Reviewer's report

Title: Cardiac thromboxane A2 receptor activation does not directly induce cardiomyocyte hypertrophy but does cause cell death that is prevented with gentamicin and 2-APB

Version: 3  Date: 17 October 2014

Reviewer: Jun-ichi Kawabe

Reviewer's report:

In addition to indirect action contributing to hear diseases, there are many reports that TXA2 mediates the cardiac damage (as authors sited in ref 24-26). Although the role of TXA2 in vascular disorders, such as atherosclerosis and thrombus formation is clear, its direct action on the heart is less certain. Therefore, there is a merit to examine the mechanism of the cardiotoxic effects of TXA2.

In this article, the authors demonstrated that a TXA2 analog, U46619 caused cell death of mouse cardiomyocytes. The effects were blocked by IP3-signal pathways inhibitors. The experimental studies have well been designed, and these data are supportive for their conclusion. However, the originality about the findings in this article is somewhat low. The negative finding that `Ca-mobilizing agonist` did not induce cardio-hypertrophy is not surprising, and scientific merit is not high.

There are several reports that U46619 (dose 1-10µM) affect the several cardiac functions including arrhythmia (ref 16-19, 24 including the authors report). In this study, the detrimental effect of U46619 on cardiomyocytes, i.e. induction of cell death was too high. If so, most of the functional abnormality in the presence of U46619 is somewhat non-specific phenomenon. Indeed, U46619 did not occurred cell damage in neonatal rat myocytes, assessed by the LDH leakage (ref 19), while other TXA2 receptor agonist, IBOP induce apoptosis in adult rat cardiomyocytes (ref 28). Please explain the discrepancy about the effects of U46619, and also a consistency with the myocardial functional disorder and severe cytotoxicity.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

No competing interests.