Reviewer's report

Title: Regulation of MCP-1 secretion in a novel bone-tumor coculture model

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Reviewer: Jian Zhang

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The authors, in this well-written manuscript, tried to test an ex vivo co-culture model in monitoring of the production and regulation of paracrine factors during interactions of an intact femur explant and tumor cells.

This is a technical manuscript using an interesting “intact femur explant-tumor cells” coculture model. However, there are some minor essential concerns: 1) They presented that MCP-1 can be produced by tumor cells as well as by bone cells that have been previously published by other research groups. The critical concern is that they used neonatal femurs in the current study as the authors stated that “intact femur retains the 3-dimensional, multi-cell architecture including ossified bone and hematopoietic cells, stroma and matrix tissue and therefore, is similar to adult bone”. What would happen if the authors use adult femurs to conduct the same experiments? Are they going to achieve the same results? 2) From the key data figure 5, the authors stated that “it is possible that the sarcoma cells may be the major contributor to the MCP-1 secretion observed in the cocultures”. Yes, it is possible. However, to distinguish the major source of MCP-1 secretion in this coculture system would be the critical study. In that case, MCP-1 knockout mice could be used and now the knockout mice are commercial available. 3) The next concern is the fact that MDA-MB-231 cells do produce detectable levels of the cytokines they measured, for example, MCP-1. These facts have been published elsewhere. However, they did not detect them. These questionable results that co-culturing with the breast cancer cells resulted in a reduction in TGFbeta and MCP-1 are therefore hard to be interpreted. 4) In this study, real-time PCR was used to test the MCP-1 mRNA expression in isolates of femurs and sarcoma cells cultured alone or cocultured in serum-free conditions. In tumor cells, co-coculture caused 1.9 fold (day 1) and 3.3 fold (day 2) inductions. In bone cells, coculture caused 1.3-fold induction on day 1, but no significant change was observed in day 2 cocultures. What is the interpretation?

Level of interest: An article of importance in its field

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.