Author's response to reviews

Title: Loss of Annexin I Expression in B-Cell Non-Hodgkin's Lymphomas and Cell Lines

Authors:

Prof Jamboor K Vishwanatha (jvishwan@unmc.edu)
Eric Salazar (ers2010@med.cornell.edu)
Dr Velliyur K Gopalakrishnan (vkgopal@unmc.edu)

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Dear Editor:

Thank you for considering our manuscript for publication. The manuscript got enthusiastic response from the reviewers. Reviewer 1 considered this a very nice paper and wanted us to update the literature list. Reviewer 2 had some comments. We carefully considered the comments of the reviewers and made appropriate changes, including providing additional data. With these revisions, we hope the manuscript is acceptable for publication.

Responses to critiques of Reviewers

Reviewer 1:
1. For completeness, the authors should include a few of the most recent new publication on annexin I expression changes in human tumors.

We have revised the introduction section to include new publications that have appeared since our original submission.

Reviewer 2:

Minor Essential Revisions
1. The conclusion in the abstract is too broad for the data presented.
With the additional data presented as per the reviewer’s suggestion, we believe our conclusion is still valid and indicates the importance of annexin I in B-cell lymphoma development.
2. The descriptions of cell lines used are imprecise or incorrect in some cases.
We have revised the descriptions of the cell lines and provided details. TK-6 is a lymphoblast cell line that is heterozygote for thymidine kinase. TK-6 is a derivative of the WI-L2, a lymphoblast cell line. DW-10 and WI-L2 are EBV transformed mature B-cell lines. PBE-1 and NALM-6 are both precursor B cell acute lymphoblastic leukemia cell lines. NALM-6 is a long established cell line and PBE1 is a line established short term from a patient with ALL at the University of Nebraska Medical Center.
3. The authors say that all the B-cell lines are negative for Annexin I by RT-PCR, but it looks like there are weak bands present for Namalwa and DW-10 and may be others.
We have performed RT-PCR several times to confirm our results and we find that there is no annexin I expression in the indicated cell lines.
4. The 3 lymphomas in Fig. 7 all look follicular to me. Maybe they could just be described as B-cell lymphomas.
The tissues used in our studies have been examined by 2 independent pathologists who are experts in Lymphomas. The pathological classification was according to these experts.

Major compulsory Revisions
1. The title should be changed to Absence of Annexin I since no loss has been demonstrated in the
We have modified the title as per the reviewer's suggestion.

2. I am not convinced that the authors have demonstrated any annexin I expression in normal B-cells.

In response to the reviewer's comments, we performed additional experiments and these data are shown as Figure 1b. We isolated normal B-cells from PBL of a volunteer, and immunoblot analysis clearly indicates presence of annexin I in these cells (Lane 1, Figure 1b).

3. It may be worthwhile to try a follicular B-cell lymphoma line or mature B-cell line since all the lines tested are immature and the result may be different.

In response to the reviewer's suggestion, we performed immunoblot analysis of 2 additional cell lines, DHL-16 and Raji. Data from these are included in Figure 1b.