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Developing effective stem cell therapies for heart disease will hinge on collaboration between multiple specialties

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Opportunities for multidisciplinary collaboration have never been more important if the development of effective regenerative therapies for heart disease is to be realised, according to the first paper in this week's *Lancet* Series on stem cells. The breaking down of traditional barriers between individual areas of specialisation, from cardiovascular medicine to device technology, and the creation of interdisciplinary teams from both academia and the private sector will be key.

"The development of regenerative strategies to reverse the progression of advanced heart failure is one of the most urgent clinical needs of this century…and has become a holy grail of modern cardiovascular science", explains Kenneth Chien from Harvard University, USA, lead author of the paper. "But if we are to move beyond stem cell biology towards the development of true cardiovascular regenerative therapy…a parallel regenerative effort to change the existing academic culture and environment might be necessary…the fate of patients with heart failure will probably hinge on the outcome."

To date, clinical trials have focused on three heart conditions—heart attack, chronic heart failure, and dilated cardiomyopathy. Although regenerative therapies based on several types of non-cardiac cells appear safe, their clinical efficacy remains to be demonstrated. But recent advances in cardiac stem cell and regenerative biology are beginning to yield potential new targets and treatment strategies.

The heart was previously thought to have only a minimal capacity for self-renewal, with little hope of reversing the loss of healthy heart muscle and function. This has changed with the recent discovery of a number of distinct embryonic progenitor cell types, some of which persist in the adult heart. Certain cells in this population can be activated in the context of cardiac injury, and are a novel target for cardiac regenerative therapeutics, either by delivery of the cells or finding ways to activate expansion and conversion to functioning heart cells. For example, recent clinical studies showed that cells derived from a patient's own heart tissue can be used to decrease scar formation after a heart attack. While it is not clear that the delivered cells are truly stem cells, these studies represent early, informative steps toward the goal of harnessing the heart's potential to heal itself.

Much work remains to be done. Because of the complexity of the heart, restoring function will require not just the regeneration of one cell type, but also the recreation of the native architecture of the heart. "An ideal cardiac regenerative therapy would possess a key cell and paracrine factor combination, a cardiac tissue niche optimized to enhance cell engraftment and differentiation, and a safe, minimally invasive delivery procedure that introduces the regenerative therapy specifically to the affected areas with the least risk of acute and long-term side effects", say the authors.

To this end, they conclude, multidisciplinary partnerships between the arenas of stem cell biology, tissue engineering, transplantation, grafting, rejection biology, and clinical cardiovascular medicine and device technology will be vital.

In an accompanying Comment, Dusko Ilic from King's College London, UK, and Julia Polak from Imperial College, London say: "Governments and the private sector will have to show confidence in stem cell research by continuous investment in a new generation of researchers who will

move science forward and translate discoveries into reliable clinical outcomes."

Provided by Lancet