Direct CD32 T cell cytotoxicity: implications for breast cancer prognosis and treatment.

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Scientific Editor: Novella Guidi

Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)
August 26, 2022

Re: Life Science Alliance manuscript #LSA-2022-01590-T

Dr. Giuseppe Sconocchia
CNR Institute of Translational Pharmacology (IFT), Rome Italy
Biomedicine
Via Fosso del Cavaliere 100
Rome, RM 00133

Dear Dr. Sconocchia,

Thank you for submitting your manuscript entitled "Antibody-independent antitumor effects of CD32-chimeric receptor T cells: implications for breast cancer prognosis and treatment." to Life Science Alliance. The manuscript was assessed by an expert reviewer, whose comments are appended to this letter. We invite you to submit a revised manuscript addressing the Reviewer comments.

To upload the revised version of your manuscript, please log in to your account: https://lsa.msubmit.net/cgi-bin/main.plex

You will be guided to complete the submission of your revised manuscript and to fill in all necessary information. Please get in touch in case you do not know or remember your login name.

While you are revising your manuscript, please also attend to the below editorial points to help expedite the publication of your manuscript. Please direct any editorial questions to the journal office.

The typical timeframe for revisions is three months. Please note that papers are generally considered through only one revision cycle, so strong support from the referees on the revised version is needed for acceptance.

When submitting the revision, please include a letter addressing the reviewer comments point by point.

We hope that the comments below will prove constructive as your work progresses.

Thank you for this interesting contribution to Life Science Alliance. We are looking forward to receiving your revised manuscript.

Sincerely,

Novella Guidi, PhD
Scientific Editor
Life Science Alliance

A. THESE ITEMS ARE REQUIRED FOR REVISIONS

-- A letter addressing the reviewers' comments point by point.
-- An editable version of the final text (.DOC or .DOCX) is needed for copyediting (no PDFs).
-- High-resolution figure, supplementary figure and video files uploaded as individual files: See our detailed guidelines for preparing your production-ready images, https://www.life-science-alliance.org/authors
-- Summary blurb (enter in submission system): A short text summarizing in a single sentence the study (max. 200 characters including spaces). This text is used in conjunction with the titles of papers, hence should be informative and complementary to the title and running title. It should describe the context and significance of the findings for a general readership; it should be written in the present tense and refer to the work in the third person. Author names should not be mentioned.
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B. MANUSCRIPT ORGANIZATION AND FORMATTING:
Full guidelines are available on our Instructions for Authors page, https://www.life-science-alliance.org/authors

We encourage our authors to provide original source data, particularly uncropped/-processed electrophoretic blots and spreadsheets for the main figures of the manuscript. If you would like to add source data, we would welcome one PDF/Excel-file per figure for this information. These files will be linked online as supplementary "Source Data" files.

***IMPORTANT: It is Life Science Alliance policy that if requested, original data images must be made available. Failure to provide original images upon request will result in unavoidable delays in publication. Please ensure that you have access to all original microscopy and blot data images before submitting your revision.***

Reviewer #1 (Comments to the Authors (Required)):

It has been shown that the Fc receptor CD16 can bind to surface ligands in addition to immunoglobulins, triggering the activation of NK cells and ADCC. In this novel and interesting paper, Sconocchia and coll, used CD32-CAR T cells that they previously generated to identify putative surface ligands recognized by the Fc receptor CD32 on tumor cells. They examined 20 distinct cell types of which 15 were cancer cell lines and demonstrated that CD32-CAR T cells recognize putative ligands on two triple negative cancer cell lines (MDA-MB-468 and MDA-MB-23), as well as other tumor cell lines, including HER2+ HCC-1954 cells, and CRC HT29. Importantly, CD32-CAR T cells did not recognize normal cell lines, such as primary fibroblasts and a myoblast cell line. The authors further performed differential gene expression analysis between cells positive and negative for CD32-CAR T cell recognition, identifying a number of potential candidate molecules. Finally, they showed that target cell expression of ICAM1 is essential for CD32-CAR T cells recognition.

This is a brilliant application of a novel biosensor for the identification of CD32 unknown ligands. Moreover, this work has also led to demonstrate a role of CD32-CAR mediated cytotoxicity independent from ADCC which may be important for therapeutic avenues of intervention. The experiments are extensive and convincing. The paper is well-organized and written. I have only minor suggestions that the authors may consider

1. In introducing Fc Receptors it is unclear whether the authors are describing human or mouse Fc receptors. The authors should clarify this from the beginning
2. In the beginning of the results, the authors say that they purified T cells for scRNA seq. It is unclear from where these cells were purified. From the xenograft mouse model in which the cells were transferred? From in vitro cultures with tumor cells?
Concern 1: in introducing Fc Receptors, it is unclear whether the authors are describing human or mouse Fc receptors. The authors should clarify this from the beginning.

Author’s reply: we have clarified the human nature of the Fc-CR utilized in our study. Please, in find the addition. Changes are indicated in red and are located in the abstract and introduction.

