Author's response to reviews

Title: ACE2 Gene Expression is Up-regulated in the Human Failing Heart

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PDF covering letter
Re: MS: 1249940712238591

Dear Dr Gadd,

Thank you for your recent correspondence. I have read with interest the reviewer's reports. The points raised regarding the statistical analysis are well made and have been carefully considered. I have tried to address these points as follows.

The point regarding the use of log values has been dealt with in the methods section (page 7, line 10).

The second valid point raised pointed to the increased risk of family-wise Type I error associated with multiple comparisons using a Student's t test. As a result we took advice from a Statistical Consultancy company (PRISM Training & Consultancy Ltd; www.prismtc.co.uk), specialising in analysis of biological data, regarding the most appropriate statistical analysis to carry out.

A two-way analysis of covariance, with Target Genes and Treatment Groups as factors and GAPDH values as a covariate, has now been performed in order to provide a potentially more sensitive analysis. Whilst the use of a covariate proved beneficial, the significance of the TargetGene x Group interaction term (p=0.013) indicated that differences between Groups were not consistent across the target genes, hence separate one-way analyses of covariance were performed for each target gene. In order to allow for the multiplicity mentioned above, Dunnett's test was used to compare adjusted means for each diseased group (IDC and ICM) to that for the control group.

We appreciate the constructive comments of the reviewer and hope that with the new statistical analysis, the manuscript is now suitable for publication.

Kind regards

Andrew Goulter