Reviewer's report

Title: Developing an Animal Model of Dupuytren's Disease by Orthotopic Transplantation of Human Fibroblasts into Athymic Rat

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Reviewer: Sandra Kraljevic Pavelic

Reviewer's report:

The authors tried to establish a successful animal model of Dupuytren's disease (DD). To that aim, they transplanted carpal tunnel (CT)-derived and DD-derived fibroblasts in the forepaw of the nude rats. They have established that transplanted fibroblasts survived for 62 days in nude mouse after which forepaw connective tissues were harvested for histological analysis and total RNA isolation. DD is a very specific type of fibrosis because it develops through long period of time with no clear molecular causes so it is extremely difficult to create an animal model that would serve the purpose of better understanding of DD disease. Presented research certainly contributes to the growing need of establishing animal model of DD, but more could have been done on the presented model.

As the authors stated, development of a frank tissue contraction analogous to the clinical presentation in humans was not obtained, however DD cells have greater persistence over time than control CT cell, and retain a distinct pro-fibrotic physiology, that could have been accomplished without their transplantation into nude mice.

Major compulsory revisions:

Cell transplantation was done after max 6 passages: why did the authors use these high passages instead of early (1-3rd passage) passages? Perhaps greater persistence of DD cell is a result of lower proliferation capacity, especially after 6th passage prior to transplantation. My major concern is that DD cells have almost the same expression level of alpha-SMA after isolation from the patients' cords and after 62 day in mouse forepaw. The authors did not specify at what time point was the expression of alpha-SMA analysed in the DD derived cells. The results show no dramatic changes in alpha-SMA during 62 day which even though this protein is a key protein involved in the development of DD symptoms. Also there were no dramatic changes in the expression of Type I collagen and Type III Collagen, whose expression rose cca. 6 times (difficult to evaluate from the picture), which is clearly not sufficient to establish DD in proposed model. It would be highly useful to perform some protein analyses (i.e. of myofibroblast markers) and known signalling molecules involved in disease progression. Please explain why these analyses were not included in the study?

The proposed animal model is definitely a step in the right direction but deeper and more comprehensive research is necessary.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

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