Editorial Comment

Muscling up damaged hearts through cell therapy

Chi Van Dang

Johns Hopkins University School of Medicine

Molecular and cellular processes gleaned from the most fundamental of biomedical studies are now harnessed for their potential healing properties. In the US and throughout the world, millions of patients suffer from myocardial infarction and many succumb to the morbidity and mortality of the ensuing cardiac failure, a protracted condition in need of healing. While pharmacological agents have been the mainstay intervention that ameliorates cardiac failure through increased contractility or reduction of cardiac workload, these agents do not inherently heal the wounds inflicted by poor perfusion of the affected cardiac tissue. Cell therapy, however, holds the promise of repleting the damage heart with new contractile cells that can be engineered to secrete concoctions that promote healing by recruiting new blood vessel development or angiogenesis. Such cell therapeutic promise has already been fulfilled for many decades for hematological diseases through transplantation of bone marrow stem cells, which are now more broadly implicated for their healing potential of other tissues.

In the study by Ye and coworkers in this symposium issue of the Journal of Geriatric Cardiology, proof-of-concept is provided that human skeletal myoblasts could be engineered to heal myocardial infarction in a porcine model of coronary ischemia. Specifically, the authors sought to compare the effects of human myoblasts engineered to secrete either vascular endothelial growth factor (VEGF) or angiopoietin (Ang-1), two key factors that promote new blood vessel development, on their ability to promote healing after experimentally induced infarction. While VEGF promotes angiogenesis primarily through mitogenic stimulation of endothelial cells, Ang-1 is known to stabilize newly developed blood vessels. Intriguingly, Ye et al. found that while ectopic VEGF expressing myoblasts injected directly into the infarcted heart increased vascularization and regional blood flow only early on, Ang-1 causes these effects in a sustained fashion. The proof-of-concept provided by this study suggests that myocardial regenerative cell therapy may well benefit from the addition of Ang-1 secreted from the engineered cell grafts themselves. These findings provide sufficient ground to determine whether the effects of Ang-1 is cell type specific or whether this approach could be generalized to engineer other regenerative cell sources, such as cardiac stem cells or bone marrow mesenchymal stem cells. Although it remains to be determined whether this therapeutic approach could positively affect hemodynamics of the damaged heart and the clinical course of myocardial infarction complicated by cardiac failure, the findings of this study invite additional studies that will hopefully reduce the morbidity and mortality of ischemic heart failure in the future through cell therapy. While promising findings such as these are indeed encouraging for those in need of healing, the researcher-healer community is obliged to refrain from mustering false hope beyond the envelope of scientific rigor.

Reference