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Multi-Investigator Letter on Reproducibility of Neonatal Heart Regeneration following Apical Resection

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We appreciate the interest that Andersen et al. (2014) have shown in our work on neonatal cardiac regeneration. Their recent paper relates directly to resection methodology first presented by Porrello et al. (2011) and describes a failure to reproduce the observations made in that study regarding regeneration after resection. We are puzzled by the results and conclusion because in the hands of the seven different groups who authored this letter, this methodology has proved robust and reproducible and has been used in several ongoing studies across our different laboratories that are in various stages of completion (Heallen et al., [2013], as well as studies by the Lee, Takeuchi, and Nei groups that are currently under review). Importantly, several independent groups had similar observations using various types of neonatal injury (Strungs et al., 2013; Haubner et al., 2012; Naqvi et al., 2014; Jesty et al., 2012), where an increase in cardiomyocytes was also observed. Having carefully examined the study published by Andersen et al. (2014), it is our overall impression that methodological differences are likely to account for the difference in published results. Although it is difficult to draw clear conclusions about such differences without a detailed analysis of primary data, our impression is that variations in surgical technique, amount of resected myocardium, methods of quantification of resected and regenerated myocardium, and methods of assessment of myocyte proliferation form the basis of the differences seen. In particular, we used ventricular weight and surface area immediately after resection and 21 days later to assess the degree of injury and regeneration, while the Andersen group used HW/BW immediately after resection and ventricular weight 21 days later. Notably, in Figure 1E of the Andersen et al., 2014, paper, the amount of resected myocardium by ventricular weight 2 days after resection was in excess of 40%. We have not examined the effect of resection of such a large segment of the myocardium, but it is plausible that it is not compatible with regeneration. We stand by the reproducibility of the initial report and we would be happy to assist Andersen et al. (2014) with various technical aspects of the neonatal apical resection method.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this letter.

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