Author's response to reviews

Title: Fetal exposure to bisphenol A enhances the development of experimental asthma

Authors:

Yoichi Nakajima (ynakaji@fujita-hu.ac.jp)
Randall M Goldblum (rmgoldbl@utmb.edu)
Terumi Midoro-Horiuti (tmidoro@utmb.edu)

Version: 3 Date: 20 January 2012

Author's response to reviews: see over
January 20, 2012

Dear Editor,

We would like to resubmit a revised manuscript “Fetal exposure to bisphenol A enhances the development of experimental asthma” for publication in *Environmental Health*. We appreciate the helpful comments from the reviewers and have used them to improve and clarify the manuscript. Described below are the answers to the reviewer’s questions, as the editor requested.

“Major comments:
“Airway reactivity is only one measure of allergic lung disease. The paper would be stronger if the authors included other pulmonary endpoints such as immune cytokines, cell differentials in the lung, pathology etc.” “Results of analysis of allergic inflammation in the pups are not presented or discussed, but should be.”

Response: We have included a new figure (Figure 3) showing eosinophil counts in the BAL fluids. We previously attempted to measure immune cytokines in the BAL fluid from the pups by Bioplex. However, most of the levels were below the detectable range even in the OVA sensitized pups from BPA exposed mothers pre and postnatally. This finding may be due to poor recovery of fluid from the lining fluid of the peripheral airways, but proving require tissue sampling, which is beyond the scope of the current manuscript.

“The levels of BPA are given for the pups that were exposed in utero and in breast milk. Some idea of BPA in the breast milk only and control animals would be good addition for comparative purposes.”

Response: We agree that more detailed measurement of BPA metabolism in our model would be interesting, but feel this is beyond the scope of the current manuscript. We have added a statement indicating that an alternative explanation for the differences between BPA effects *in utero* and postnatally via breast milk could be due to the extent of BPA exposures.

“Some discussion of potential molecular mechanisms by which BPA causes this effect is needed.”

Response: The proposition that BPA acts via its known estrogenic activity is discussed in the several places in the introduction. We have referred to one of our previous studies of *in vitro* effect of environmental estrogens on mast cells to suggest that BPA’s effects are most likely mediated through ERα on immune cells. Further speculation about mechanism is probably not appropriate at this point.

All of the minor comments were answered in the manuscript.

We hope that you will agree that these important observations provide important new information to the controversy related to the potential pathological effect of BPA, as well as, a potential mechanism for enhanced susceptibility to prenatal exposure we noted. We feel that studies such as these may help us justify human studies that may provide new understanding about environmental causes of the increased frequency and severity of asthma in children, and thereby, promote new approaches to prevent excess asthma morbidity.
Sincerely,

J. M. Horiuti

Terumi Midoro-Horiuti
Associate Professor