Zinc Oxide Nanocrystals and high energy Shock Waves as promising anticancer agent

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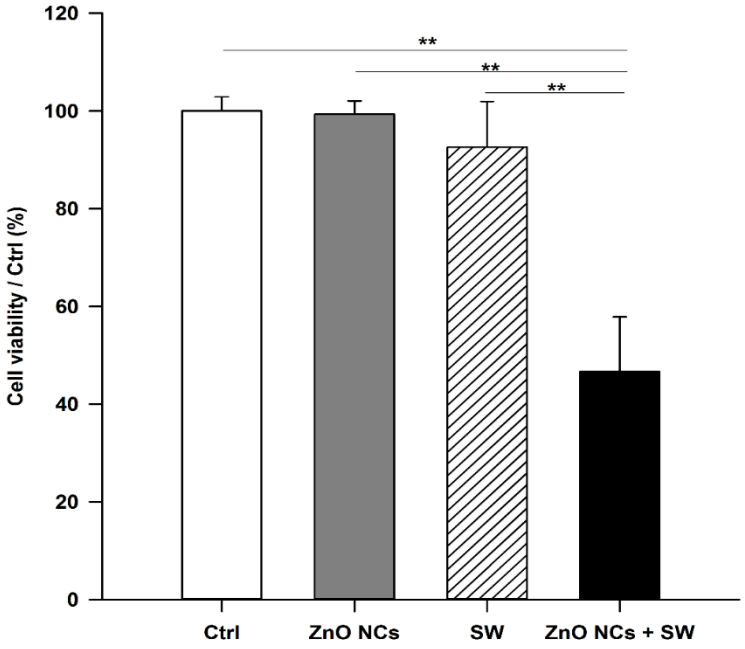
High energy Shock Waves (SW) are mechanical shock waves characterized by a positive pressure, sometimes up than 100 MPa with a phase duration of 0.5-3 μs, and a negative pressure of 10 MPa, whit a duration of 2-20 μs. SW have been clinically exploited for lithotripsy, the treatment of musculoskeletal pathologies, rehabilitative and regenerative purposes. Some authors have proposed SW in combination with sonosensitizers to inhibit tumor growth in *in vitro* and *in vivo* studies. In this investigation, we explored the possibility to exploit Zinc Oxide Nanocrystal (ZnO NCs) assisted SW treatment to achieve enhanced cytotoxic effects on cancer cells. The presence of a synergistic effect between ZnO NCs and SW was evaluated performing singular and multiple SW treatments per day (3/day) on cervical carcinoma KB cells pre-incubated with 10 μg/mL ZnO NCs for 24 h. A significant decrease of cell viability was recorded when cells incubated with ZnO NCs were treated 3/day with SW 50 MPa, 500 shots, 4 shots/s. Pilot studies on the mechanism have been performed. The addition of two different reactive oxygen species (ROS) scavengers revealed ROS marginal role in the pathway involved in cell inhibition growth, whereas kinetic evaluation of cell death highlighted the progressive increase of apoptosis and secondary necrosis caused by the combined effect of ZnO NCs and SW.



*Study of the combined effect of ZnO NCs and SW in cancer cells. Percentage of viability 24 h after the SW treatment of untreated cells (Ctrl), cells incubated with ZnO NCs (ZnO NCs), cells treated with SW (SW), and cells incubated with NCs and treated with SW (ZnO NCs + SW). Bars represent mean percentage of cell viability compared to Ctrl + SEM, n=6, **p<0.01.*

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