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Stem cell therapies for heart and brain: Failed promises or new hope?

Chrishan J. A. Ramachandra[1,2], Cesario V. Borlongan[3]

Over the past decades, several groups have demonstrated the effectiveness of stem cell transplantation to improve organ function in the setting of heart failure and stroke. A search for relevant literature accounts for over 3000 related articles and yet, it is a conundrum as to why these cell-based therapies are yet to be implemented in standard clinical practice. In this special issue of Conditioning Medicine, the success and failure of stem cell therapy is critically reviewed with emphasis given to novel approaches that may facilitate better translation from bench to bedside.

When repairing the damaged myocardium of experimental animal models, several types of stem cells have been shown to have therapeutic properties, with some being more potent than others (Nguyen et al., 2016). Surprisingly, neither type has fared well in larger clinical trials. To comprehend these discrepancies, Yap and colleagues (2021) aptly review the implementation of first- and second-generation stem cells for cardiac repair and surmise that better clinical outcomes may be achieved by bolstering various cellular properties through the incorporation of transgenes.

Despite the creation of stem cells with augmented therapeutic properties, cell engraftment remains a pressing concern. This could be circumvented by using bioprinting technology to generate 3D bioengineered myocardial tissue that could be patched on to the damaged region, similar to a band-aid (Coulombe et al., 2014). Cong and colleagues (2021) discuss this approach and though it is very much in its infancy, cardiac patches could serve as an alternative to cell transplantation by providing structural support, promoting direct remuscularization, and secreting cardioprotective paracrine factors.

The disappointments associated with stem cell therapy for heart failure are no different to what has been observed in stroke patients. Though solid safety profiles have been established, clinical efficacy following cell transplantation remains low, again due to modest engraftment. Kingsbury and colleagues (2021) review the current status of stem cell therapy for stroke and surmise hypoxic pre-conditioning of transplanted cells to likely improve clinical outcomes.

An alternative to cell replacement therapy for primary cell death could be the targeting of inflammation associated with secondary cell death. Considering the implication of the gut-brain axis in stroke pathology, Moscatello and colleagues (2021) highlight the importance of the gut microbiome and its role in neurodegeneration, and also discuss the implication of stem cell therapy for suppressing gut inflammation.

Finally, induced pluripotent stem cell (iPSC)-derived progenies are fast emerging as viable alternatives to adult stem cells (Ja et al., 2016). However, the requirement for large cell quantities and adult-like physiology poses a hindrance towards their clinical adoption. In order to establish safe and efficient differentiation protocols for cell therapies, Lees and colleagues (2021) discuss the dynamic continuum of metabolic states that underly pluripotency and differentiation to achieve physiological relevant cellular states.

In summary, this special issue on Stem Cells highlights important points that need to be considered when moving forward in order for cell-based therapies to be effective in heart failure and stroke. While several unique approaches have been proposed, validation must be performed on clinically relevant models with appropriate controls to prevent recurring disappointments as seen over the past few decades.

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[1]National Heart Research Institute Singapore, National Heart Centre Singapore, Singapore. [2]Cardiovascular & Metabolic Disorders Program, Duke-National University of Singapore Medical School, Singapore. [3]Center of Excellence for Aging and Brain Repair, University of South Florida Morsani College of Medicine, Tampa, FL, USA.

Correspondence should be addressed to Chrishan J.A. Ramachandran (chrishan.ramachandra@nhcs.com.sg) or Cesario V. Borlongan (cborlong@usf.edu).

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