Reviewer’s report

Title: PAF-R dependent pathways control tumor growth and tumor response to chemotherapy

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Reviewer: Benedetta Bussolati

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The paper by Oliveira and colleagues investigates the effect of PAF inhibition on tumor response to chemotherapy in two different tumor experimental models. In a model of an Ascitic mammary tumor, WEB2170 reduced tumor growth, but did not show an additive effect with chemotherapy. Moreover, WEB2170 reduced the tumor-induced production of PGE2, NO and VEGF by the microenvironment and abrogated the promoting effect of apoptotic tymphocytes on tumor growth.

In a second model, a subcutaneous implantation of murine melanoma cells, WEB2170 showed an additive effect on survival with chemotherapy and a parallel effect on vessel density and inflammatory infiltration.

The authors propose that PAF-R, known to be involved during the phagocytosis of apoptotic tumor cells, may also be responsible for the inhibition of tumoricidal activity of macrophages. In this setting, PAF may contribute to tumor chemoresistance following the drug-dependent generation of apoptotic cells and activation of an M2 tumor macrophage phenotype. This idea is original and very interesting. However, the hypothesis is not clearly demonstrated but rather deduced by experiments on different aspects of tumor biology.

Major Compulsory Revisions

In my opinion, the paper should be re-presented in a more logic way and some experiments performed to clearly demonstrate the hypothesis. Moreover, part of the results are not novel and should be removed to focus on the novel part of the study.

In particular, in the EAT model, the effect of PAF inhibition on tumor growth and PGE2 production has been previously shown. In addition the result that PAF inhibition did not ameliorate the chemotherapy effect is against the role of WEB on apoptosis-dependent chemoresistance. In parallel, the effect of PAF inhibition on melanoma tumor growth and angiogenesis has been previously shown. The interesting result on the effect of WEB2170 plus chemotherapy should be expanded with experiments using combined administration of apoptotic cells and WEB. Moreover, experiments investigating the macrophage phenotype in the presence or absence of WEB in the melanoma model are needed.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

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