Author’s response to reviews

Title: Significant cross reactive antibodies to influenza virus in adults and children during a period of marked antigenic drift

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Version: 4 Date: 13 May 2014

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13.5.2014

Dear Editor,

Thank you for your email. We corrected the manuscript in complete accordance with the editor comments. We remove the red font of the previous revision and added the requested corrections (the new changes are marked in red).

I hope that you will now accept this manuscript for publication.

Best wishes,
Michal

Comment: "I just want to readdress that the authors need to clarify the immunization history of those children, otherwise the cross-reactive antibodies could be associated with vaccination. In addition, the authors need to refer some literature when introducing the antigenic relatedness among those H3N2 viruses circulated since 2000. Some of the conclusion is inaccurate in the current manuscript."

Response: The children were not vaccinated or immunized against influenza. We now better emphasize it in the material and methods section, page 5, lines 97-98. To verify that indeed the children studied here were not vaccinated against influenza we tested the sera of the children for recognition of the H1N1 virus (A/New Caledonia/20/1999) that was applied in the vaccine given in the study period and against the influenza B viruses (B/Sichuan/379/99, in 2001-2002 and B/Malasia/2506/04 in 2006-2007) and found them to be negative. We now
mention it on page 8 lines 153-158. We also now discuss it in length in the discussion section, page 11, lines 226-231. I hope this is sufficient and I will be happy to clarify this further if needed.

Regarding the antigenic relatedness among the H3N2 viruses circulated since 2000. We have added a new Figure 1 in which we made a phylogenetic tree based on hemagglutinin sequence demonstrating the A/Sydney and A/Panama are closely related while all other viruses are substantially different and are closely related to A/Wisconsin. We also refer to some literature as requested please see page 7 lines 136-147. Please see also discussion page 11 lines 220-223.