Reviewer's report

Title: Degranulating mast cells in fibrotic regions of human tumors and evidence that mast cell heparin interferes with the growth of tumor cells through a mechanism involving fibroblasts.

Version: 1 Date: 21 July 2005

Reviewer: Francesca Levi-Schaffer

Reviewer's report:

General

The aim of the work was to test the hypothesis that mast cells can suppress the growth of tumor via an indirect mechanisms involving peri-tumoral fibroblasts.

In the first part of their study the Authors performed an IHC survey of a variety of human tumors to determine the distribution of mast cells. It was found that mast cells in the human tumors examined are located almost exclusively at the edges and within the fibrosis stroma of the tumors. In the second part, in an in vitro system they assessed the activity of heparin, in the presence of fibroblast on the growth of an human breast cancer line. Heparin is shown to reduce the clongenic growth of breast cancer cells. Heparin is therefore proposed as a main mast cell derived mediator that can inhibit the growth of primary and metastatic tumor cells.

The topic of the study is important since few works to date have been performed on the role of mast cells in tumor growth, and the work is well performed.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The two parts of the work do not harmonically complement each other. The first is there mostly to demonstrate that mast cells must have an interaction with fibroblasts in tumors since they are mostly localized in fibrous areas. However no staining for heparin or mast cell signs of activation that would substantiate the hypothesis of heparin release, were performed. Also, one would expect an IHC staining of FGF-7 in these sections since they find that heparin effects are strengthened by the presence of this factor.

The second part focuses on the role of heparin and FGF-7 on the reduction of tumor cell clonogenic potential, after that the role of tryptase was excluded.

However, a number of other mediators from the mast cells and fibroblast side can influence tumor growth, such as COX metabolites, heparanase, etc. Therefore, the work needs strengthening to demonstrate the role of heparin either by adding to the system mast cells, or mast cell extracts/supernatants in the presence of polyarginine to neutralize heparin.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

What is the tissue origin of the “normal human fibroblasts”? An heparin dose-response would be useful, instead of a single (1 unit/ml) concentration.

Is “heparin mediated anti-tumor effect” specific or can heparin influence the proliferation of normal epithelial cells? This should be discussed.
Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

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