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Titel des Beitrags: Cytosolic DNA triggers mitochondrial apoptosis via DNA damage signaling proteins independently of AIM2 and RNA polymerase III.

Abstract: A key host response to limit microbial spread is the induction of cell death when foreign nucleic acids are sensed within infected cells. In mouse macrophages, transfected DNA or infection with modified vaccinia virus Ankara (MVA) can trigger cell death via the absent in melanoma 2 (AIM2) inflammasome. In this article, we show that nonmyeloid human cell types lacking a functional AIM2 inflammasome still die in response to cytosolic delivery of different DNAs or infection with MVA. This cell death induced by foreign DNA is independent of caspase-8 and carries features of mitochondrial apoptosis: dependence on BAX, APAF-1, and caspase-9. Although it does not require the IFN pathway known to be triggered by infection with MVA or transfected DNA via polymerase III and retinoid acid-induced gene I-like helicases, it shows a strong dependence on components of the DNA damage signaling pathway: cytosolic delivery of DNA or infection with MVA leads to phosphorylation of p53 (serines 15 and 46) and autophosphorylation of ataxia telangiectasia mutated (ATM); depleting p53 or ATM with small interfering RNA or inhibiting the ATM/ATM-related kinase family by caffeine strongly reduces apoptosis. Taken together, our findings suggest that a pathway activating DNA damage signaling plays an important
independent role in detecting intracellular foreign DNA, thereby complementing the induction of IFN and activation of the AIM2 inflammasome.

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