Reviewer's report

Title: Expression profiling in canine osteosarcoma: identification of biomarkers and pathways associated with outcome

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Reviewer: Françoise REDINI

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The manuscript describes a profiling study performed on osteosarcoma bearing dogs treated with limb amputation followed by doxorubicin or platinum-based drug chemotherapy. Potential new biomarkers were identified to predict patient outcome in osteosarcoma together with new pathways that may be targeted for therapeutic intervention. This is a nice, well written study with potent clinical transfer.

Gene expression was assessed with Affimetrix canine microarrays and a subset of genes was confirmed using RT-qPCR. The genes identified were then converted to their human homologues and assigned to functional pathways. Pathway analysis revealed alterations in pathways associated with oxidative phosphorylation, hedgehog and parathyroid hormone signaling, immune responses, cytoskeletal remodeling and focal adhesion.

This study clearly demonstrated that complementary technologies must be used to determine significant markers which must be validated by RT-qPCR for example. This is an important point for translational research.

One minor point has to be clarified before publication.

The number of samples used in the analyses is not clear: In the abstract, it is said that 8 biopsies from dogs with DFI<100 days and 7 biopsies from dogs with DFI>300 days are used, corresponding to the 15 donors described in the material & methods section (page 7), but it is not clear what the term “cohort” means in this paragraph; then in page 8, the study included 20 samples: the 15 previously describes plus 5 that met the selection criteria: which criteria? And in the results section, the authors said that the DFI<100 and the DFI>300 groups are composed of 10 donors each (5 males and 5 females) ; why these 5 other donors were added ? from which cohort ?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests