Reviewer’s report

Title: Molecular, cellular and physiological characterization of the cancer cachexia-inducing C26 colon carcinoma in mouse

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Reviewer: Francisco J Lopez-Soriano

Reviewer’s report:

In this paper, the authors characterize the C26 colon carcinoma as a cachectic tumour model in mice. This is an important feature, because good animals models of cachexia are scarce but necessary as tools in the characterization of the molecular mechanisms underlying this complex syndrome often associated with cancer. This tumour model has been used for approximately 30 years, although very few papers have considered the consequences of its growth from the point of view of cachexia, so the points concerning this question are particularly outstanding. The methodology used is appropriate but there are some major points to be considered concerning the results presented.

Perhaps the most important feature of cachexia is a progressive waste of both skeletal muscle and adipose tissue, this leading to an important body weighty loss. In this case, the maximum cachectic effect seems to be achieved on day 16 (Figure 3b), which corresponds to the beginning of the exponential growth phase (Figure 2a). This is not an usual finding in other cachexia models, where cachexia progresses with tumour growth. This needs some clarification or comment. In addition, it would be useful to express the statistic variability of the data present in Figure 2a, particularly because only a reduced number of animals can survive till this moment.

The authors state that body weight loss is largely explained by muscle wasting, also indicating that numerous skeletal muscles were affected. However they do not shown these important data whereas Figure 3d shows the weights of liver, kidney and heart, which are organs no affected by tumor growth. Form the point of view of a characterization of a cachectic model, the data of individual skeletal muscles and also white adipose tissues depots along tumour growth are necessary in order to evaluate the cachexia status of the animals.

Both immunohistochemical and Western blot analysis have been performed by using tibialis anterior muscle samples, whereas the functional analysis has been done with EDL muscles. I can understand the suitability of EDL in such functional studies. However, because different muscles can be differentially affected by cachexia, it could be necessary to extent such studies to other muscles with different fiber composition. Again, the factor time of tumour growth must also be considered here in order to have a good characterization of the model.
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.