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Cucurbitacin F as inducer of cell cycle G2/M arrest and apoptosis in human soft tissue sarcoma cells

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Aim of the Study: Soft tissue sarcomas represent a rare group of malignant tumors that frequently exhibit chemotherapeutic resistance and increased metastatic potential. In this study, we evaluated the cytotoxic, apoptosis inducing and cell cycle arresting effects of 25-O-acetyl-23,24-dihydro-cucurbitacin F which has been isolated from leaves and twigs of Quisqualis indica. Q. indica is used in traditional Chinese medicine to treat cancer and related syndromes and also known for its anthelminthic effects.
Material and Methods: The present study investigates the effects of 25-O-acetyl-23,24-dihydro-cucurbitacin F (1) on cell viability, cell cycle distribution, and apoptotic induction of three human sarcoma cell lines of various origins by using the CellTiter 96® AQueous One Solution Cell Proliferation Assay, flow cytometrical experiments, real-time RT-PCR, Western blotting, and the Caspase-Glo® 3/7 Assay
Results: We could show that 1 reduced cell viability in a dose-dependent manner and arrested the cells at the G2/M interface. The accumulation of cells at the G2/M phase resulted in a significant decrease of the cell cycle checkpoint regulators cyclin B1, cyclin A, CDK1, and CDK2. Interestingly, 1 inhibited surviving expression significantly, which functions as a key regulator of mitosis and programmed cell death, and is overexpressed in many tumor types including sarcomas. Moreover, 1 induced apoptosis in liposarcoma and rhabdomyosarcoma cells caspase-3 dependently.
Conclusion: Our data strongly support 1 as a very interesting target for further investigation and development of novel therapeutics in sarcoma research.