Data Supplement for "The Emerging Role of MicroRNAs in Cardiac Remodeling and Heart Failure

To compare and contrast the altered expression profiles of miRNAs in various animal models of heart disease and in human heart failure we have generated a two-dimensional graphical map (see Online Figure I) that displays the relevant human and experimental studies in columns with the accompanying changes in miRNA expression levels depicted in rows. Analogous to conventional heat maps that have been used for gene and miRNA arrays, we have used red to indicate changes in miRNAs that are reported to be up-regulated, and green to indicate miRNAs that were reported to be down-regulated. miRNA expression that was reported as unchanged is depicted in black, whereas miRNAs that were either not reported, or whose change in expression was not statistically interpretable were left uncolored. The definitions for changes that were considered to either up- or down-regulated in the various reports are given in the table below:

Online Table I

Study	Experimental model	Criterion	Reference
A.	Human HF vs control	> 1.5 fold change	Thum et al.[1]
B.	Human HF vs control	> 1.3 fold change	van Rooij et al.[2]
C.	Human DCM vs control	$p < 0.05$ and $q < 5\%$	Ikeda et al.[3]
D.	Human ICM vs control	$p < 0.05$ and $q < 5\%$	Ikeda et al.[3]
E.	Human Aortic stenosis vs control	$p < 0.05$ and $q < 5\%$	Ikeda et al.[3]
F.	Mouse TAC vs sham	$p < 0.05$	Sayed et al.[4]
G.	Mouse TAC vs sham	30 % change	Cheng et. al.[5]
H.	Mouse TAC (or CnA Tg) vs sham	> 1.5 or < 0.5 fold change	van Rooij et al.[5]
I.	Mouse TAC vs sham at 14 days	None	Tatsuguchi et al.[6]
J.	Cardiomyocytes treated with PE	> 1.5 fold or < 0.75 fold	Tatsugchi et al.[6]

Key: TAC: trans-aortic constriction, HF: heart failure, DCM: dilated cardiomyopathy, ICM: ischemic cardiomyopathy, CnA Tg: calcineurin transgenic mouse, PE: phenylephrine, q: false discovery rate. Reference article numbers refer to the references in the online supplement.

However, unlike a conventional heat-map, the color intensity of the miRNAs depicted in Online Figure I has not been adjusted to reflect the magnitude of change in miRNA expression. Using this approach, we obtained miRNA expression profiles on 172 miRs from a total of ten different experimental and clinical models, of which 5 were in human tissue, 4 were in-vivo studies in animals, and 1 was an in vitro study in cultured cardiac myocytes. An abridged version of this map that illustrates microRNAs that were changed in at least two studies is shown in Figure 2 of the main body of the manuscript.

References

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Online Figure I: miRNA expression profiles in experimental models and human heart failure. A Pubmed search (May-June 2008) was conducted using the MeSH titles: 'microRNA', 'heart disease' and/or 'heart failure.' A total of 2314 articles were identified of which 614 review articles were excluded. The content of the 1696 original articles were reviewed for relevance with respect to the role of miRNAs in cardiac remodeling. Six studies reported global miRNA expression data (miRNA profiling) using micro-RNA micro-arrays, of which 3 evaluated miR expression in two or more experimental model systems.[1-6] Red indicates miRs that were significantly up-regulated; green indicates miRs that were significantly down-regulated; black indicated no change in miR expression levels; white indicates miRs that were either unreported, equally expressed or not significantly different ($p>0.05$) between disease phenotype and controls (Reference article numbers in Online Figure I refer to the references in the Data Supplement)