Reviewer's report

Title: Novel TBX1 loss-of-function mutation causes isolated conotruncal heart defects in Chinese patients without 22q11.2 deletion

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Reviewer: Edward Lammer

Reviewer's report:

This MS describes DNA sequencing of TBX1, from 199 Chinese subjects born from 2008-09 and diagnosed with a variety of conotruncal heart defects. Among infants who do NOT have the 22q11 microdeletion, the authors found one de novo missense mutation within an evolutionarily conserved T-box domain of TBX1. The authors further show compelling in vitro studies of the novel human mutation and showed that it loses transactivation activity.

This MS describes a novel de novo human TBX1 mutation found in a subject with pulmonary valve atresia with VSD.

Minor Essential Revisions
1. The introduction and discussion should include comments and references to CRKL, another gene that is within the common 3MB 22q11 microdeletion and that has been associated with conotruncal defects when deleted, even if TBX1 is not affected.

Level of interest: An article of outstanding merit and interest 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.

Declaration of competing interests:

no competing interests other than that my lab does similar research