Reviewer's report

Title: A redundant role for dectin-1 in experimental colitis models.

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Reviewer: Colin de Haar

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A redundant role for dectin-1 in experimental colitis models

In this manuscript S.E.M Heinsbroek et al. examine the role of dectin-1 in two established mouse colitis models. An increase of dectin-1 expressing cell has previously been reported to occur during intestinal inflammation. As such, further assessment of its role is of great interest. With their research Heinsbroek et al also touch upon the interesting question whether fungi as part of the microbiota contribute to IBD pathogenesis.

Major Compulsory revisions:

1: In figure 1A and 1B the expression of dectin-1 in colon of normal WT and DSS colitic mice is shown. The pictures are of very bad quality and there is a lot of tissue damage after the cryosection that make it impossible to see what kind of cells is expressing the dectin-1. Double staining on this tissue to answer whether we are looking at macrophages, neutrophils or other cell is needed to support the use of macrophages in the in vitro experiments.

2: In figure 1C and D the cytokine production by macrophages isolated from wt and dectin-1 deficient mice is shown. From the material and methods section I understand that the isolated macrophages were first cultured ON and then plated out and stimulated. This process could greatly affect the expression of various PRR and thereby affect their response to the various ligands. Since the hypothesis for the mouse colitis experiments seems based on these observations the changes in PRR expression between the freshly isolated macrophages and those stimulated in vitro should be presented. Also the effect on cell death by the various compounds, especially that of the cecum preparation should be reported.

3: In comparison to zymosan or the LPS stimulation the macrophages make very little TNF-alpha in response to the cecum preparation. An explanation should be provided.

4: Based on the in vitro observation the authors hypothesize that the dectin-1 deficient mice will have a less severe colitis. Their data showed a slight decrease in IL-10 and a stronger effect on TNF-alpha. Based on this observation it might be even more likely that the mice will have a milder colitis because there will be relatively more IL-10 then TNF-alpha. This alternative hypothesis should be addressed.
5: The role of mannan binding lectin (MBL) has previously been studied in DSS colitis. Mice deficient for MBL did not show any difference with regard to DSS colitis, but had enhanced disease severity when DSS was combined with C. albicans infection in MBL-deficient mice. Does the fungal part of microbiota present in mice represent those in humans? Is the contribution of dectin-1 simply not picked up because the right fungus is not present in the current models? How does infection with C. albicans influence the DSS colitis in dectin-1 deficient mice?

6: Is there a difference between cecum preparations from WT vs dectin-1 deficient mice and control vs DSS colitis?

7: The authors discuss that other PRR may compensate for the loss of dectin-1. This is in line with the idea that there are other PRR involved in the recognition and response to fungi and food components. Does anti-fungal treatment affect DSS colitis?

8: The rationale for using the H. hepaticus model is not clear. Especially since these mice are treated with anti-IL-10 as cytokine that seems reduced in dectin-1 deficient macrophages exposed to feces.

Minor essential revisions:

1: In their discussion the authors state that although PRR are important in human IBD, their data suggest that dectin-1 is redundant in intestinal inflammation. The last part should be extended with.....experimental colonic inflammation induced by either DSS or H. hepaticus in mice. Because based on this study we cannot draw conclusions for the human situation.

2: The role of dectin-1 in TLR-2/6 signaling should be discussed

3: The current study only addressed the role of dectin-1 in the innate component of intestinal inflammation. We cannot draw any conclusions on its potential effect on the adaptive immune system. Since this latter plays a very important role in established IBD, this should be discussed.

Discretionary revisions

1: Some data on ROS production by the macrophages in vitro would be nice.

**Level of interest:** An article of limited interest

**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:**