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Human Adult Stem Cells: Their Biosafety and Current Status in Cell-based Therapy

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Human adult stem cells have attracted considerable interest in the field of regenerative medicine in recent years [1,2]. Adult stem cells include mesenchymal stem cells, neural stem cells, hematopoietic stem cells, cardiac stem cells, hepatic stem cells etc. [3]. They are capable of differentiating into the major specialized cells of the tissue in which they resided, therefore helping to repair and regenerate damaged tissues and organs. With its regenerative potential, human adult stem cells have been studied in numerous clinical settings, including musculoskeletal, neurological, vascular, immune-mediated, respiratory, liver, cardiac diseases etc. [4]. The ability to engineer these cells without compromising their genotypes and phenotypes offers the opportunities to expand their therapeutic potentials for advancing human health [5]. However, the biosafety and bioefficacy concerns associated with their use in cell-based therapy have restricted their applications [6].

For therapeutic use, human adult stem cells should meet the following criteria: (i) ability to proliferate to produce large amount of viable cells, (ii) ability to differentiate into desirable cell types, (iii) ability to survive in the recipient after transplantation, (iv) ability to maintain their functionality after transplantation, with (v) low risk of generating biosafety issues after transplantation such as genetic instability, tumourigenesis, and immunogenesis [7]. To date, there exist a numbers of biosafety issues in stem cell-based therapies, including chromosomal aberration and tumour formation [8,9]. Significant efforts have been devoted to manipulate their culture conditions in order to generate healthy stem cells and to improve its bioefficacy for therapeutic purpose. For example, human mesenchymal stem cells (MSCs) have been treated with cytokines (e.g., IL-6, HGF and TNF-α) or hypoxic condition to increase the expression of CXCR4 (a crucial receptor for homing and engraftment) hence enhances their homing and engraftment potential [10-12]. Besides that, human MSCs have been genetically engineered to overexpress CXCR4. This genetic manipulation has been found to enhance their engraftment potential to heart and improve cardiac function in the mice model of myocardial infarction [13]. Electrical stimulation has also been applied to human MSCs to direct the migration of MSC to the injured areas and increase the expression of CXCR4 [14]. In addition, the transplanted human MSCs have also been encapsulated into a scaffold that resembles extracellular matrix of the injured tissue to serve as a temporary substrate for cell adhesion. This approach could prevent cell death and provide sufficient duration for the interaction between the transplanted stem cell and injured tissue [15]. With advances in molecular and imaging technologies, several approaches such as advanced molecular cytogenetic techniques, microRNA analysis and non-invasive cellular imaging have also been introduced in cell-based therapies to improve the biosafety of human adult stem cells [16].

As mentioned, human adult stem cells hold tremendous potential in cell-based therapies as utilizing these cells could eliminate the ethical and safety concerns related to the use of other types of stem cells, including human embryonic stem cells and human induced pluripotent stem cells [17]. Nonetheless, while the outcomes of numerous preclinical and clinical studies support the potential of human adult stem cells in various clinical fields, multiple challenges are yet to be addressed to achieve successful clinical translations. In view of the growing need for human adult stem cell therapy, it is important to understand all the steps required in developing a stem cell-based therapy, including bioprocessing, safety and efficacy assessment, cell administration route and delivery strategies. This will aid in establishing the strategies to maximize the therapeutic efficacy of human adult stem cells for clinical applications in the future.

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