X-linked Lymphoproliferative Syndrome

## Abstract

Human X-linked inhibitor of apoptosis, or XIAP, is a member of the IAP family of proteins that has been shown to be a potent regulator of the cell death pathway, and has also been implicated as a mediator of other signal transduction pathways. Mutations in XIAP have been identified as a cause of X-linked lymphoproliferative disorder (XLP), a rare but fatal disease associated with aberrant response to Epstein-Barr virus (EBV). Surprisingly, mice that lack XIAP have not thus far been shown to have any major defects in apoptotic signaling, though JNK and NF- $\kappa$ B-dependent transcription have been implicated in defective responses to bacteria. The studies presented here show that XIAP is not a universal mediator of TGF- $\beta$  signaling or NF- $\kappa$ B-dependent transcription. However, cells derived from *Xiap*-null mice exhibit increased sensitivity to apoptotic stimuli over their wildtype counterparts, but interestingly only under highly specific experimental conditions. A closely related family member, c-IAP2, is also shown to be protective from similar apoptotic stimuli, while another, c-IAP1, is not observed to protect cells from apoptosis. Our data also demonstrate that XIAP does not cause XLP in the same manner as another protein mutated in the same disease, SAP. Cells from *Xiap*-null mice respond differently to a murine  $\gamma$ -herpesvirus closely related to EBV, which may explain the role of XIAP in XLP. These studies will not only shed light on the function of XIAP in the regulation of the immune system, but will also help to understand the pathogenesis of XLP.