Crystal structure of Staufen1 with a physiological RNA sheds light on substrate selectivity

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Report:

(Note: Letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)

Please note that the manuscript was previously reviewed at another journal and the reports were taken into account in the decision-making process at Life Science Alliance. Since the original reviews are not subject to Life Science Alliance's transparent review process policy, the reports and author response cannot be published.

1st Editorial Decision 31 August 2018

August 31, 2018

Re: Life Science Alliance manuscript #LSA-2018-00187-T

Fulvia Bono

Dear Dr. Bono,

Thank you for transferring your manuscript entitled "Crystal structure of Staufen1 in complex with a physiological RNA sheds light on substrate selectivity" to Life Science Alliance. The manuscript was assessed by expert reviewers at another journal before, and the editors transferred those reports to us with your permission.

The reviewers at the other journal appreciated that you provide the first crystal structure of a tandem dsRBD construct from Staufen1 with a natural substrate. However, they also thought that the biological relevance of your findings remains unclear at this stage, and that the conclusion that RNA binding by Staufen1 requires a sequence-specific RNA is not sufficiently supported. Both reviewers provided constructive input on how to revise your work to strengthen your conclusions. Based on these reports already at hand, we would like to offer publication of a revised version of your manuscript in Life Science Alliance. Please provide a point-by-point response to the concerns raised and accordingly text changes as well as more definitive proof for base-specific interactions (following the constructive input of both reviewers). We think that testing RNA mutant versions that probe specifically the highlighted GC base pair in the 3'-UTR, as suggested by Reviewer 2, is a

straightforward experiment that would elevate your paper significantly (or allow changing your interpretation).

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.

We would be happy to discuss the individual revision points further with you should this be helpful.

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.

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

Sincerely,

Andrea Leibfried, PhD
Executive Editor
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2nd Editorial Decision 27 September 2018

September 27, 2018

RE: Life Science Alliance Manuscript #LSA-2018-00187-TR

Dr. Fulvia Bono
University of Exeter
Living Systems Institute
Stocker Road
Exeter EX4 4QD
United Kingdom

Dear Dr. Bono,

Thank you for submitting your revised manuscript entitled "Crystal structure of Staufen1 with a physiological RNA sheds light on substrate selectivity". The reviewers who evaluated your work at another journal before re-assessed this version, and as you can see below both reviewers appreciate the introduced changes and support publication in Life Science Alliance. We would thus be happy to publish your paper in Life Science Alliance pending final revisions necessary to address the comments made by reviewer # 2 and to meet our formatting guidelines.

- please update the manuscript to address the few comments made by reviewer #2
- please move the figure legends for supplementary figures into the docx file and upload the S figures as individual files not larger than a single page (=> please make sure that figure S6 is on a single page)
- please make sure that all figure panels are called out in the manuscript text (not all S figure panels are currently called out, Fig 5A and Fig 6B are not called out either)

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.

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, http://life-science-alliance.org/authorguide

-- 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 FORMATTING:

Full guidelines are available on our Instructions for Authors page, http://life-science-alliance.org/authorguide

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.

Submission of a paper that does not conform to Life Science Alliance guidelines will delay the acceptance of your manuscript.

It is Life Science Alliance policy that if requested, original data images must be made available to the editors. Failure to provide original images upon request will result in unavoidable delays in publication. Please ensure that you have access to all original data images prior to final submission.

The license to publish form must be signed before your manuscript can be sent to production. A link to the electronic license to publish form will be sent to the corresponding author only. Please take a moment to check your funder requirements.

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 this transparent process, 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,

Andrea Leibfried, PhD
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Reviewer #1 (Comments to the Authors (Required)):

I am happy with the response to the reviewers and the additional data provided and the text changes. I do not have further request.

Reviewer #2 (Comments to the Authors (Required)):

The revision is improved. A few remaining issues are below.

1. p9, line 2 from the bottom, what is "(5,1% of the surface)"? and which surface?

2. p10, line 222, which figure "(Fig, B-C)"?

3. Many single-sentence paragraphs - p10, p13, p14, and p16 - should be avoided.

4. p13, line 297, make sure to include the "water-mediated" in the sentence: S187 makes a similar water-mediated contact in ...

5. p13, line 307, the side chain of Q293 is directed towards the edge of C90 - please include the information about the inter-atomic distance from the current structure, and include the sentences from Response to the Reviewers' Comments in the same paragraph of the main text: the side chain of Gln293 is not in hydrogen bonding with the base pair of C90-G197, and it does not establish a clear base-specific interaction but is in the vicinity of C90.

2nd Revision – authors' response 3 October 2018

Response to reviewer #2:

Reviewer #2 (Comments to the Authors (Required)):

The revision is improved. A few remaining issues are below.

1. p9, line 2 from the bottom, what is "(5,1% of the surface)"? and which surface?

5,1% of the combined surface of dsRBD3A and 4. The surface is the heterodimerization interface between dsRBD3A and 4. We clarified this point at p. 9, line 219.

2. p10, line 222, which figure "(Fig, B-C)"?

Thank you for noticing this. The Figure we refer to is Fig. 2. We added it in the text.

3. Many single-sentence paragraphs - p10, p13, p14, and p16 - should be avoided.

Changed.

4. p13, line 297, make sure to include the "water-mediated" in the sentence: S187 makes a similar water-mediated contact in ...

Done.

5. p13, line 307, the side chain of Q293 is directed towards the edge of C90 - please include the information about the inter-atomic distance from the current structure, and include the sentences from Response to the Reviewers' Comments in the same paragraph of the main text: the side chain of Gln293 is not in hydrogen bonding with the base pair of C90-G197, and it does not establish a clear base-specific interaction but is in the vicinity of C90.

We included the distance between Q293 and C90, which is 4.4 Å, and clearly above H-bonding distance. In Fig. 4B-E, H-bonds are conventionally marked with a dashed line while the interaction between Q293 and C90 is not. From the inter-atomic distance (now included) and from the close ups of interactions in Fig.4 it is clear that Q293 and C90 are not in H-bonding interaction. Therefore, we feel that it is not necessary to state that this interaction is NOT an H-bond in the main text. We find also that “directed towards” is a milder description of the interaction than “in the vicinity”.

3rd Editorial Decision 5 October 2018

October 5, 2018

RE: Life Science Alliance Manuscript #LSA-2018-00187-TRR

Dr. Fulvia Bono
University of Exeter
Living Systems Institute
Stocker Road
Exeter EX4 4QD
United Kingdom

Dear Dr. Bono,

Thank you for submitting your Research Article entitled "Crystal structure of Staufen1 with a physiological RNA sheds light on substrate selectivity". I appreciate the introduced changes, and 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 (PMC) as soon as we are allowed to do so, the application for PMC indexing has been filed. You may be eligible to also deposit your Life Science Alliance article in PMC or PMC Europe yourself, which will then allow others to find out about your work by Pubmed searches right away. Such author-initiated deposition is possible/mandated for work funded by eg NIH, HHMI, ERC, MRC, Cancer Research UK, Telethon, EMBL.
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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 this transparent process, 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.

DISTRIBUTION OF MATERIALS:
Authors are required to distribute freely any materials used in experiments published in Life Science Alliance. Authors are encouraged to deposit materials used in their studies to the appropriate repositories for distribution to researchers.

You can contact the journal office with any questions, contact@life-science-alliance.org

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,

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