Reviewer's report

Title: Missense mutations in Desmocollin-2 N-terminus, associated with Arrhythmogenic right ventricular cardiomyopathy, affect intracellular localization of desmocollin-2 in vitro

Version: 1 Date: 27 August 2007

Reviewer: Luisa Mestroni

Reviewer's report:

General
The authors screened 54 ARVC probands for mutations in desmocollin-2 (DSC2), and identified two heterozygous mutations (304G>A, E102K and 1034C>T, I345T) in two probands and in four family members. The two mutations map to the N-terminal region of DSC2. cDNA with the 2 mutations was cloned and transfected in neonatal rat cardiac myocytes and in HL-1 cells. Functional studies demonstrated that, the two N-terminal mutants were predominantly in the cytoplasm and were unable to properly localize in the membrane.

The work of Beffagna et al. confirms the role of DSC2 in ARVD and contributes to the understanding of the mechanism causing the disease. The paper is clear, well written and accompanied by excellent illustrations.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

None

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Discretionary Revisions (which the author can choose to ignore)

Only one clarification requested: I would be interested to know what the rationale was for using the two cell lines for their transfection experiments. Other than that I found the methods clearly explained, and the paper very interesting.

What next?: Accept after discretionary revisions

Level of interest: An article of outstanding merit and interest in its field
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 interests