Reviewer's report

Title: Autophagy and apoptosis-related genes in chronic liver disease and hepatocellular carcinoma

Version: 2 Date: 10 May 2012

Reviewer: Muriel Priault

Reviewer's report:

The article by Kotsafti et al, entitled « autophagy and apoptosis-related genes in chronic liver and hepatocellular carcinoma » investigates the correlation, if any, between one autophagic gene (beclin 1) and some pro- or anti-apoptotic proteins of the Bcl-2 family. The purpose is to address the debated question of the interplays between apoptosis and autophagy, with respect to the healthy vs pathological status of liver samples.

The article is on the whole very well written. A fair confrontation of the data available in the literature is provided. The topic addressed is well delineated, and the methods used are adequate and sufficiently described. The data presented are convincing, and most of all, they provide information which have either never been investigated so far, or data which are at odds with previous reports thus adding a useful contribution to the scientific debate.

The discussion would benefit from more hindsight on some points which will be specified below.

In line with this, the abstract does not recapitulate all the noteworthy pieces of information: notably, no mention is done of the results obtained with Bcl-2.

Major Compulsory Revisions

1- Figure 1:
Levels of mRNA for Beclin 1 seems to show a stronger correlation with Bad than with Bcl-xL. This could have drawn a more striking graph than the plot presented in figure 4. Although it makes sense to assess the correlation between beclin 1 and bcl-xl with regards to their ability to interact physically, it is also relevant to view beclin 1 and bad as competitors for Bcl-xl and therefore assess their correlation.

2- The reader's attention might be drawn also to the fact that Bcl-2 and Bcl-xL, which are often looked at as redundant proteins show quasi opposite profiles on figure 1. The authors are encouraged to comment on that point in the discussion section, just as they did for Bax and Bak.

3- Figure 3:
Moreover, it is necessary to show the expression levels of the protein Bcl-xL, to confront extensively figure 3 to figure 1. This will help analyze throughly the correlation assayed throughout the manuscript.
4- Figure 3: Finally, since the Material an Methods section mentions a densitometric analysis of the western blots, providing a quantification on figure 3 would give more strength to the work.

Minor Essential Revisions :
the statement that beclin 1 is « the main autophagic agent » (as can be read both in the abstract background and discussion) : several other ATG genes are known to be essential to either the onset or the execution of autophagy ; therefore, this should be rephrased.

Minor concern not for publication:
The materials and methods section shows inconsistent pieces of information: the primers section mentions sequences for p53, p21 and Bl-1, while no related data is presented in the result section.
Same observation for the western blot section mentioning p53 and Bl-1.
Finally, a densitometric analysis is evoked, which is not shown in any graph.

Level of interest: An article of importance in its field

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 interest