The novel curcumin derivative 1g induces mitochondrial and ER-stress-dependent apoptosis in colon cancer cells by induction of ROS production

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Abstract

Background and Purpose A novel curcumin (Cur) derivative 1g can inhibit the proliferation of colon cancer in vitro and in vivo. The purpose of this study was to explore the role of 1g in inducing apoptosis of colon cancer cells, especially mitochondrial apoptosis and endoplasmic reticulum (ER)-stress caused by reactive oxygen species (ROS). Experimental Approach Bioinformatics was used to analyze differentially expressed mrnas. Gene expression was measured by using qRT-PCR and protein expression was measured by using western blotting. Cell apoptosis, cycle, mitochondrial membrane potential and ROS were analyzed by flow cytometry. Experiments on transplanted tumors in animals. Key Results The mechanism of this effect was a change in mitochondrial membrane potential caused by 1g that increased its pro-apoptotic activity. In addition, 1g produced ROS, induced G1 checkpoint blockade, and enhanced ER-stress in colon cancer cells. On the contrary, pretreatment with the ROS scavenging agent N-acetyl-l-cysteine (NAC) inhibited the mitochondrial dysfunction caused by 1g and reversed ER-stress, cell cycle stagnation, and apoptosis. Additionally, pretreatment with the p-PERK inhibitor GSK2606414 significantly reduced