Fas death receptor signalling: roles of Bid and XIAP.

Abstract:
Fas (also called CD95 or APO-1), a member of a subgroup of the tumour necrosis factor receptor superfamily that contain an intracellular death domain, can initiate apoptosis signalling and has a critical role in the regulation of the immune system. Fas-induced apoptosis requires recruitment and activation of the initiator caspase, caspase-8 (in humans also caspase-10), within the death-inducing signalling complex. In so-called type 1 cells, proteolytic activation of effector caspases (-3 and -7) by caspase-8 suffices for efficient apoptosis induction. In so-called type 2 cells, however, killing requires amplification of the caspase cascade. This can be achieved through caspase-8-mediated proteolytic activation of the pro-apoptotic Bcl-2 homology domain (BH)3-only protein BH3-interacting domain death agonist (Bid), which then causes mitochondrial outer membrane permeabilisation. This in turn leads to mitochondrial release of apoptogenic proteins, such as cytochrome c and, pertinent for Fas death receptor (DR)-induced apoptosis, Smac/DIABLO (second mitochondria-derived activator of caspase/direct IAP binding protein with low Pi), an antagonist of X-linked inhibitor of apoptosis (XIAP), which imposes a brake on effector caspases. In this review, written in honour of Juerg Tschopp who contributed so much to research on cell death and immunology, we discuss the functions of Bid and XIAP in the control of Fas DR-induced apoptosis signalling, and we speculate on how this knowledge could be exploited to develop novel...
regimes for treatment of cancer.