Reviewer’s report

Title: A case report of recessive restrictive cardiomyopathy caused by a novel mutation in cardiac troponin I (TNNI3)

Version: 0 Date: 04 Feb 2019

Reviewer: Charles S. Redwood

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The manuscript by Pantou and colleagues describes a proband presenting with severe restrictive cardiomyopathy at 41. Genetic analysis showed that the proband is homozygous for a missense mutation (Asp196His) in TNNI3, the gene encoding cardiac troponin I. Both parents (third cousins) were heterozygous for this mutation and asymptomatic while the twin sister (also homozygous) also has RCM and the brother, also homozygous, had a HCM phenotype.

This straightforward report provides clear evidence of recessive inheritance of RCM and provides some incremental advance in the field of cardiomyopathies. It is largely convincing and well written. This precise mutation is novel but it is notable that there are many cardiomyopathy mutations in this region of TNNI3, indeed two other mutations of the same residue - to Asn and to Gly. All of these seem to cause disease in an autosomal dominant fashion. The authors should attempt some speculative explanation why the Asp196Pro does not seem to act via an autosomal dominant mechanism in contrast to the other mutations in this region.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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