Nanomedicine & Biotherapeutic Discovery

Extended Abstract

Mesenchymal stromal cells and therapeutic nanoparticles as multimodal treatment of osteosarcoma

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Abstract

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 selfassembly 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. 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. An osteogenic sarcoma (OS) or osteogenic sarcoma (OGS) (or merely bone cancer) could be a cancerous tumour in an exceedingly bone. Specifically, it's associate aggressive malignant tumor that arises from primitive remodeled cells of mesenchymal origin (and therefore a sarcoma) which exhibits osteoblastic differentiation and produces malignant osteoid. cancer|sarcoma} is that the commonest histologic kind of primary bone sarcoma. it's most rife in teenagers and young adults. several patients 1st complain of pain which will be worse in the dark, is also intermittent and of varied intensity and should are occurring for a few time. Teenagers UN agency square measure active in sports typically complain of pain within the lower leg bone, or instantly below the knee. If the tumour is giant, it will gift as barefaced localised swelling. generally a fulminant fracture is that the 1st symptom, as a result of the affected bone isn't as robust as traditional bone and should fracture abnormally with minor trauma. In cases of a lot of established tumors that don't seem to be as near to the skin, like those originating within the pelvis, localised swelling might not be apparent. Mesenchymal stem cells (MSCs) additionally called mesenchymal stromal cells or healthful sign cells square measure potent stromal cells that may differentiate into a spread of cell sorts, together with osteoblasts (bone cells), chondrocytes (cartilage cells), myocytes (muscle cells)

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and adipocytes (fat cells that create to marrow fatty tissue). Mesenchymal stem cells square measure characterised morphologically by alittle cell body with many cell processes that square measure long and skinny. The cell body contains an outsized, spherical nucleus with a outstanding nucleole, that is enclosed by finely spread body substance particles, giving the nucleus a transparent look. the rest of the cell body contains alittle quantity of dictyosome, rough endoplasmic reticulum, mitochondria and polyribosomes. The cells, that square measure long and skinny, square measure wide spread and therefore the adjacent extracellular matrix is inhabited by many crisscross fibrils however is empty of the opposite kinds of scleroprotein fibrils.

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