Reviewer's report

Title: The Spectrum of Resistance in SR/CR Mice: the Critical Role of Chemoattraction in the Cancer/Leukocyte Interaction

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Reviewer: Elizabeth A. Repasky

Reviewer's report:

The manuscript by Riedlinger et al. details generally interesting, but largely descriptive, information regarding an interesting mouse model (ST/CR) which has significant natural anti-tumor activity. Here, the growth characteristics of other cell lines are evaluated (both in adult SR/CR mice and "naïve pups") and their compared to that which occurs in WT mice. While there is overall greater protection from tumor growth noted in the SR/CR mice, the authors note some differences in the individual responses to various cell lines, showing that the growth of some is blunted nearly completely, while the growth of others progresses as expected. Data suggests that the relatively unimpaired growth of MethA and LL/2 tumors is due to their inability to attract leukocytes, whereas the blockage of growth of tumor cells such as S180 and EL-4 lymphoma cells is due to their attraction of leukocytes. If S180 cells are co-injected with MethA or LL/2 cells, then there is improved survival. Further, injection of S-180 induced cell-free ascites also helps increase anti-tumor activity, suggesting that the chemoattraction by cancer cells is mediated by diffusible molecules.

- Major Compulsory Revisions

In general, these data do not address immunological mechanisms, and are highly descriptive. In general, the amount of experimentation is limited. Nevertheless, some modest advances in our knowledge regarding this model can be discerned. However, several concerns must be addressed.

The written text results in multiple questions and concerns. Some are listed here. Overall, there seems to be a lot of missing information and details.

The use of/or interpretation of data from the the Naïve Pups is not clearly explained, and is not included at all in the Abstract.

It is not immediately clear how this data (page 8) differs from previous studies. Please clarify.

Where is the data showing the fact that in vitro, "all these cancer cell lines tested could be killed"? (page 8, first line, second paragraph.)

It is not clear why the co-injection of tumors which do result in an infiltrate also controls the growth of another distinct tumor. Do the authors suspect a non-specific, antigen independent mechanism?
Where is the data described on Page 9, top (related to co-injection)?)

There is insufficient methodological information on the co-injection of tumor cells (and other assays used). The authors indicate that both were injected IP. But, under these conditions, is there a growth rate difference for the cell lines vs if they were injected alone. Is the retardation of one cell line due to immune mechanisms, or a growth retarding mechanisms coming from the other tumor cell?

The authors indicate that S180 only enhances the resistance of SR/CR mice to LL/2 locally. However, here they are (presumably) also comparing IP growth and solid tumor growth (although the details of the "remote" site are not provided.

The authors need more data to support their conclusion that “the ability to induce leukocyte infiltration along with the number of infiltrating leukocytes may be directly related to the number of cancer cells the SR/CR mice can resist...". I do not see any data that the there is actually survival of the 2nd (non-immunogenic) cells in the co-injection model. How do the authors know that they are examining a leukocyte infiltrate that is controlling both tumors?

The fact that a remote tumor survives suggests to this reviewer that the co-injection model (IP) may not result in the survival of both tumor cells).

Why do the authors say (top page 13) that the outcome of the co-injection experiment with S180 and CFAC was unexpected?

**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’