

## Format for ANSWERING REVIEWERS

November 13, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14501-review.doc).

**Title: Contribution of miRNAs to ion-channel remodelling in atrial fibrillation**

**Author:** José Manuel Vilches, Diego Franco, Amelia E Aránega

**Name of Journal:** World Journal of Hypertension

**ESPS Manuscript NO:** 14501

We appreciate the comments provided by the reviewers, and found them of great help in improving our manuscript. These suggestions have helped us to enhance our results. Thus, we have edited our manuscript based on reviewer suggestions

Reviewer 1: It is a review on the role of microRNAs on the development/persistence of atrial fibrillation and on myocardial ion channel remodeling. The text is up-to-date and the issue is relevant. My only suggestion is that, for the common reader interested in cardiovascular diseases but not with specific knowledge on molecular genetics and on cardiac ion channels (as is this reviewer), the text reading is rather hard, with so many abbreviations, most of them without previous definition (e.g. on page 4: Drosha/DGCR8, Dicer, sno-miRNAs, sh-miRNAs, t-miRNAs, and so on). Beyond defining each abbreviation at first appearance, maybe an abbreviation list could be helpful. Figure 2, for example, has several abbreviations without any definition in its legend. There was also some typo errors (e.g. therapeutical - page 4; targeting - page 7; highliting - page 8, and

others) and also English language errors. A complete revision is needed. Regarding the scientific content, my only suggestion is to rephrase the last sentence of the introduction "their role in AF caused by electrical remodelling", because AF is not caused by electrical remodeling, in fact AF causes electrical remodeling and this induces AF maintenance

In agreement with reviewers comment in this version of the manuscript we have include definitions of abbreviations as well as a list of abbreviations. Typo errors have been corrected and English language has been revised for a native expert. In addition, we have rephrased the last sentence of the introduction-

Reviewer 2: This review summarized the role of miRNAs in the regulation of ion channel gene expression and electronic remodeling, which is the main cause of atrial fibrillation (AF). Overall, the authors provided new insights for the pathogenesis of AF and highlighted the importance of miRNAs in regulating this process. While the scientific significance of this paper is sound, the writing and format should be deeply polished. For example, P2, a blank space should be used to separate "(APD)" and "[4,5,6]". P3, "two clases" should be "two classes".

In accordance with reviewer's suggestion we have corrected the typo errors and this version of the manuscript has been revised for a native expert

Reviewer 3: This is a review article from a well-respected group in the related research filed. It contains updated information regarding the Contribution of MiRNAs to Ion Channels Remodeling in Atrial Fibrillation. I am sure that this manuscript will be an important contribution to the field. This reviewer has few comments that can be addressed. Minor comments: 1. Authors need to correct few English errors. 2. As mentions in the abstract, this has focused to summarize micRNAs and ion channel remodel. As known, the extracellular matrix remodeling has been shown to play critical role in the onset and progression process of AF (Kallergis et al. JACC 2008;52:211-215; Fujita et al JAHA 2013;2;00504). The authors add one paragraph related information (ECM remodeling and micRNA) with citing these references. In addition, recent studies have highlighted circulating micRNAs as biomarkers

for the AF. It will be also considered to discuss in the revised manuscript. 3. Finally, give a brief clinical perspective.

In accordance with reviewer's suggestion 1) this version of the manuscript has been revised for a native expert 2) The role of the extracellular matrix remodelling in the onset and progression of AF has been discussed (pages 3 and 5) and the suggested references included.3) Finally a brief clinical perspective has been added together with concluding remarks

**Amelia E Aránega**

Cardiac and Skeletal Myogenesis Group

Department of Experimental Biology

University of Jaén

CU Las Lagunillas B3-362

23071 Jaén Spain

[aaanega@ujaen.es](mailto:aaanega@ujaen.es)