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Title: Alcoholic Liver Disease: Current Insights into Cellular Mechanisms

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Comments:

1. Please add page and line numbers.

Page and line numbers have been added.

2. In the EPIDEMIOLOGY AND PREVALENCE section, why have the authors discussed up to 2016 and not more recent years?

On page 6, ONS data has been added for the UK up to 2020. A 20% increase in ALD deaths occurred from 2019-2020 with a 72% increase in deaths from 2001-2020. Projected prevalence stats for the USA have been included up to years 2040. The WHO report is published every 4 years and thus the most recent WHO data is included.

3. Please explain how table 1 was evaluated and prepared?

The models for staging of ALD were compared using the different variables for each model to develop prognostic scoring. The references used for each model to define and compare the variables as well as the scoring cut off values have been added to column 1.

4. The inflammasome section needs to be discussed in more detail.

The inflammasome section has been discussed in more detail on pages 10-11. Inflammasome components have been discussed in more detail as well as their assembly. Further discussion including the activation of pro-inflammatory cytokines and infiltration of immune cells has been included. Research showing IL-1 $\beta$  signalling and elevated inflammasome components (including NLRP3, ASC) have been discussed in patients with AH and in liver fibrosis.

5. What about the impact of other cytokines and inflammatory mediators?

The impact of relevant cytokines and inflammatory mediators such as TNF- $\alpha$ , LPS are discussed throughout the review.

6. The Adaptive Immunity section does not describe sufficiently the role of alcohol consumption on T cells and rather explains more the TH17 subfamily of T cells.

The different phenotypes of T cells implicated in ALD have been discussed in more detail as well as chemokines such as CCL5. Antigen-specific activation and proliferation of CD4<sup>+</sup> T cells via the presentation of neoantigens caused by protein adducts from alcohol metabolism has been included as well as non-specific activation via cytokines, PAMPs and DAMPs. The involvement of T cells in the progression of ALD requires further research. See pages 14-15.