Apoptin-induced cell death is modulated by Bcl-2 family members and is Apaf-1 dependent

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Abstract

Chicken anemia virus (CAV) is the causative agent of chicken infectious anemia, which is primarily an immunosuppressive disease of young chickens, but also affects chickens of all age groups (1). The death of infected cells is caused by Apoptin (VP3), a small 14 kDa virally encoded and proline-rich protein, which has no homologous cellular counterparts (2). Apoptin Selectively induces apoptosis in transformed cell but not in normal cells, thus making it a promising candidate as a novel anticancer therapeutic (3). The authors report that contrary to previous assumptions, Bcl-2 and Bcl-xL inhibit apoptin-induced cell death in several tumor cell lines. In contrast, deficiency of Bax conferred resistance, whereas expression of Bax sensitized cells to apoptin induced death. Cell death induction by apoptin was associated with cytochrome c release from mitochondria as well as with caspase-3 and -7 activation. The protein zVAD-fmk highly protects against apoptin-induced cell death. Apoptosis induced by apoptin required Apaf-1, as immortalized Apaf-1 deficient fibroblasts as well as tumor cells devoid of Apaf-1 were strongly protected. Thus, the results indicate that apoptin-induced apoptosis is not only Bcl-2 and caspase dependent, but also engages an Apaf-1 apoptosome-mediated mitochondrial death pathway.

References