Reviewer's report

Title: Dronabinol has preferential antileukemic activity in acute lymphoblastic and myeloid leukemia with lymphoid differentiation patterns.

Version: 1 Date: 9 July 2015

Reviewer: Hideki Yagi

Reviewer's report:

Major Compulsory Revisions

General comments
This manuscript describes that Dronabinol, synthetic tetrahydrocannabinol (THC) has the cytotoxic activity to lymphatic leukemia cells and AML cells expressing lymphatic markers by preclinical examinations. THC shows cytotoxicity by CB2 receptor.

The cytotoxic effect of THC on Jurkat cells is confirmed by authors, generalized in leukemia and discussed the applications of Dronabinol. The main research findings of this paper will be important for the medical Marijuana as anti-cancer drug.

Do myeloid or lymphoid cells in healthy donors express CB1 or CB2 on cell surface? Is there a difference in expression levels of CB1 or CB2 on the cell surface between AML patient and healthy donor?

An FACS profiles of more typical apoptosis (Annexin V+/PI-) is provided if you acquire data in shorter incubation time (12 or 24 hrs).

In Fig. 3, why can you identify AML1-13 or ALL1-13 cells with a clonal cell?

Statistical analysis is incorrect. Cytotoxic data must be analyzed by Williams' test, not Student's t-test, if prove dose-dependency (Figs. 1A, 1C, 2A, 2D and S1-S6). Statistical analysis should be corrected by a biostatistical professional if necessary.

In my opinion, a substantial revision is needed to make this manuscript suitable for publication.

Specific comments
1. In IC50, "50" has to be displayed text as a subscript.

2. In Fig.2, flow cytometrical analysis indicates that PI+ /Annexin V+ cells are dead or late apoptotic cells. Apoptotic cells are PI- / Annexin V+ cells. You should change the y-axis label of the bar graph into "Apoptotic cells (%)" from "Dead cells (%)".

3. In Fig. 3 A, C, D or E, you should change the numbers under FACS histogram into percentages.
4. In Fig. 4B, Western blot pattern is corrected to the position of cell name in anti-CB2.
5. In Fig. 5A & B, statistical analysis is necessary.
6. In Fig. 5B, you should change into the x-axis label of the bar graph appropriately.
7. In Fig. 5C right, are “Cleaved” and “Caspase 3” reverse positions?
8. In Methods, the second paragraph in “Cell lines” section is lengthy and repeat.

I hope that my comment is very useful for the improvement of the article.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.