

Enhancing the efficiency of cell and gene therapy- Challenges and potential solutions

演者 : Dwaipayan Sen先生

Centre for Biomaterials, Cellular and Molecular
Theranostics, VIT, Vellore, TN, INDIA

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Abstract

The regenerative and multi-differentiation potential of mesenchymal stem cells (MSCs), along with their ubiquitous source of origin, offers vast opportunities with respect to the applications in diverse interdisciplinary sectors of research. Although the MSCs boast of several applications in terms of regenerative medicine and also in the field of tissue engineering, their usage is limited still due to the marked loss of transplanted MSCs. The major factors contributing to such a hostile post-transplant environment are demarcated by the following: Reactive Oxygen species (ROS), Hypoxia-reperfusion (H/R), inflammation and anoikis. The conglomeration of all these pathophysiological conditions result in increased apoptosis and necrosis, leading to untimely death of MSCs. The plethora of these harsh conditions contributes to an upsurge of endoplasmic reticulum stress. Endoplasmic reticulum (ER) is an intracellular organelle that contributes to efficacious protein synthesis, folding, assembly and transportation. When the normal functions of the ER are perturbed, ER stress is generated which in turn activates an unfolded protein response (UPR). Our lab at VIT tries to greatly resolve the inefficacy of tissue-specific engineered transplants of MSCs via a focussed elucidation in the UPR-mediated pathological conditions, leading to the dearth of MSC survivability. In addition we also utilize adeno associated viral (AAV) as a gene therapy vector to treat inherited as well as non-inherited disorders.

お問い合わせ : 金属生体材料学分野 埴 隆夫(内線:8006)

E-mail: hanawa.met@tmd.ac.jp