Reviewer’s report

Title: Search for Cardiac Calcium Cycling Gene Mutations in Familial Ventricular Arrhythmias Resembling Catecholaminergic Polymorphic Ventricular Tachycardia

Version: 3 Date: 22 December 2008

Reviewer: Christopher H George

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The inclusion of data relating to the exon 3 deletion is interesting and the paper has been slightly improved. It is mystifying why the paper’s characterisation of the variant N3308S (which appears functionally benign) is presented in preference to functional data from the two novel mutations.

I am wholly unconvinced by the authors’ claim that the in vitro effects of S616L and R1051P need not be studied simply because the clinical phenotypes associated with these ‘hot-spot’ mutations are typical and thus any functional characterisation are unlikely to extend current knowledge. I disagree with this statement. If, for some reason the authors are unable to perform this characterisation of the two mutations, then it should be clearly stated as a limitation of the study.

Minor essential revisions.

The quality of the figures is poor throughout- the new Figure 3 is illegible.

The authors should clearly state that they consider the S616L mutation to extend the N-terminal hot-spot region of RyR2.

Level of interest: An article whose findings are important to those with closely related research interests

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 interest