Zinc oxide nanocrystals and ultrasound: A new strategy to fight cervical cancer

Zinc oxide nanocrystals and ultrasound: A new strategy to fight cervical cancer

L. Racca*, T. Limongi, V. Vighetto, B. Dumontel, A. Ancona, M. Canta, G. Canavese, N. Garino, V. Cauda

Department of Applied Science and Technology, Politecnico di Torino, Corso Duca degli Abruzzi, Turin, Italy

**luisa.racca@polito.it, Phone number: +39 0110907380*

OBJECTIVES

Cervical cancer is the fourth most common cancer in women, and is in the top three cancers affecting women younger than 45 years old. Traditional therapeutic protocols include surgery, radiation therapy and chemotherapy [1]. Nanomedicine, however, could represent a new strategy to decrease the mortality of this pathology, reducing the negative outcomes related to traditional anticancer approaches [2]. An innovative proposal in this field is the administration of nanotools remotely activated by an external physical stimulation. In this study thus the possibility to exploit the synergism between ZnO NCs (ZnO NCs) and ultrasound (US) to affect the viability of cervical cancer cells was investigated.

METHODS

The cytotoxicity and internalization of aminopropyl-functionalized ZnO NCs was evaluated on cervical adenocarcinoma KB cells. Furthermore, the presence of a synergistic effect between ZnO NCs and US was evaluated performing single and multiple US treatments per day on KB cells pre-incubated with ZnO NCs. Pilot studies on the mechanism of the observed synergism have been performed, evaluating cell proliferation, after the incubation of ZnO NCs and US treatments, whit the addition of reactive oxygen species (ROS) scavengers, and the kinetics of cell death.

RESULTS

ZnO NCs resulted to be non-toxic for KB cells and they were efficiently internalized in cancer cells. Regarding the evaluation of the synergism, a significant decrease of cell viability was recorded when cells incubated with

ZnO NCs were treated multiple times with US. The addition of two different ROS scavengers revealed ROS marginal role in the pathways involved, whereas the kinetic evaluation of cell death highlighted the progressive increase of apoptosis and secondary necrosis caused by the combination of ZnO NCs and US.

CONCLUSIONS

Herein, for the first time, the synergistic action of ZnO NCs and US to achieve cervical cancer cell death was demonstrated. Further studies are going to focus on the evaluation of the US-assisted therapy with ZnO NCs shielded into a lipid envelop, to improve their biocompatibility and let them a biomimetic property, decorated with monoclonal antibodies for targeting.

ACKNOWLEDGMENTS

This work has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement No 678151 – Project Acronym "TROJANANOHORSE" – ERC starting Grant). We wish to gratefully thank the ELvation Medical company for the supply free of charge of the PW2 instrument (R. Wolf).

REFERENCES

[1] Arbyn et al. 'Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis' *The Lancet Global Health,* 8: e191-203

[2] Racca L. et al. 'Zinc Oxide Nanocrystals and High-Energy Shock Waves: A New Synergy for the Treatment of Cancer Cells' *Front Bioeng Biotechnol*, 8, 577, 2020.