Reviewer's report

Title: M1 and M2 macrophages derived from THP-1 cells differentially modulate the response of cancer cells to etoposide

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Reviewer: wenxiang sun

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Major Compulsory Revisions

The study by GENIN et al titled as “M1 and M2 macrophages derived from THP-1 cells differentially modulate the response of cancer cells to etoposide” reports that human monocytic cell line THP-1 derived M1 and M2 macrophages have different modulated effects on cancer cells when treated with chemotherapeutic agent etoposide. M1 and M2 macrophages were polarized from THP-1 and characterized by several markers and specific cytokines production. They used these two polarized macrophages studying their effects on cancer cell sensitivity to etoposide. The authors claimed THP-1 M2 macrophages inhibited but THP-1 M1 macrophages accelerated etoposide-induced cancer cell apoptosis.

Although it is important to study the role of TAMs in cancer cells sensitivity to chemotherapeutic agents, I don’t think the experiments in this manuscript sufficiently support the authors’ conclusions. When characterizing M1 and M2 macrophages, they used several makers, which were not significant to show the differentiation. The western blot results showing accelerating effects of M1 macrophages in etoposide-induced apoptosis were not obvious. The inhibition of cancer cell apoptosis is also just slightly affected by M2 macrophages. More evidences to show the apoptosis are needed here.

Some special comments for authors:

1. In Fig1, the imaging of differentiation markers is not showing in the same scale level between before and after differentiation. The differences seemed caused by scale differences. More markers need to be detected for the differentiation, like CD14 and CD68. To characterize THP-1 derived M1 and M2 macrophages, additional markers including CCR7, CD80 and CD163 need to be tested. (Tjiu JW et al, J Invest Dermatol 2009; Zhang F et al, Proteomics. 2014; Engström A et al, Int J Oncol. 2014).

2. In Fig3 A, the authors showed TNF-# and IL-1# expression levels are also high in control M0 macrophages and decreased after 24 hours. Why their expression decreased after 24 hours? The IFN-# alone or with LPS induced IL-1# was nearly comparable with M0 macrophages. In previous work, IFN-# or LPS can induced much higher expression of IL-1# in M1 than in M0 macrophages, which was not observed in this manuscript. The author should give explanation to this (Tjiu JW

3. In Fig6 B and D, although the cleavages of procaspase-3 and PARP-1 are slightly inhibited in cancer cells co-cultured with THP-1 M2 macrophages, the cleavages are not significantly increased in the case of THP-1 M1 macrophages. More evidences about the different effects of THP-1 M1 and M2 macrophages in etoposide-induced cancer cell apoptosis are needed here. The molecular weight of protein also needs to be labeled.

4. In Fig4 C, it’s better to show CD206 expression level using histogram. It is hard to see the real positive population using dots.

5. In line 38, “THP-1 deried macrophages”, should be “THP-1 derived macrophages”; In line 616, “western bloting” should be “western blotting”.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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.