Reviewer's report

Title: Kinetics of cancer

Version: 1 Date: 25 July 2005

Reviewer: Darryl Shibata

Reviewer's report:

General
The reviewer apologizes for the delay, but I was waiting for reference 6 to be published in order to evaluate the data used in this manuscript.

The authors apply a quantitative approach (ie Armitage-Doll type model) usually used with human data to mouse cancer models. Essentially frequency-age data can be analyzed to infer cancer dynamics. Overall this is an excellent idea because it may more readily translate concepts between human cancers and mouse models.

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

I have several comments, which mainly address some of the practical difficulties of using this type of analysis on mouse models.

1) One common assumption is that the gap between transformation and “discovery” is small, because one can only document when a cancer is found and not when transformation occurs. For humans, this gap is likely to be small (perhaps a year?), which is small relative to age. For example, one year is 2% of a 50 year old. However, in the mouse models, tumors are found with median ages of a few months. For Mhl1-/-, the median is about 8 months. Even if the cancers transform a month before discover, the gap is relatively large (12% of a lifetime at 8 months), and proportionally more of a problem with younger mice. It seems appropriate to comment on the this limitation, and perhaps point out that better data (at least for this type of analysis) could be obtained by killing asymptomatic cohorts of mice at different ages.

2) The data used for the GI “cancer” analysis (ref 6) appears to combine adenomas and cancers. For example, Table 1 in ref 6, GI tumors in Mlh3-/ mice consists of 9 adenomas and 4 cancers. Analyzing adenomas and cancers together does not seem appropriate for log-log plots, and the reasoning for this combination should be explained more fully.

3) The limitations of log-log plots for relatively small numbers of tumors should be discussed, given that human data sets typically contain thousands of individuals whereas most mouse studies contain less than 50 individuals. Specifically, how many tumors are needed to perform a reasonable quantitative analysis?

4) It would be interesting to calculate or estimate “n” for the different mouse models, given that “n” is typically 5-7 for human colorectal cancers.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) Figure 1: “a” and “b”---- the Y-axis is mislabeled
2) Figure 2 should be better labeled. What exactly do the symbols indicate?

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