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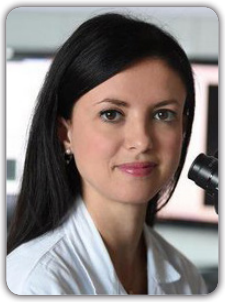

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Mesenchymal stromal cells and therapeutic nanoparticles as multimodal treatment of osteosarcoma

Osteosarcoma (OS) is a highly malignant primary bone tumor and the most frequent bone sarcoma in children and adolescents. Standard treatments include surgery and chemotherapy. The current survival rate is 65%. The poor outcome is mostly due to an inability to deliver drugs to the infiltrative tumor cells. Therefore, significant efforts need to be undertaken to develop new delivering strategies. One approach is to dispense therapeutic agents using mesenchymal stromal/stem cells (MSC) which have the unique ability to home and engraft in the tumor stroma. They therefore represent an ideal vehicle for targeted drug delivery. Our aim is to evaluate the efficacy of MSC as delivery vehicle for a bimodal treatment consisting of photodynamic therapy (PDT) and of the cytostatic drug Paclitaxel (PTX). We engineered biodegradable nanoparticles (NPs) able to induce cell death through a dual synergic action (PTX and PDT). Then we loaded these NPs into MSC and we used these cells as Trojan horse vehicles. Albumin (HSA) and Keratin (Ker) based NPs were conjugated with the photosensitizer chlorin e6 (Ce6), and the PTX was introduced through de-solvation or drug-induced protein self-assembly techniques. Human MSC were loaded with different dosages of NPs, co-cultured with different OS tumor cell lines and irradiated with infrared light. Results show that MSC efficiently internalize NPs, release PTX by exocytosis and after irradiation generate ROS, inducing an overall 90% mortality of tumor cells. Our data demonstrate the excellent ability of MSC to function as a carrier of photo-killing agents *in vitro*. The proposed bimodal therapy could minimize the side effects of the systemic chemotherapy administration and enhance its efficacy through the synergic effect of PTX and PDT and could be intended as a future innovative co-adjuvant approach for treatment of OS affected patients.

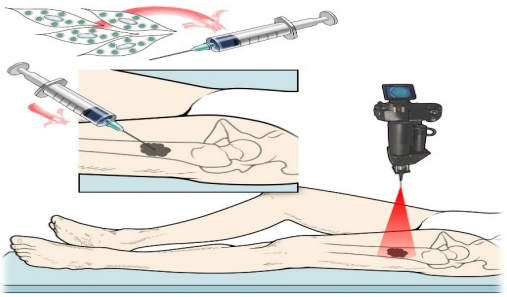

Figure-1: Schematic representation of the proposed clinical approach: infusion of MSC loaded with therapeutics nanoparticles able to synergically release the chemotherapeutic drug Paclitaxel and generate toxic ROS after photodynamic activation, to kill tumor cells in OS affected patients.

Recent Publications

1. Duchi S, Dambruoso P, Martella E, Sotgiu G, Guerrini A, Lucarelli E, Pessina A, Cocce V, Bonomi A, Varchi G (2014) Thiophene-based compounds as fluorescent tags to study mesenchymal stem cell uptake and release of taxanes. *Bioconjug Chem.*: 649-55.

2. Duchi S, Sotgiu G, Lucarelli E, Ballestri M, Dozza B, Santi S, Guerrini A, Dambruoso P, Giannini S, Donati D, Ferroni C, Varchi G (2013) Mesenchymal stem cells as delivery vehicle of porphyrin loaded nanoparticles: Effective photoinduced *in vitro* killing of osteosarcoma. *J Control Release*: 225-37.

References

1. J B Hayden, B H Huang (2006) Osteosarcoma: Basic Science and Clinical Implications. *Orthopedic Clinics of North America:* 1-5.

2. Y L Hu, Y H Fu, Y Tabata, J Q Gao (2010) Mesenchymal stem cells: a promising targeted-delivery vehicle in cancer gene therapy. *J. Control. Release*: 154-162.

Biography

Serena Duchi has completed her PhD in Molecular and Cellular Physiology in 2009. She has then specialized in the Treatment of Musculoskeletal Tumors at the Rizzoli Orthopedics Institute, Bologna, Italy, where she leads different projects as Research Fellow. She has a passion and strong knowledge in different imaging techniques for epifluorescence, confocal and time-lapse microscopy, FRET, TIRF, and light-sheet microscopy.

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