Reviewer's report

Title: Neoplastic transformation of rat liver epithelial cells is enhanced by non-transferrin-bound iron.

Version: 2 Date: 27 November 2007

Reviewer: Kyle E Brown

Reviewer's report:

General
The authors have provided a reasonable response to the critiques, although the use of the MTT assay to address the issue of cytotoxicity is not wholly satisfactory. The MTT assay measures a metabolic activity (reduction of a tetrazolium compound) that is assumed to be proportional to the number of cells present. In the current work, the MTT assay confirms the the overall result of the cell counts but does not provide additional information regarding the mechanism by which iron acts as a tumor promoter. This issue would be more appropriately addressed by measurements of cell membrane integrity (e.g., Trypan Blue exclusion, LDH release, etc.) or, better yet, reproductive integrity (clonogenic survival). Since the effects of high-dose FAC on cell number were apparent as early as 3 days, these parameters might be informative after a single exposure to FAC.

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

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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)

On the top of page 16, the authors make reference to "local NTBI concentrations that exist in necrotic regions of an iron loaded cirrhotic liver." While I accept the point regarding potential differences in iron citrate levels between the liver and the periphery, the implication that there is widespread necrosis in iron-loaded liver (whether human disease or animal models) in incorrect and may be misleading to readers who are not expert in this area. This should be changed.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
**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.