

## Author's response to reviews

**Title:** Commentary: Mechanistic Considerations for Associations Between Formaldehyde Exposure and Nasopharyngeal Carcinoma

### Authors:

Chad M Thompson ([cthompson@toxstrategies.com](mailto:cthompson@toxstrategies.com))

Roland C Grafstrom ([Roland.Grafstrom@ki.se](mailto:Roland.Grafstrom@ki.se))

**Version:** 3 **Date:** 1 November 2009

### Author's response to reviews:

Dear Editor:

Please find included the revised manuscript "Commentary: Mechanistic Considerations for Associations Between Formaldehyde Exposure and Nasopharyngeal Carcinoma" (MS: 8656361972995718). This manuscript has been revised in accordance with the very minor suggestions made by the reviewer, as well as the accompanying suggestions for conforming the article to the journal style. Given the very favorable review of the manuscript, we made very few changes to the manuscript as a whole, which are outlined below.

Sincerely,

Chad M. Thompson

Reviewer 1:

A list of abbreviations...Abbreviations were added at the end of the Conclusion section per the journal's instructions.

Figure deserves a drastic shake-up...We took the reviewer's advice to make a three panel figure. Panel (a) describes the dual role ADH3 plays in formaldehyde metabolism and nitrosothiol homeostasis. Panel (b) shows how the EBV protein LMP1 and NO both converge on NF- $\kappa$ B pathways. It also summarizes experimental data that show that depletion of NO reactivates EBV. Per the reviewer's suggestion, panel (c) simply combines panels (a) and (b), with minor modifications.

Needs a clear figure legend...Considerable attention was paid to expanding and clarifying the legend.

In addition to these suggested changes, based on the Reviewer's comment that the mechanisms described might also apply to leukemia, we added the following sentence at the end of the Conclusion section: "Finally, the mechanisms presented herein might also be operative for other diseases associated with formaldehyde exposure that have etiologies involving EBV, such as lymphoproliferative disorders."

#### Journal Style:

All changes suggested to conform to the journal style were made with one exception. It was stated, "The format of the abstract is background, methods, results and conclusions" and "Please format the manuscript into a background, methods, results and discussion and conclusions sections." However, this article is clearly a Commentary and not amenable to such changes. Instead, we have formatted the article in accordance with the guidelines for a Commentary in Environmental Health. In addition, we removed non-standard abbreviations from the abstract.

#### Additional Non-substantive Change:

Introduction, second paragraph, first sentence: we edited the language of this sentence to improve the flow of the text