Reviewer’s report

Title: NPC1L1 knockout protects against colitis-associated tumorigenesis in mice

Version: 5 Date: 15 January 2015

Reviewer: Robert Eferl

Response to authors (points of Major Compulsory Revisions)

1) The reviewer appreciates that littermates have been used for the tumor experiments which is essential and now clarified in the methods of the revised manuscript. The reviewer assumes that the last sentence of the authors’ response (Regretfully, we didn’t use heterozygous knockout mice in this study) should mean that no heterozygous mice have been used which is, however, not a drawback.

2) The reviewer did not fully understand the explanation of the authors “As shown in Fig 3A, that N-cadherin was not detected in membrane proteins from adjacent colorectal mucous membranes and tumors indicated that samples should not be contaminated with interstitial tissue”. Because N-cadherin is neither present in the membrane fractions of normal tissue nor tumor tissue, a mixture of normal and tumor tissue would also not display detectable expression. The absence of N-cadherin can therefore not be used as a valid marker to exclude contamination. IHC-staining is still an option to address this issue.

Response to authors (points of Minor Essential Revisions)

1,2) The language has improved significantly and the spelling mistakes were replaced.

3) The additional explanations in the Legend of Supplementary Figure 1 are appreciated but it is still unclear why some of the parameters (e.g. length of small intestine) have been measured (despite of the considerable length of the legend). Moreover, the legend is hardly readable and contains many typos. Proofreading by a native speaker (like it was done for the main manuscript) is recommended. Can the authors find a way to express the main message in one or two sentences?

4) The reviewer trusts the authors that the livers of NPCL1-/- mice are not bigger than those of controls. It is not meaningful to show the same livers from two different angles. Supplementary Figure 1F should be deleted to avoid misleading of readers.

5) In the original manuscript, Figure 4 had a meaningful title but no further explanation. In the revised version, the figure is called “Western blot” and a meaningful explanation is included. A meaningful title should also be provided.
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

no competing interests