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Novel Cardiac troponin C(TNNC1) variant causing familial dilated cardiomyopathy

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Introduction

Cardiac troponin C (cTnC), expressed by the gene TNNC1 is the calcium sensing component of the cardiac troponin complex. Disease causing mutations in TNNC1 have been described in some families with dilated cardiomyopathy(DCM). We describe a novel DCM causing mutation in TNNC1 in which aspartic acid at position 151 is replaced by valine (D151V).

Methods

We studied a large 3 generation Asian family with a strong pedigree suggestive of autosomal dominant DCM with 7 affected individuals of which 3 died between ages 13 and 35 years. Complete exon sequencing for 77 known cardiac genes was performed and all identified variants were validated by Sanger sequencing.

Results

We identified a novel missense mutation in the C-terminus calcium binding site of cTnC, resulting in a p.D151V amino acid substitution. The mutation co-segregates with all screened clinically affected family members and is absent in a control population of 300 healthy individuals. Furthermore phylogenetic analysis shows that aspartic acid-151 of cTnC to be highly conserved across all Metazoa.

Conclusion

We describe a novel disease causing mutation at a highly conserved residue in a family with dilated cardiomyopathy. Given its location, we postulate its effect relates to the modulation of calcium binding to cTnC.