



Investigating tumour intrinsic PD-1/PD-L1 signalling in canine osteosarcoma cell lines as a potential model for human disease.

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Abstract

Osteosarcoma (OS) is a fatal disease both in dogs and humans. One of the problems in development of novel treatment approaches is relatively low frequency of osteosarcoma in humans. In fact, no major changes in osteosarcoma therapy have been applied in clinics over last 30 years and chemotherapy remains the first-line treatment. Although rarely diagnosed in humans, osteosarcoma is 27 times more prevalent in dogs. Interestingly, the disease in both species shares many pathological and genetic similarities. Recently, much attention has been brought to immunotherapies as a potential breakthrough in cancer treatment. Indeed, PD-1/PD-L1 monoclonal antibodies showed great success rates in number of patients and types of cancer. Even though the implementation of immunotherapy is getting wider, there are still some diseases with no significant progress in therapeutic approach over decades, including osteosarcoma. Until recently, the mechanism underlying PD-1/PD-L1 monoclonal antibodies activity solely considered the blockade of interaction between PD-1 receptor localized on T-cells and PD-L1 expressed by cancer cells. Interestingly, some recent studies reported the ability of cancer cells not only to express PD-L1 but also PD-1. PD-1/PD-L1 intrinsic signalling was also proved to stimulate pathways regulating tumour growth, proliferation and survival regardless of the functional immune system. This led to hypothesis that tumour PD-1/PD-L1 intrinsic signalling may play currently undefined role in cancer cells. Better understanding of this phenomenon could have potential to maximize immunotherapy outcomes and explain why it is only successful in a group of cancer patients. Our preliminary data showed for the first time that canine osteosarcoma cell lines spontaneously express PD-1. Moreover, either PD-1 or PD-L1 overexpression stimulates mTOR signalling and accelerates cellular growth in 3D culture. The aim of this work is to further investigate PD-1/PD-L1 intrinsic signalling in canine osteosarcoma cell lines as a potential model for human disease. Taking into consideration higher prevalence of the disease in dogs and many pathological and genetic similarities between the disease in both species, make dogs a perfect model to study osteosarcoma and to potentially apply the results into human studies.

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