Reviewer’s report

Title: p53 expression is significantly correlated with high risk of malignancy and epithelioid differentiation in gastrointestinal stromal tumors. An immunohistochemical study with 104 GISTs.

Version: 2 Date: 21 April 2008

Reviewer: Jon Gunnlaugur Jonasson

Reviewer’s report:

The authors have in this study addressed an interesting area in the field of gastrointestinal stromal tumours. They aim to find out if genetic alterations leading to dysregulation of the cell cycle are associated with a more aggressive behavior of GIST. In this attempt they stain a little over one hundred such tumours with p53, bcl2 and cyclin D1.

Overall the manuscript is interesting and it is well written. Although there is not much in the way of new and unexpected results presented in this paper it is an important addition to the expanding literature of GIST. The text could be shortened somewhat without harming the message of the paper.

The English language in general is clear and correct although it needs some minor amendment.

Some additional criticism:

Major Compulsory Revisions:
1) What were the actual criteria used for including a tumour into this study? From the Material and methods chapter it appears that a c-kit positive staining was obligatory. For a significant part of the time period 1973-2001 the diagnosis of GIST was not possible and therefore it needs to be clarified how the tumours were retrieved and how the GIST diagnosis was made.

2) Since the study attempts to evaluate staining results with regard to aggressive tumour behavior and patients survival it would be of interest to present Kaplan-Meier survival curves in order to demonstrate the separation of p53 positive and p53 negative cases.

Minor Essential Revisions:
1) How were the tumours selected for the study? Were they all tumours of certain type in a specific pathology department? It would be interesting to have this clarified for epidemiological interests in an assessment of the data.

2) References are needed for a statement like this one: “Because 50% of GISTs become malignant…….” This is actually a debatable statement and should perhaps be rephrased accordingly.

3) Much of what is being written within the background (introduction) chapter should preferably be presented within the Material and Methods chapter. There is
a rather detailed description of what actually was done in this study presented within this chapter of the manuscript. This should preferably be presented in the Materials and Methods chapter and possibly shortened.

4) Each tumour apparently was evaluated by two pathologists with regard to assessing certain pathological parameters. How was that actually performed? Did they evaluate the specimens together with a joint decision or separately? If the latter was the case how was the final decision made?

5) It needs to be added to the Material and Methods chapter that mitoses were evaluated as other pathology parameters.

6) CD34 staining is being reported in the results chapter although not mentioned in the Material and Methods chapter.

7) The conclusions in the main text should not imply an association between positive p53 staining and intestinal location since this did not prove significant in the paper.

Discretionary Revisions:

1) Frequently sentences are being initiated by a numerical number. In general I would attempt to rephrase these sentences and avoid that.

2) I would recommend rephrasing the first sentence of the conclusions both in the abstract and the main text.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests