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Chemotherapy and photodynamic therapy as multimodal approach for a synergic treatment of osteosarcoma tumor: *In vitro* results

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The insurgency of multi drug resistance (MDR) is the major obstacle in osteosarcoma treatment. Nano-formulation of chemotherapeutics has improved both drugs solubility of and drug delivery tumor but did not have an effect on MDR. In this work, we tested *in vitro* if the efficacy of keratin nanoparticles loaded with paclitaxel (PTX) could be improved by photodynamic therapy. Keratin (Ker) based nanoparticles loaded with PTX and with the photosensitizer Chlorin-e6 (Ce6) were obtained through desolvation (des) and drug-mediated aggregation (ag) methods (PTX-Ce6@Kerdes and PTX-Ce6@Kerag respectively). *In vitro* experiments were performed on three OS cell lines, e.g. MG63, SaOS-2 and U2-OS, exposing them for 24 hours to the nanoparticles and then irradiated with a LED light (λmax=668±3 nm) for 5 min at RT (fluence 263 J/cm2) and compared to not-irradiated samples. IC50 values were determined and we observed that PTX-Ce6@Kerag NPs were able to release PTX and block OS cells with a kinetic similar to that of free PTX, whereas PTX-Ce6@Kerdes provided a slower release profile. Cells viability tests show the synergic effect arising from the cytostatic activity of the released PTX and the reactive oxygen species (ROS) produced upon Ce6 irradiation. Our results prove that our bimodal nanoparticles are able to augment PTX cytotoxicity. If *in vivo* experiments will confirm *in vitro* data, this approach would significantly enhance the efficacy of drug based treatments, increasing the life expectancy of OS patients.

Recent Publications

1. Perteghella S, Martella E, de Girolamo L, Perucca Orfei C, Pierini M, Fumagalli V, Pintacuda D V, Chlapanidas T, Viganò M, Faragò S, Torre M L, Lucarelli E (2017) Fabrication of Innovative Silk/Alginate Microcarriers for Mesenchymal Stem Cell Delivery and Tissue Regeneration. *Int J Mol Sci*.; 18(9): 1829.

2. Di Maggio N, Martella E, Frismantiene A, Resink T J, Schreiner S, Lucarelli E, Jaquiery C, Schaefer D J, Martin I, Scherberich A (2017) Extracellular matrix and α5β1 integrin signaling control the maintenance of bone formation capacity by human adipose-derived stromal cells. *Sci Rep*.; 7: 44398.

Biography

Elisa Martella holds her Bachelor's degree in Pharmaceutical Biotechnology (2009) and received her PhD in Cellular Biology and Biotechnology at University of Bologna (2013) in a Regenerative Medicine project in collaboration with University of Basel (CH). She is currently a Post Doctorate Fellow at Italian National Research Council, and she is involved on a project focused to investigate novel approaches for osteosarcoma treatment. She has experience in cellular biology, regenerative medicine, nanomedicine and oncology research.

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