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ABSTRACT

Stem cell therapy is one of the most promising therapeutic innovations to help restore cardiac structure and function after ischemic insults to the heart. However, phase I and II clinical trials with autologous "first-generation stem cells" have yielded inconsistent results in ischemic cardiomyopathy patients and have not produced the definitive evidence for their broad clinical application.
Recently, new cell types such as cardiac stem cells (CSC) and new allogeneic sources have attracted the attention of researchers given their inherent biological, clinical and logistic advantages. Preclinical evidence and emerging clinical data show that exogenous CSC produce a range of protein-based factors that have a powerful cardioprotective effect in the ischemic myocardium, immunoregulatory properties that promote angiogenesis and reduce scar formation, and are able to activate endogenous CSC which multiply and differentiate into cardiomyocytes and microvasculature. Furthermore, allogeneic CSC can be produced in large quantities beforehand and can be administered "off-the-shelf" early during the acute phase of myocardial ischemia. The distinctive immunological behavior of allogeneic CSC and their interaction with the host immune system is supposed to produce immunomodulatory beneficial effects in the short-term, preventing long-term side-effects after their rejection. Preclinical studies have shown highly promising results with allogeneic CSC, and clinical trials are already ongoing.
Finally, unraveling questions about the biology and physiology of CSC, the characterization of their secretome, the conduction of larger clinical trials with autologous CSC, the definitive evidence on the safety and efficacy of allogeneic CSC in humans and the possibility of repeated administrations or combinations with other cell types and soluble factors will pave the road for further developments with CSC, that will undoubtedly determine the future of cardiovascular regenerative medicine in human beings.

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