Author's response to reviews

Title: Use of a Targeted, Combinatorial Next-Generation Sequencing Approach for the Study of Bicuspid Aortic Valve

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1. Page 6 paragraph 2 should revise as: Only 2 of these variants (rs72541816 at APC and rs116164480 at GATA5) were de novo that were not segregated from the parents. These two variants were present in an individual with a family history of coarctation of the aorta.

I corrected that sentence as requested, and I also clarified again in the discussion that de novo= not in either parent

2. Abstract & discussion: The current text needs clarification that cost saving refers to 78 samples, not per sample. The abstract should also put in the cost saving as compared to targeted capture without pooling since the genome coverage is more comparable to the current study.

Clarified the sample number/entire cohort concept, also changed abstract to reflect the effect of pooling alone with targeted capture

3. Table 1: Were these mutations found in only one patient? Please add the count of patients carrying each of the mutation for comparison with the 1000G.

Added a sentence to results to say each variant was identified in only one proband

4. Supplementary table 2: Since individuals could carry 1-5 putative damaging mutations, it would be useful to add an ID variable to indicate if an individual carry more than one mutation. Alternatively, the authors could present the table based on sample ID (anonymous) rather than gene name and provide the respective clinical & variant information."
Added a column for "sample identifier" and sorted by that rather than by gene name

5. EDITORIAL REQUIREMENTS (2ND REQUEST):
*Please include the email address of all authors in the title page.

Added, apologies on missing this with the previous revision