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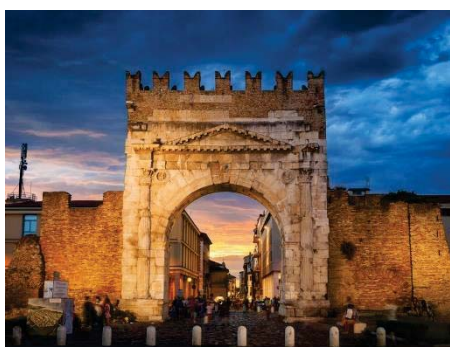
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Biomimetic hybrid nanoconstructs for cancer therapy

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In the last few years there has been an increasing interest in nanomedicine and in particular in developing nanoparticles to fight cancer [1].

Zinc oxide nanocrystals (ZnO NCs), thanks to their peculiar properties, can be employed for cancer diagnosis and therapy. Even if the cytotoxicity mechanism of ZnO NCs is not totally understood yet, it is most probably due to the combination of intracellular Zn²⁺ cations release and the production of reactive oxygen species: in vitro tests have also shown an increased cytotoxic effect of ZnO on cancer cells with respect to the healthy counterpart [1].

In order to promote the stability of ZnO NCs in physiological environment, increase their biocompatibility and reduce their immunogenic effects, we covered ZnO NCs with a biomimetic phospholipidic bilayer [2] derived from extracellular vesicles, in particular exosomes, obtaining a nanoconstruct called TrojaNanoHorse (TNH).

Exosomes are naturally produced by many types of cells as vehicle of intercellular communication and, when autologous, they are not recognized by the immune system. We extracted exosomes from living cells and we re-used them as a biomimetic, nature-derived coating to stabilize and reduce the immunogenicity of the ZnO NCs. Most importantly, we would like to exploit the natural communication function of exosome to drive the therapeutic nanoparticles towards the cancer cells [3].

We optimized the coupling process between ZnO NCs and exosomes through a systematic study of the thermodynamic, kinetic and electrostatic parameters of the process and then we tested the efficiency of coupling by combining different characterization techniques.

These experiments on the TNH preparation are the starting points to further study the TNH internalization process, mechanisms of causing cell damages, stability in biological fluids, and targeting mechanisms, to make TNH a new theranostic nanoconstruct against cancer.

[1] L. Racca, M. Canta, B. Dumontel, A. Ancona, T. Limongi, N. Garino, M. Laurenti, G. Canavese, V. Cauda, *Smart Nanoparticles for Biomedicine* **1** (2018) 171-187.

[2] B. Dumontel, M. Canta, H. Engelke, A. Chiodoni, L. Racca, A. Ancona, T. Limongi, G. Canavese, V. Cauda, *J. Mater. Chem. B* **5** (2017) 8799-8813.

[3] M.P. Zaborowski, L. Balaj, X.O. Breakefield, C.P. Lai, *Bioscience* **65** (2015) 783–797.