Reviewer’s report

Title: The KCNE genes in hypertrophic cardiomyopathy: a candidate gene study

Version: 1 Date: 26 May 2011

Reviewer number: 1

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- Major Compulsory Revisions

In the present manuscript, the authors performed mutation screening of the KCNE gene in 93 unrelated patients with hypertrophic cardiomyopathy (HCM), but failed to identify pathogenetic KCNE variants associated with HCM. This is an interesting trial in an area that needs investigating. However, the number of probands seems to be not enough to draw definitive conclusions from their results. In fact, the authors could not find mutations even in some known genes associated with HCM (TCAP, CSRP3 and TNN) from their patients. It is important that the authors should revise their manuscript and delete unsound reasoning.

1) The cohort size in this study was apparently small. It is therefore still premature to relinquish their hypothesis (a possible link between genetic KCNE alterations and HCM). As the authors know, the mutation rate in the KCNE gene in the long QT syndrome is very low (~1%), despite its general importance. The authors should be careful about their definitive descriptions and clarify the limitation in their study.

2) Recently, Roepke et al. (2009, Nat Med. 15:1186-1194) reported cardiac hypertrophy caused by targeted disruption of KCNE2 gene in mouse model. Why do the authors think that the altered expression of the KCNE gene in cardiomyopathic hearts is a secondary result?

- Minor Essential Revisions

The authors should clarify the ethnicity and geographical region of habitat in their patients.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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