Concern 2: in the beginning of the results, the authors say that they purified T cells for scRNA seq. It is unclear from where these cells were purified. From the xenograft mouse model in which the cells were transferred? From in vitro cultures with tumor cells?

Author’s reply: a clarification sentence has been added to the beginning of the first paragraph of the result section in page 7.

Based on the guide lines of LSA policy, we had to shorten the title down to 100 characters without changing the meaning.
September 5, 2022

RE: Life Science Alliance Manuscript #LSA-2022-01590-TR

Dr. Giuseppe Sconocchia
Istituto di Farmacologia Traslazionale
Biomedicine
Via Fosso del Cavaliere 100
Rome, RM 00133
Italy

Dear Dr. Sconocchia,

Thank you for submitting your revised manuscript entitled "Direct CD32 T cell cytotoxicity: implications for breast cancer prognosis and treatment.". We would be happy to publish your paper in Life Science Alliance pending final revisions necessary to meet our formatting guidelines.

Along with points mentioned below, please tend to the following:

- please add a category for your manuscript to our system
- please add a callout for Figure 4F and Figure 7 to your main manuscript text
- please remove the panel A from the figure 7 legend; since this is the only panel, you do not need to label the panel individually

If you are planning a press release on your work, please inform us immediately to allow informing our production team and scheduling a release date.

LSA now encourages authors to provide a 30-60 second video where the study is briefly explained. We will use these videos on social media to promote the published paper and the presenting author (for examples, see https://twitter.com/LSAjournal/timelines/1437465065917124608). Corresponding or first-authors are welcome to submit the video. Please submit only one video per manuscript. The video can be emailed to contact@life-science-alliance.org

To upload the final version of your manuscript, please log in to your account: https://lsa.msubmit.net/cgi-bin/main.plex
You will be guided to complete the submission of your revised manuscript and to fill in all necessary information. Please get in touch in case you do not know or remember your login name.

To avoid unnecessary delays in the acceptance and publication of your paper, please read the following information carefully.

A. FINAL FILES:

These items are required for acceptance.

-- An editable version of the final text (.DOC or .DOCX) is needed for copyediting (no PDFs).

-- High-resolution figure, supplementary figure and video files uploaded as individual files: See our detailed guidelines for preparing your production-ready images, https://www.life-science-alliance.org/authors

-- Summary blurb (enter in submission system): A short text summarizing in a single sentence the study (max. 200 characters including spaces). This text is used in conjunction with the titles of papers, hence should be informative and complementary to the title. It should describe the context and significance of the findings for a general readership; it should be written in the present tense and refer to the work in the third person. Author names should not be mentioned.

B. MANUSCRIPT ORGANIZATION AND Formatter:

Full guidelines are available on our Instructions for Authors page, https://www.life-science-alliance.org/authors

We encourage our authors to provide original source data, particularly uncropped/-processed electrophoretic blots and spreadsheets for the main figures of the manuscript. If you would like to add source data, we would welcome one PDF/Excel-file per figure for this information. These files will be linked online as supplementary "Source Data" files.

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Reviews, decision letters, and point-by-point responses associated with peer-review at Life Science Alliance will be published online, alongside the manuscript. If you do want to opt out of having the reviewer reports and your point-by-point responses displayed, please let us know immediately.

Thank you for your attention to these final processing requirements. Please revise and format the manuscript and upload materials within 7 days.

Thank you for this interesting contribution, we look forward to publishing your paper in Life Science Alliance.

Sincerely,

Novella Guidi, PhD
Scientific Editor
Life Science Alliance
September 7, 2022

RE: Life Science Alliance Manuscript #LSA-2022-01590-TRR

Dr. Giuseppe Sconocchia
Istituto di Farmacologia Traslazionale
Biomedicine
Via Fosso del Cavaliere 100
Rome, RM 00133
Italy

Dear Dr. Sconocchia,

Thank you for submitting your Research Article entitled "Direct CD32 T cell cytotoxicity: implications for breast cancer prognosis and treatment.". It is a pleasure to let you know that your manuscript is now accepted for publication in Life Science Alliance. Congratulations on this interesting work.

The final published version of your manuscript will be deposited by us to PubMed Central upon online publication.

Your manuscript will now progress through copyediting and proofing. It is journal policy that authors provide original data upon request.

Reviews, decision letters, and point-by-point responses associated with peer-review at Life Science Alliance will be published online, alongside the manuscript. If you do want to opt out of having the reviewer reports and your point-by-point responses displayed, please let us know immediately.

***IMPORTANT: If you will be unreachable at any time, please provide us with the email address of an alternate author. Failure to respond to routine queries may lead to unavoidable delays in publication.***

Scheduling details will be available from our production department. You will receive proofs shortly before the publication date. Only essential corrections can be made at the proof stage so if there are any minor final changes you wish to make to the manuscript, please let the journal office know now.

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Again, congratulations on a very nice paper. I hope you found the review process to be constructive and are pleased with how the manuscript was handled editorially. We look forward to future exciting submissions from your lab.

Sincerely,

Novella Guidi, PhD
Scientific Editor
Life Science Alliance