Coronary artery disease (CAD) persists as a leading cause of morbidity and mortality in the industrialized world. Patients with myocardial damage who have not adequately responded to medical therapy and revascularization may, if eligible, be treated by surgical ventricular restoration, ventricular assist devices, and, ultimately, by transplantation. Although these treatments can extend the lives of some patients, they can only be offered to a minority of affected patients and remain “mechanical” in that they do not biologically address the functional deficit of the heart. This has led to great interest in cell replacement strategies, with the goal of functionally address the functional deficit of the heart. This has led...
occurrence of the hemorrhage, suggesting that the angiogenic function of erg may act through direct regulation of this endothelial junction molecule. However, this association was not investigated in the fli1 morphants, and therefore it is unknown whether erg and fli1 act additively on angiogenesis through the same mechanism.

These findings improve our understanding of the function and mechanisms that link ETS domain genes to hematopoiesis and vessel development and provide insight into the identification of targets for improving stem/progenitor cell function and their use in angiogenic therapies. For example, the expansion of stem cells in culture can lead to alterations in their genome and function, and these changes may negatively impact on their clinical safety and efficacy.16 The development of techniques to control the changes of stem/progenitor cells in culture will benefit from greater knowledge of the genes responsible for the regulation of their differentiation and function.

Depressed CPC number/function may represent a cardiovascular risk factor with a significant genetic contribution,12 making it is plausible that CPC dysfunction is a multigene disorder with a complex relationship to the other traditional cardiovascular risk factors.17 In this scenario, the identification and study of single candidate genes based on function would be less likely to provide targets for improving the efficacy of autologous progenitor cells in therapy. This is because with multiple contributing genetic factors, the effect of each gene is only a fraction of the resultant phenotype in CAD.17 Support for this concept comes from the observation in the study by Liu and Patient that 2 ETS domain genes under investigation acted cooperatively in regulating angiogenesis.13 Whereas these studies are essential to elucidate the function of the known suspects, unbiased genome-wide association studies, such as those being performed to identify genetic contributors to coronary disease,18,19 may uncover genetic loci containing genes with previously unsuspected links to CPC function. Such information could define mechanisms of importance for individual patients, toward the development of strategies to enhance autologous progenitor cell function and ultimately enable personalized cell-based regenerative therapy.

Regardless of the approach, namely candidate gene versus genome-wide association studies, it is probable that major improvements in the success of regenerative strategies can be translated from understanding the regulators of stem/progenitor cell differentiation and function. The success of therapy using solely autologous cells in CAD patients may come from the study of genes and development.

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None.

References


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