Reviewer's report

Title: SCN5A Allelic Expression Imbalance in African-Americans Heterozygous for the Common Variant p.Ser1103Tyr

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Reviewer: Connie Bezzina

Reviewer's report:

This manuscript addresses the interesting hypothesis that disease severity / risk of sudden cardiac death in SCN5A-related channelopathy could be modulated by the level of expression of the particular SCN5A-allele on which the nucleotide variant resides. The authors of this manuscript tested this hypothesis specifically in heterozygotes for the p.Ser1103Tyr variant, a variant which is common in African-Americans and which has been previously associated with increased risk for cardiac arrhythmia and sudden death in this population. Allelic imbalance was assessed in cardiac RNA extracted from hearts of victims of SIDS as well as control hearts.

The study is carefully designed and executed and is well-written. Although the authors identified allelic imbalance in p.Ser1103Tyr heterozygotes, they did not identify an association with sudden death. In spite of the lack of association with sudden death in the small sample sets studied, the findings of this study are interesting because they demonstrate that allelic imbalance occurs for the SCN5A transcript, a phenomenon that very likely contributes, together with a multitude of other factors, on disease expression and risk of sudden death.

This reviewer has no further comments.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.