ER-stress and reversed the apoptosis induced by colon cancer cells. Conclusion and Implications This study not only found that 1g inherits the safety of Cur and has a more inhibitory effect on colon cancer cells than Cur, but also revealed that excessive production of ROS is one of the mechanisms of anti-tumor action.

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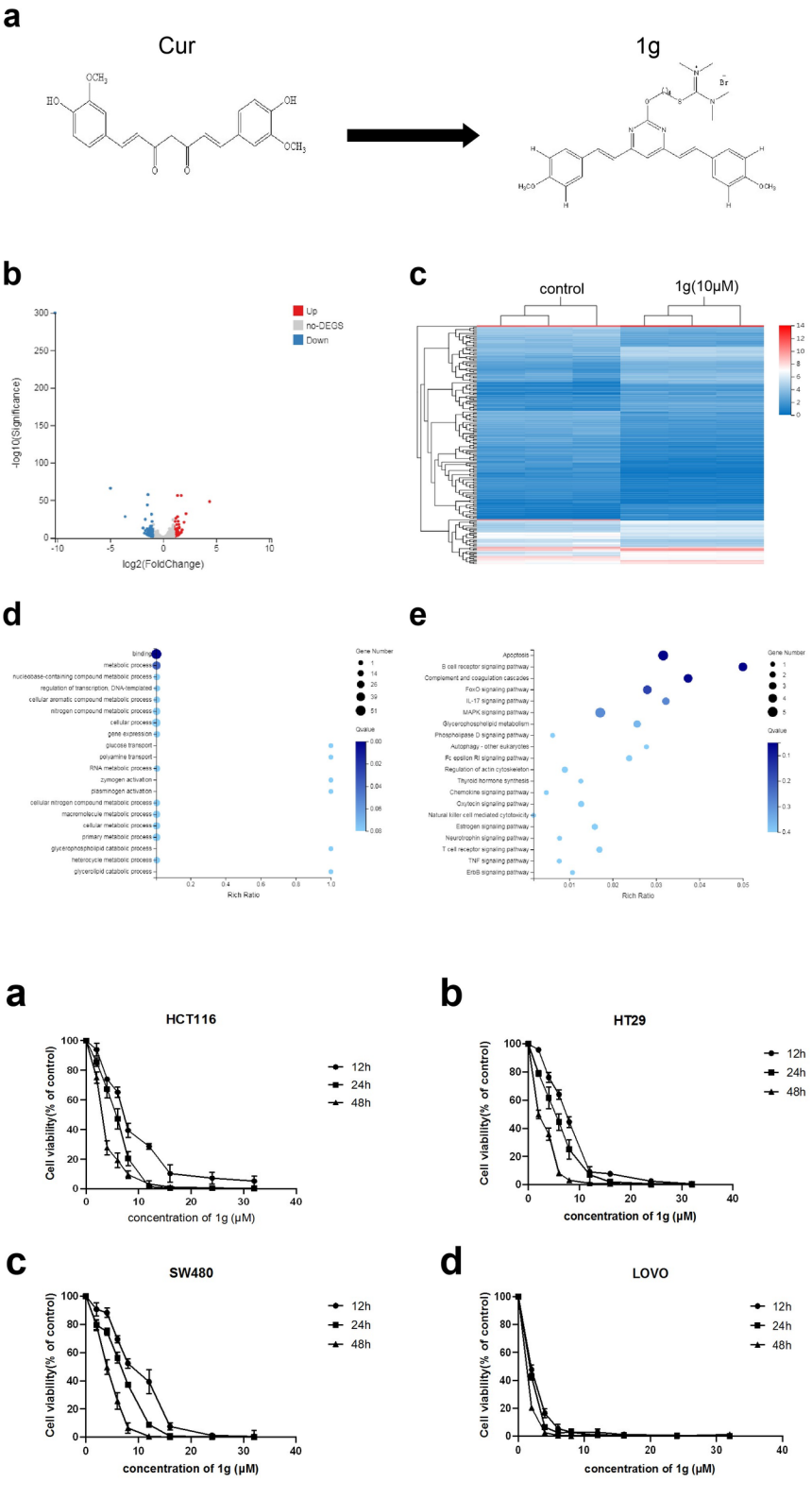

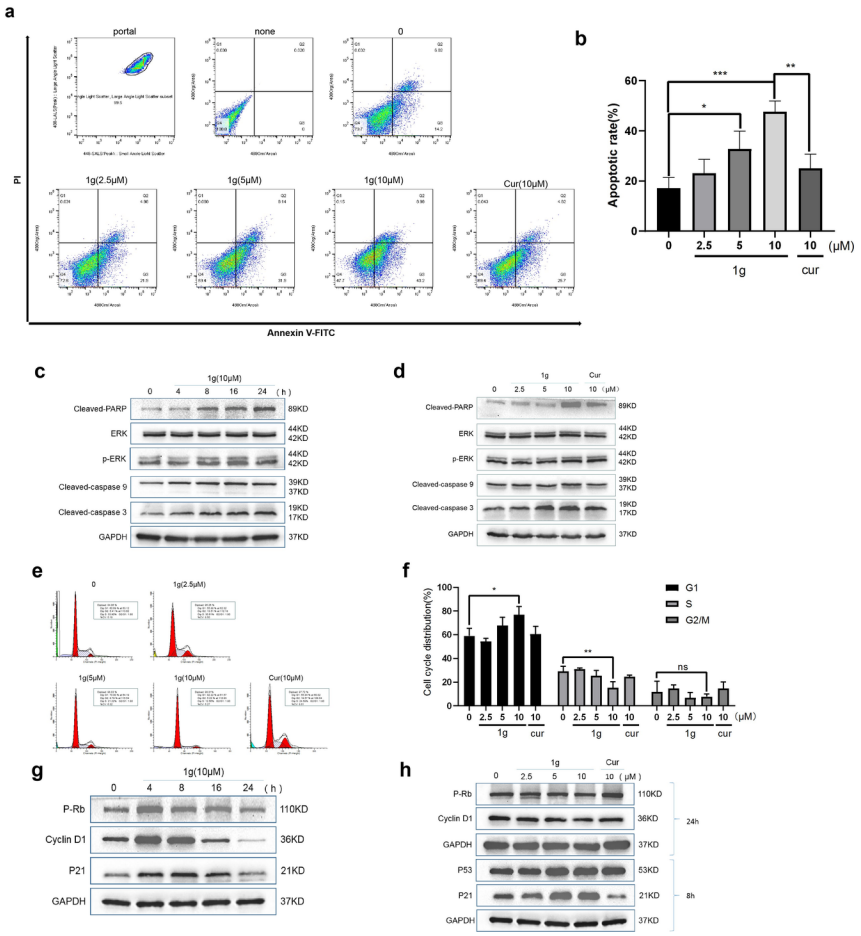

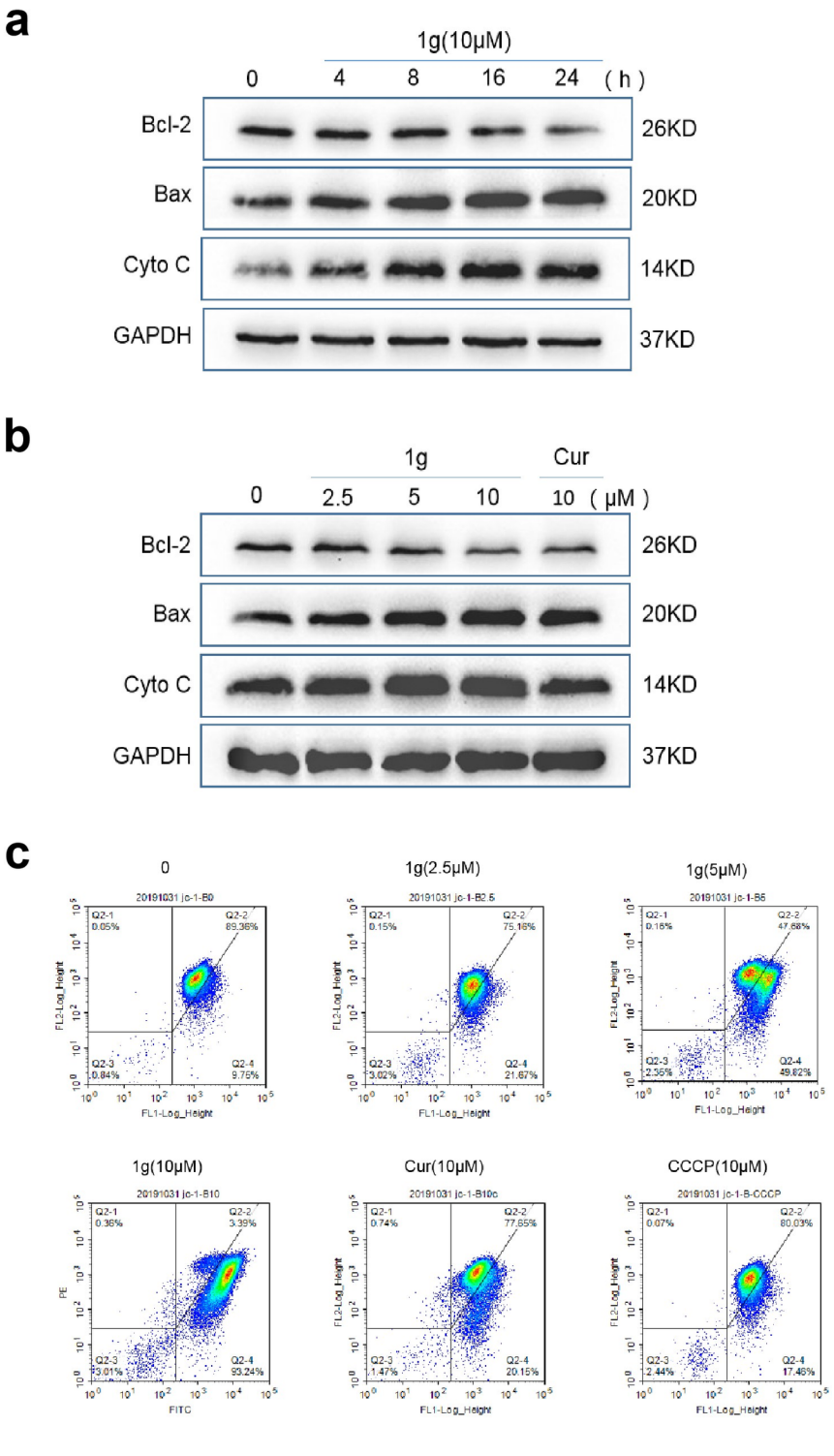

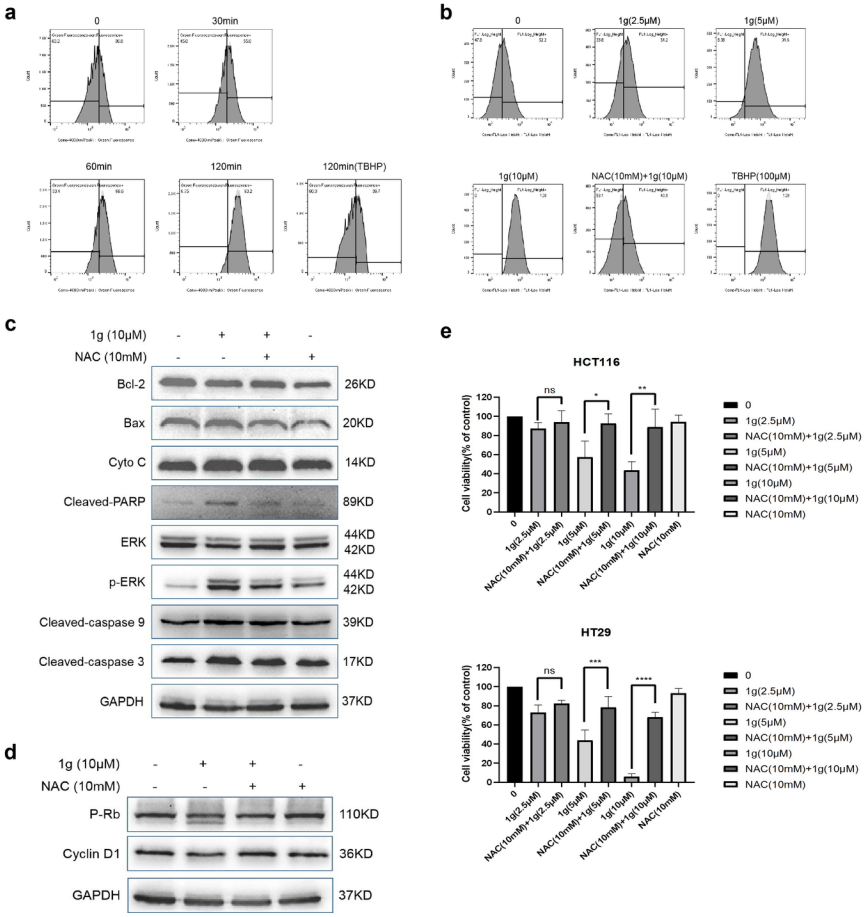

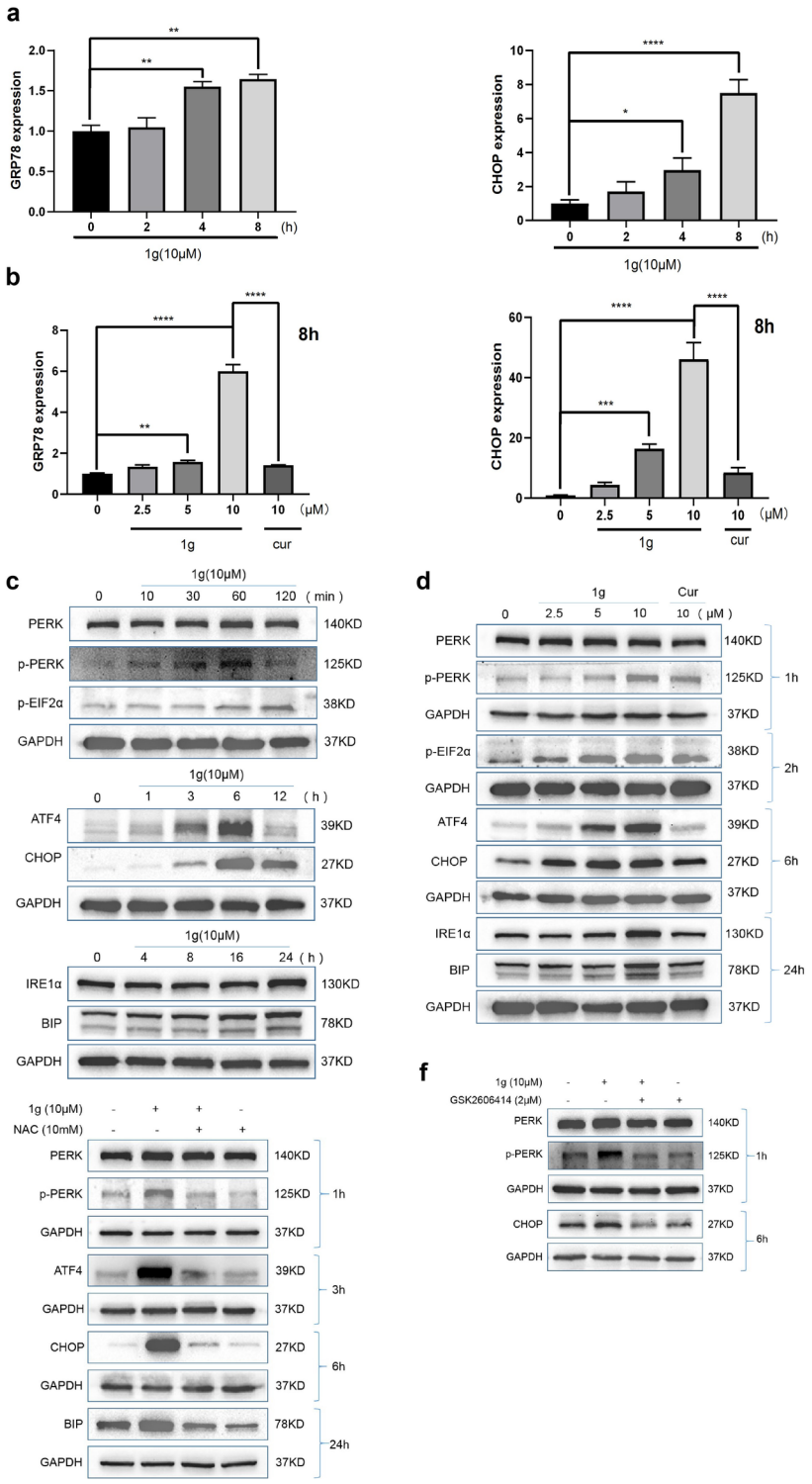

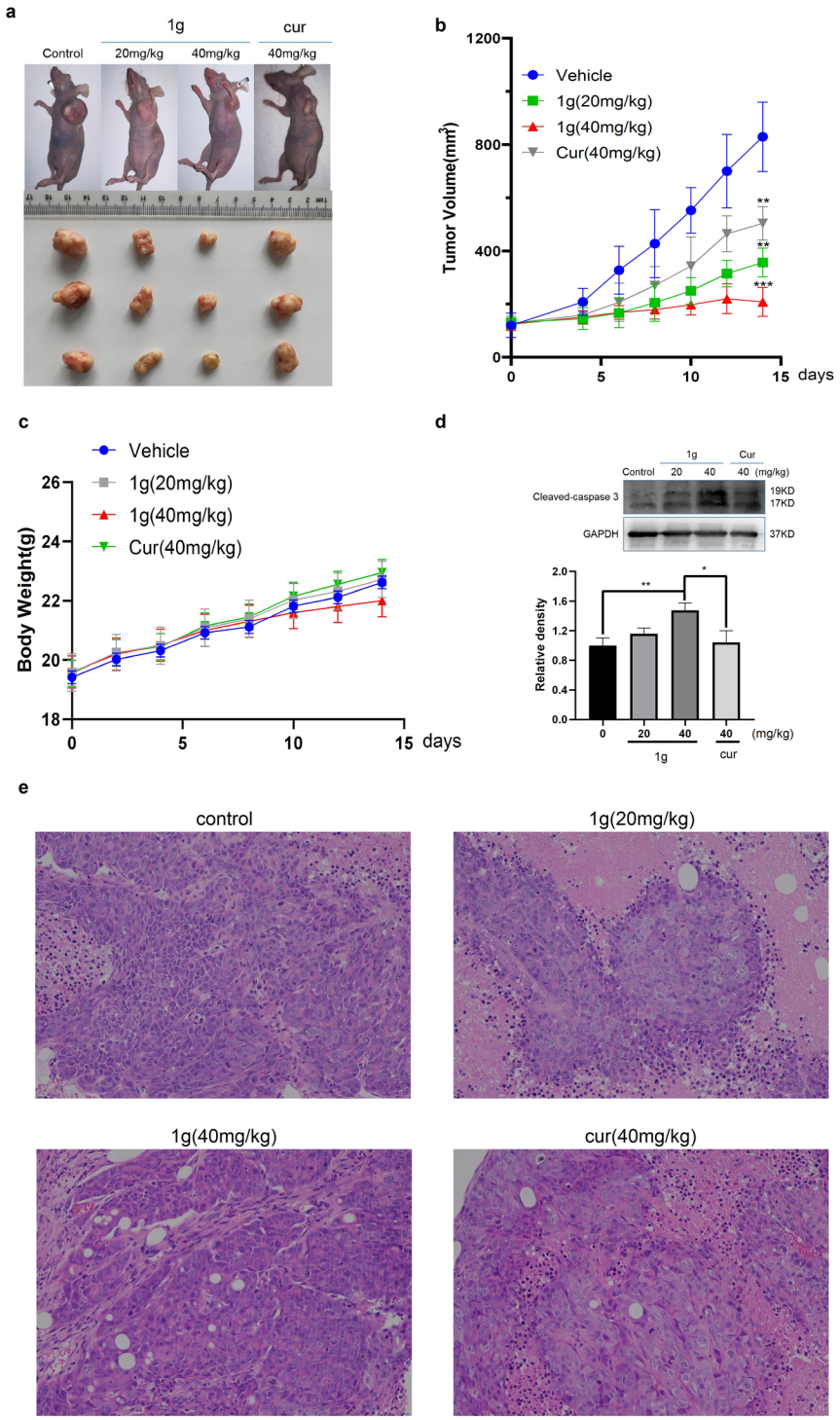

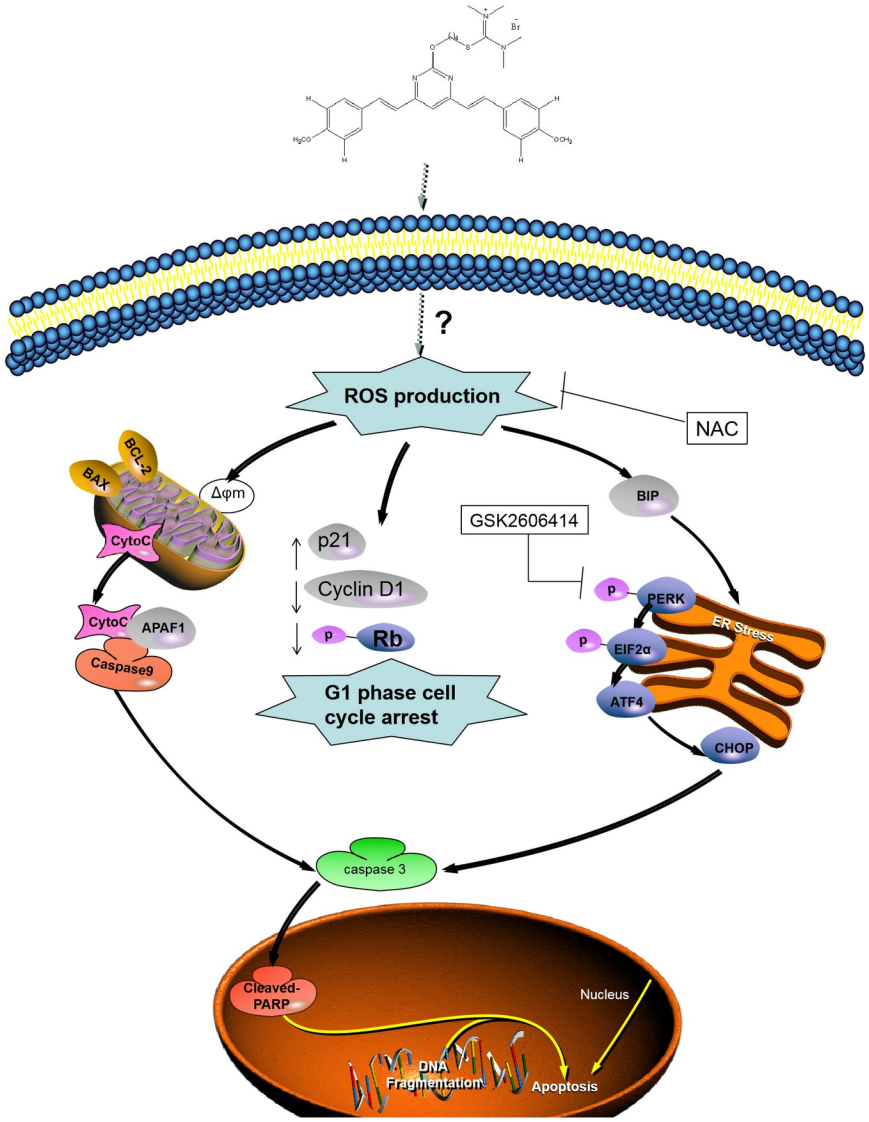

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