Ácido betulínico pode ser eficaz contra o hepatoblastoma: apoptose

Betulinic acid treatment promotes apoptosis in hepatoblastoma cells.

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Source

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Abstract

Hepatoblastoma (HB) represents the most common malignant liver tumor in children with a dismal prognosis for patients with advanced disease. This study provides evidence that the naturally occurring pentacyclic triterpenoid betulinic acid (BA) is highly effective against HB. We demonstrate that BA has a strong cytotoxic effect on HB cells in a dose-dependent manner by impinging on cell viability and causing massive induction of programmed cell death. Apoptotic features including morphological changes, membrane asymmetry and proteolytic cleavage of caspase 3 and poly(ADP-ribose) polymerase were frequently found in BA-treated HB cells, which is suggestive of the mitochondrial intrinsic apoptotic pathway. In contrast, the hepatocellular carcinoma (HCC) cell line HepG2 was resistant to BA treatment. This insensitivity was dependent on the high expression of survival factors, such as Survivin and BCL2. Interestingly, BA treatment led to a significant decrease in expression of the hedgehog target genes GLI1, PTCH1 and IGF2 in HepT3 cells. In conclusion, we demonstrate that BA is capable of inducing apoptosis in HB cells and thereby might be a hopeful new strategy for treating HB, especially those with an activated hedgehog signaling pathway.

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