**Short Commentary**:

RE: CIRCHF/2015/002210R1: Tang *et al* “Effects of intracoronary infusion of escalating doses of cardiac stem cells in rats with acute myocardial infarction”

Although c-kitpos cardiac stem cells (CSCs) have been shown to impart salubrious effects in the setting of post-infarction heart failure, the dose of these cells is unknown. So far, doses of CSCs have been chosen arbitrarily. Here we examined the effects of escalating doses of CSCs in a rat model of postinfarction cardiomyopathy. The results indicate a binary rather than a dose-related response to intracoronary administration of CSCs infused after acute myocardial infarction in this rat model. Thus, once a therapeutic effect is achieved, increasing the dose of cells does not necessarily increase the magnitude of the response, suggesting that the occurrence of beneficial remodeling may be observed only after reaching a threshold stimulus necessary to jumpstart multifaceted intrinsic myocardial reparative mechanisms. Regarding direct translational value, similar to most small animal models, this study may not be directly applicable to humans in terms of exact extrapolation of the effective cell dose used in rats. For example, the SCIPIO trial suggested efficacy in humans with a dose of one million CSCs, which when measured in cells per gram of myocardium, is much less than the 0.3 x 106 cell dose used herein, which did not show any benefit. The important concept is that once a therapeutic threshold is achieved, increasing the number of CSCs may not necessarily result in increased efficacy. Given the apparent binary response to therapy with CSCs, this study implies that additional therapeutic benefit might be achieved by repeated lower doses of CSCs rather than a single higher individual dose.