Reviewer's report

Title: The host response to the probiotic Escherichia coli strain Nissle 1917: Specific up-regulation of the proinflammatory chemokine MCP-1

Version: 1 Date: 3 October 2005

Reviewer: David R Mack

Reviewer's report:

General

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

1) Abstract: This needs to be re-written as in the current form it is too general for the research conducted. For example in the background “molecular mechanisms…remain unclear” ignores a substantial amount of research. Was there a more specific aim rather than just a fishing expedition of 22,000 genes? The results do not include anything about the 2nd cell line or the mice findings. The final sentence is not a conclusion of the research conducted but speculation.

2) Background: There is no proof in humans that bacteriocins or microcins are important in bacterial interference but merely speculated.

3) Background: The last sentence “counteraction of inflammatory processes by stabilization of the gut microbial environment and the intestine’s permeability barrier” does not make sense. Clarification of what is trying to be said is needed.

4) Methods: Were pH determinations made before and after the bacterial incubation period? If there was a pH change, were the alterations in gene expression on the basis of the pH change?

5) Methods: DTT treatment of intestinal pieces would be expected to do far more than remove excess mucus. Was simple washing with PBS not enough?

6) Methods: Explain why the 10 genes were of major interest? Were they of major interest at the outset of the experiments? Did they gain interest as they had some of the most prominent changes among the different genes whose expression levels were modulated by EcN?

7) Conclusions: Page 18, last paragraph. The Authors speculate that upregulation of MCP-1, MIP-2a and MIP-2b upon contact with the probiotic EcN might reflect being part of the host defense process against pathogenic bacteria through the establishment of a protective immunologic barrier. A more direct conclusion is that the removal of the protective mucus layer by the various methods used for this study and then exposing to a gram negative bacteria and an E. coli strain lead to the response against EcN and should be considered by the authors. Additionally, there was no evidence provided that a protective immunologic barrier was established with the current experimentation.

8) Abstract: Conclusion. As valid a speculation as the last sentence currently in the abstract is that the use of EcN could lead to worsening of mucosal inflammation in those with a reduced mucosal barrier. While the authors may choose to include this speculation in the discussion neither the current last sentence of the current abstract nor the speculation in this point should be part of the abstract.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
9) Background: It is not clear what the authors mean by “probiotic genes”. The sequence of some microbes used as probiotics have been delineated.

10) Background: The authors should include the dose off mesalamine (1,500 mg) used in the comparative trial and the recurrence rate (approx. 35%) as the former is quite low and the latter is high.

11) Background: “a semi-rough … known protein toxins” is written awkwardly and should be re-written.

12) Methods: Caco cells are well known to have significant alterations depending on the passage number. Details of the cells should be included.

13) Methods: What specifically was the inoculum corresponding to the low bacterial MOI?

14) Methods: It is not clear why lower bacterial numbers were required with intestinal pieces if they were already colonized? Please clarify.

15) Methods: It should be described that CM stands for conditioned media.

Discretionary Revisions (which the author can choose to ignore)
16) Background: It is suggested the authors use the WHO/FAO definition.

17) Background: First paragraph, 3rd sentence “To be treated” could be removed since probiotics are not always used to treat conditions but also used to maintain ‘health’.

18) Methods: What difference are photomicrographs AI, II, and III trying to depict? Are they really needed?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No

Declaration of competing interests:
Reviewer has previously received research grants from organizations associated producing other probiotic microbes than currently under study.