Clinically Relevant Models of Diabetic Cardiac Complications

To the Editor:

We read with great interest the article by Hsueh et al in a recent edition of Circulation Research. We concur with the efforts of the Animal Models of Diabetic Complications Consortium (AMDCC) to attempt to create clinically relevant models of diabetes induced cardiovascular disease. Like the AMDCC, our own group has studied extensively diabetic complications in the retina, kidney, and heart in the diabetic Ren-2 rat, a model of enhanced tissue based renin–angiotensin system. After induction of diabetes with streptozotocin, the diabetic Ren-2 rat develops many of the criteria suggested by Hsueh et al for the validation of diabetic cardiomyopathy, such as invasive evidence of systolic and diastolic dysfunction, altered gene expression, and evidence of oxidative stress, activation of profibrotic signaling pathways, and changes in myocardial calcium handling. Furthermore, the clinical relevance of any rodent model must be based on the predictive power for both negative and positive clinical trials. The diabetic Ren-2 rat, to date, has confirmed faithfully both positive and negative results that are remarkably similar to those findings in human clinical studies, validating the relevance of this model. We, therefore, encourage the AMDCC to continue its development of new models, and we suggest that amplification of the renin–angiotensin system may offer valuable insights into the pathophysiology of this complex disease.

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