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TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Concise Review: Endothelial Progenitor Cells in Regenerative Medicine: Applications and Challenges

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ABSTRACT

Endothelial progenitor cells (EPCs) are currently being studied as candidate cell sources for revascularization strategies. Significant advances have been made in understanding the biology of EPCs, and preclinical studies have demonstrated the vasculogenic, angiogenic, and beneficial paracrine effects of transplanted EPCs in the treatment of ischemic diseases. Despite these promising results, widespread clinical acceptance of EPCs for clinical therapies remains hampered by several challenges. The present study provides a concise summary of the different EPC populations being studied for ischemic therapies and their known roles in the healing of ischemic tissues. The challenges and issues surrounding the use of EPCs and the current strategies being developed to improve the harvest efficiency and functionality of EPCs for application in regenerative medicine are discussed. STEM CELLS TRANSLATIONAL MEDICINE *2016;5:1–9*

SIGNIFICANCE

Endothelial progenitor cells (EPCs) have immense clinical value for cardiovascular therapies. The present study provides a concise description of the EPC subpopulations being evaluated for clinical applications. The current major lines of investigation involving preclinical and clinical evaluations of EPCs are discussed, and significant gaps limiting the translation of EPCs are highlighted. The present report could be useful for clinicians and clinical researchers with interests in ischemic therapy and for basic scientists working in the related fields of tissue engineering and regenerative medicine.

INTRODUCTION

The term "endothelial progenitor cells" (EPCs) might be fundamentally used to refer to populations of cells that are capable of differentiation into mature endothelial cells (ECs), with purported physiological roles in angiogenesis (the sprouting of new blood vessels from existing ones) and vasculogenesis (de novo formation of vascular networks) [1]. These features make EPC populations valuable cellular candidates or therapeutic targets in regenerative medicine, with several strategies being developed to use them, including direct cellular transplantation and tissue engineering approaches. Efforts to translate these efforts to the clinic have, however, been hampered by several issues, including controversies over the identity and functions of EPCs, the limited numbers of EPCs, and their clinical potency. In the present report, we begin with a description of EPC populations, leading to an overview of clinical strategies that have been developed to use EPCs in regenerative medicine. The factors limiting the use of EPCs and the current research themes to resolve these issues are also discussed.

IDENTIFICATION AND CHARACTERIZATION OF EPC POPULATIONS

The discovery of endothelial progenitor cells has been credited to Asahara et al. for identifying a hematopoietic population in adult peripheral blood capable of eliciting postnatal vasculogenesis [2]. Subsequent studies suggested that EPC numbers could be used in clinics as a biomarker of cardiovascular disease [3], an important line of investigation that continues today [4]. In the context of regenerative medicine, it is the capacity for vascular regeneration and the potential for ischemic therapy for which EPCs are most valued. However, significant controversies exist over the identity and roles of EPCs in vascular repair. Thus, a brief discourse on the major EPC populations reported in published studies is necessary to facilitate further discussion. During the past two decades, the term "EPC" has been used to describe a burgeoning range of cell types defined by their isolation and culture methods, as well as the ontological sources, ranging from fetal trophoblastic tissue to adult bone marrow. A detailed discussion of the myriad EPCs used in