

# CARDIAC FIBROSIS IN THREE DIMENSIONS- MECHANISTIC INSIGHTS INTO ARRHYTHMIC RISK DUE TO HYPERTROPHY

Kalyanam Shivkumar, Zhilin Qu, and Robert D Harvey

DOI: 10.1113/JP283710

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*The following individual(s) involved in review of this submission have agreed to reveal their identity: Mark L Trew (Referee #1)*

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## Review Timeline:

Submission Date:	21-Sep-2022
Editorial Decision:	25-Sep-2022
Revision Received:	07-Dec-2022
Accepted:	12-Dec-2022

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*Senior Editor: Harold Schultz*

*Reviewing Editor: Bjorn Knollmann*

## 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. Depending on transfer agreements, referee reports obtained elsewhere may or may not be included in this compilation. Referee reports are anonymous unless the Referee chooses to sign their reports.)

Dear Dr Shivkumar,

Re: JP-TP-2022-283710 "CARDIAC FIBROSIS IN THREE DIMENSIONS-MECHANISTIC INSIGHTS INTO ARRHYTHMIC RISK DUE TO HYPERTROPHY" by Kalyanam Shivkumar, Zhilin Qu, and Robert D Harvey

Thank you for submitting your invited Translational Perspectives to The Journal of Physiology. It has been assessed by a Reviewing Editor and an author of the focus paper. Some minor revisions have been requested.

The reports are copied at the end of this email.

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Your revised manuscript should be submitted online using the links in Author Tasks Link Not Available.

Please submit the revised version of the article in Word format and ensure the focus paper is referenced.

I look forward to receiving your revised submission and thank you very much for your contribution to The Journal.

Yours sincerely,

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EDITOR COMMENTS

Reviewing Editor:

I enjoyed reading the translational perspective, which is balanced and well-referenced. I have two suggestions for the authors:

1. Panels A and B from the figure are reproductions from the article. It is not clear how they relate to panel C, which is a classic arrhythmia mechanism diagram. Since panels A and B are not referred to in the text of the perspective, I suggest simply deleting the panel and only show the diagram of panel C as a figure.
2. There are several very long and complicated sentences in the piece. For example "The resultant changes such as conduction block, fibrosis induced source-sink mismatch and enhanced formation of triggers in turn by fibrosis can collude to provide both the trigger and the substrate for lethal arrhythmias (Figure)." Please edit for clarity, fix spelling mistakes, and adhere to J Physiol style of referencing.

Senior Editor:

The reviewers are very excited about your article, and it is thought to be highly influential. The reviewing editor does raise a couple of concerns and minor suggestions. We can not reprint figures from the published paper without author permission and proper attribution. It would be best to simply refer to the figures and submit Panel C as your figure. Also please correct the citation and reference style to that used for our Journal (format found in Instructions to Authors). It is also suggested to proof and revise for clarity and spellings. Thank you for your efforts on a great perspective.

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## REFEREE COMMENTS

Referee #1:

This is a very nice, highly informed and factually correct summary of factors driving VT/VF.

The authors of Khwaounjoo et al agree with the commentary in the perspective around the role of cardiac innervation and subsequent function control leading to cardiac VT/VF in the SHR model. There is exciting potential for further research around the plasticity and arrhythmic role of ganglionated plexi on the epicardium, and whether this precedes and/or coincides with fibrosis. The SHR is also a good model for such studies.

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END OF COMMENTS

**Confidential Review**

**21-Sep-2022**

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**RESPONSE TO REVIEWS:**

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Thank you, we have done this.

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Thank you.

Dear Dr Shivkumar,

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We are pleased to tell you that your paper has been accepted for publication in The Journal of Physiology.

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Yours sincerely,

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COMMENTS FOR AUTHOR:

Reviewing Editor:

No further concerns. Very nice piece.

Senior Editor:

Thank you for providing this insightful article to the Journal of Physiology

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Reviewer 1:

The revisions have improved the manuscript. No further comments.

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**1st Confidential Review**

**07-Dec-2022**

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