Dissertation Evaluation Report

Report No.	Diploma Number: D-BIO 1446	Applicant's Name	ZHANG XU

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Evaluation Report of Dissertation

1. Evaluation of the research purpose.

The most common pathogenesis of atrial fibrillation is atrial fibrosis. Although excessive mechanical stresses are known to play a critical role in atrial fibrogenesis, the molecular mechanism and responsible cells are unclear. This study tried to investigate the mechanism of atrial fibrogenesis in response to biomechanical stress by *ex vivo* approach. Thus, the research purpose is appropriate.

2. Evaluation of the research methods.

This study was designed to widely compare the expression of fibrosis-related genes in mouse atrial tissues using the fibrotic pathway-specific PCR array, and then the authors investigated the time-course dynamics of the transcription on several interested genes by quantitative reverse transcription-PCR. To understand the responsible cells, the atrial "explants" were daily loaded to 50 mmHg for 3 hours. Then, outgrowth cells from the "explants" were characterized by immunocytochemistry. The research method is also valid.

3. Evaluation of the analysis, interpretation and discussion.

As a result, it is suggested that the loading of atrial tissues to hydrostatic pressure could induce a profibrotic transcription, likely by activating the transforming growth factor-β (TGF-β) signal pathway, and stromal cells in atrial tissues would be the sensitized cells in response to hydrostatic pressure loading, providing indirect evidence on the common pathological feature of atrial fibrosis following pressure overload.

As stated above, the dissertation will greatly contribute to the field of basic cardiology, and the evaluators uniformly agree that the author should be awarded a Doctor of Philosophy in Medical Science.