ABSTRACT

Identification and characterization of endothelial colony-forming cells as endothelial progenitors introduced the concept of therapeutic vascularization as treatment option for correcting tissue ischemia by re-establishing blood flow through newly formed blood vessels.

The work in this thesis addresses several important aspects regarding the translation of ECFCs from bench to bedside. The main advantages as well as pitfalls of the present concepts for use of ECFCs as therapeutic means were outlined and reviewed with special emphasis on the contribution of large and small animal models in testing new concepts for clinical implementation.

Isolation and manipulation of ECFCs prior to clinical application requires standardized technology based on use of products devoid of animal-derived products. We have defined an in vitro system for isolation and manipulation of ECFCs from peripheral blood based on the use of human platelet lysate. We also have demonstrated that environmental factors such as hypoxia affect the isolation process by reducing the number of generated ECFCs colonies and impairs the proliferation capacity of isolated cells.

Besides being an attractive cell type for therapeutic neovascularization, ECFCs are of great value to study diseases, in which vascular dysfunction is one of the hallmarks of displayed phenotype as it is in case of pulmonary arterial hypertension (PAH-ECFCs). The comparison of ECFCs outgrowth between healthy subjects and PAH patients followed by functional characterization of PAH-ECFCs as reported in this thesis indicate that indeed an excessive generation and proliferation of ECFCs might play an important role in pathogenesis of PAH.

In summary, the studies presented in this paper improve our understanding of PBECFCs as well as their roles in postnatal vascularization. We anticipate that they will be helpful for future therapeutic application of ECFCs.