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Combination therapy of canine osteosarcoma with canine bone marrow stem cells, bone morphogenetic protein and carboplatin in an in vivo model.

Rici REG[1], Will SEAL[2], Luna ACL[2], Melo LF[1], Santos AC[1], Rodrigues RF[1], Leandro RM[1], Maria DA[2].
Author information

Abstract

Osteosarcoma (OSA) is the most common malignant bone cancer in children and dogs. The therapeutic protocols adopted for dogs and humans are very similar, involving surgical options such as amputation. Besides surgical options, radiotherapy and chemotherapy also are adopted. However, hematologic, gastrointestinal and renal toxicity may occur because of chemotherapy treatments. Recent study clearly showed that mesenchymal stem cells (MSCs) combined with recombinant human bone morphogenetic protein (rhBMP-2) may be associated with decreases of the tumorigenic potential of canine OSA. The aim of this study was to analyse the efficacy of chemotherapy with carboplatin and rhBMP-2 with MSCs in a canine OSA in vivo model. Canine OSA cells were implanted in mice Balb-c/nude with MSCs, rhBMP-2 and carboplatin. Flow cytometry and PCR for markers involved in tumour suppression pathways were analysed. Results showed that the combination of MSCs and rhBMP-2 reduced tumour mass and infiltration of neoplastic cells in tissues more efficiently than carboplatin alone. Thus it was demonstrated that the use of rhBMP-2 and MSCs, in combination with conventional antineoplastic, may be an efficient treatment strategy.

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Hypoxia induces senescence of bone marrow mesenchymal stem cells via altered gut microbiota.

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Abstract

Systemic chronic hypoxia is a feature of many diseases and may influence the communication between bone marrow (BM) and gut microbiota. Here we analyse patients with cyanotic congenital heart disease (CCHD) who are experiencing chronic hypoxia and characterize the association between bone marrow mesenchymal stem cells (BMSCs) and gut microbiome under systemic hypoxia. We observe premature senescence of BMSCs and abnormal D-galactose accumulation in patients with CCHD. The hypoxia that these patients experience results in an altered diversity of gut microbial communities, with a remarkable decrease in the number of Lactobacilli and a noticeable reduction in the amount of enzyme-degraded D-galactose. Replenishing chronic hypoxic rats with Lactobacillus reduced the accumulation of D-galactose and restored the deficient BMSCs. Together, our findings show that chronic hypoxia

predisposes BMSCs to premature senescence, which may be due to gut dysbiosis and thus induced D-galactose accumulation.

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