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Titel des Beitrags:
IAP antagonization promotes inflammatory destruction of vascular endothelium.

Abstract:
In this study, we show for the first time that the therapeutic antagonization of inhibitor of apoptosis proteins (IAPs) inhibits B16 melanoma growth by disrupting tumor vasculature. Specifically, the treatment of mice bearing B16 melanoma with an IAP antagonist compound A (Comp A) inhibits tumor growth not by inducing direct cytotoxicity against B16 cells but rather by a hitherto unrecognized antiangiogenic activity against tumor vessels. Our detailed analysis showed that Comp A treatment induces NF-κB activity in B16 tumor cells and facilitates the production of TNF. In the presence of Comp A, endothelial cells (ECs) become highly susceptible to TNF and undergo apoptotic cell death. Accordingly, the antiangiogenic and growth-attenuating effects of Comp A treatment were completely abolished in TNF-R knockout mice. This novel targeting approach could be of clinical value in controlling pathological neoangiogenesis under inflammatory condition while sparing blood vessels under normal condition.

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