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**Pharmacologic ascorbate induces neuroblastoma cell death by hydrogen peroxide mediated
DNA damage and reduction in cancer cell glycolysis**

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ABSTRACT

An ascorbate-mediated production of oxidative stress has been shown to retard tumor growth. Subsequent glycolysis inhibition has been suggested. Here, we further define the mechanisms relevant to this observation. Ascorbate was cytotoxic to human neuroblastoma cells through the production of H₂O₂, which led to ATP depletion, inhibited GAPDH, and non-apoptotic and non-autophagic cell death. The mechanism of cytotoxicity is different when PARP-dependent DNA repair machinery is active or inhibited. Ascorbate-generated H₂O₂ damaged DNA, activated PARP, depleted NAD⁺, and reduced glycolysis flux. NAD⁺ supplementation prevented ATP depletion and cell death, while treatment with a PARP inhibitor, olaparib, preserved NAD⁺ and

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