Author's response to reviews

Title: Breast feeding, breast milk and viruses.

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These are point by point comments made in response to the Reviewer’s report (Professor Generoso Bevilacqua) dated 5 May, 2007.

We are most grateful for the very detailed consideration of the manuscript by Professor Bevilacqua.

1. Information produced about exposure to colostrum is surely relevant.
   We completely agree. Hence the need for this study.

2. To me, this information seems relevant because it suggests a route for the transmission mother-baby of viruses in general.
   We completely agree.

3. Personal opinion 1: MMTV could have a role in human breast carcinogenesis.
   We agree.

4. Personal opinion 2: the hypothetical transmission is not via milk.
   In our view various hypotheses for the transmission of MMTV to humans can be postulated including human milk.

5. I do agree on the fact that gastric juice does not necessarily kill everything, but in the specific case there are several data about the fact that a large number of viral particles and a prolonged feeding are necessary to have a “cancerogenetic” infection in mice.
   We agree.

6. There are several data against the milk-hypothesis for human breast cancer, mainly:
   - the epidemiological studies about breast feeding protection.
     We agree.
   - the fact that viral particles were never convincingly demonstrated in human milk.
     We agree in principle, however, we have re-read in detail the Moore et al studies all from about 1970 to 1974. While not conclusive they are suggestive that viral particles in human milk are very similar to MMTV viral particles in mouse milk.
     The data of C Ford can only partially taken into consideration because without peer review; moreover it looks strange to me that after 3 years they are not published yet.
     We completely agree. Yes it does look strange re no publication of the Ford data. The reason is that funding of these projects ceased and the work was discontinued. Because the issue could cause such social distress it was considered very important to replicate the Ford results before seeking publication.

7. The following sentence does not seem to me opportune: “In contrast to this evidence, there is consistent evidence that the risk of breast cancer is double or more in daughters of women with breast cancer, a fact not accounted for by the presence of BRCA or other familial genes. This major contradiction in the evidence has yet to be explained.”
   - to find families with a high incidence of breast cancer with no mutation in known genes is not rare. In this case, there are at least two possibilities: a. it is a sporadic disease; b. it is an hereditary disease due to the involvement of genes. To rule out the second one, an accurate genetic analysis of the family has to be done.
   - Both our view and that of the reviewer are of course matters of opinion only. However we have chosen to follow his advice and we have eliminated this section of the manuscript.
   - moreover, of the 3 cited papers (3,4,6), I was not able to find the first one and I was not able to find in the second two any statement about what reported in the sentence cited above.
     Reference 3 is a major meta-analysis published as cited in the Lancet. I have rechecked the original article the citation is correct (but the authors are not consistently listed in Medline). Reference 5 (Titus-Ernstoff et al 1998) reports confirmation of previous studies “As expected, family history of breast cancer…… were associated with breast cancer” (see table 2 for data). However, the
reviewers opinion is accepted and we have “softened” and as above eliminated most of the comment in the revised manuscript.

8. About immunity and viral infection ….
We have followed the reviewers additional ideas below and accordingly we have eliminated the comments re immunity.

9. The reviewer suggests rewriting the paper along different themes. We have followed his ideas as exactly as possible.

10. We have followed all the suggestions made by the reviewer.

11. We have adopted the Title of the manuscript suggested by the reviewer. It is now “Breast feeding, breast milk and viruses”.

The reviewer has stated he would be glad to receive e-mails directly from the authors. I sent the revised manuscript to Dr Bevilacqua but there has been no response. Maybe he is away. As the deadline for resubmission is near we have resubmitted without waiting further for his response.