Reviewer’s report

Title: TSC-22 regulates collagen 3a1 gene expression in the rat heart

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Reviewer: Marcus Franz

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The manuscript entitled "TSC-22 regulates collagen 3a1 gene expression in the rat heart" by Kelloniemi and co-workers investigates TSC-22 expression during cardiac tissue remodeling occurring in response to cardiac overload induced by hypertrophic stimuli or after myocardial infarction. The authors found an increased expression in rat models of hypertrophy and post infarction remodeling and could further prove that these effects can be, at least in part, reversed by treatment with losartan and metoprolol. In a next step, by in vitro analysis, ET-1 could be shown to serve as an activator of TSC-22 expression in cultured ventricular myocytes both on the mRNA and protein level. Using adenovirus-mediated gene delivery, the authors were able to evidence that TSC-22 over-expression contributes to the regulation of col3a1 gene expression. Thus, TSC-22 has been suggested as a potential novel target for therapeutic interventions aimed to reduce fibrotic tissue remodeling.

This is an excellently performed study and the authors should be complimented for their work. Idea and motivation of the study are innovative and aimed to increase our knowledge on cardiac tissue remodeling, in particular cardiac fibrosis occurring in response to a variety of pathologic stimuli in different cardiovascular disorders. The introduction is written very well and helps the reader to easily get all important background information to follow the study. The spectrum of methods utilized in this study is wide and, among others, includes animal models, adenovirus-mediated gene delivery, cell cultures studies or descriptive analyses in human samples. All experimental procedures are described very well. The amount of data obtained in this study is impressive. Presentation of the results is clear and comprehensible. The discussion summarizes all findings in an adequate way and critically discusses all the novel observations made in this study against the background of the available literature in the field. Taken together, the study could be an important building block for further experiments addressing the role of TSC-22 in cardiac remodeling with special regard to its potential impact as therapeutic target.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.