Nonhuman Primate Progenitor Cells: Implications for Vascular Disease Therapy

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Introduction

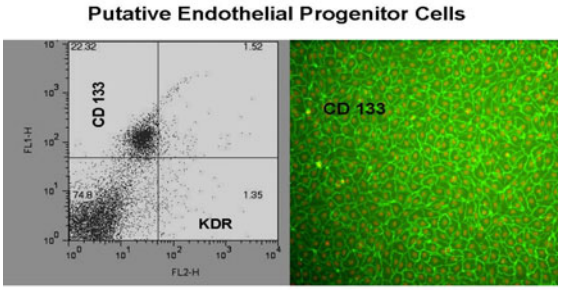
Because of their close phylogenetic similarities with human beings, nonhuman primates represent an animal model well-suited for preclinical progenitor cell-based cardiovascular therapy. However, little work has been done in this regard. The objectives of this study were to collect, identify, expand and label progenitor cell populations from the bone marrow of monkeys as a preamble for future vascular studies.

Materials and Methods

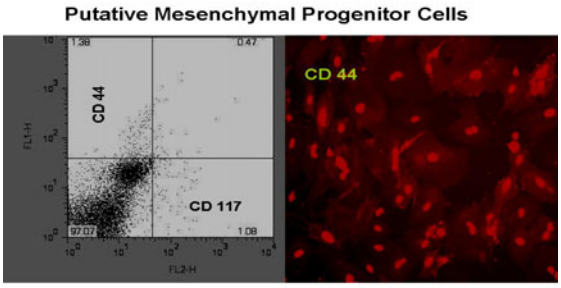
Bone marrow aspirates and peripheral blood samples were collected from five adult male cynomolgus monkeys (*Macaca fascicularis*). The mononuclear cells were isolated on a Ficoll gradient and used for:1) flourescent antibody flow cytometry (FACS - putative endothelial progenitor cells (EPCs) were identified as those with a [$CD45^-$ /$CD133^+$/ KDR^+] phenotype whereas earlier stage uncommitted mesenchymal-like progenitor cells (MPCs) were identified as those with a [$CD45^-$/ $CD117^+$/$CD44^+$] phenotype; 2) cell expansion in endothelial growth media (EGM-2) followed by immunohistochemical (IHC) analyses (using the same markers as those used in the FACS analyses) of third passage epanded cells. The expanded cells were further labeled with Vybrant®CM-dil cell tracking solution (1µl/ml).

Results and Discussion

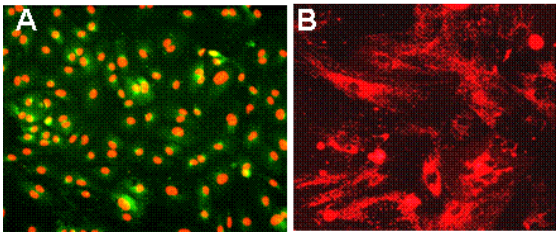
FACS analyses of collected sample indicate that EPCs comprise 1% and 0.06% of the total number of bone marrow and peripheral blood cells, respectively. MPCs comprise 4.5% and 0.25% of the total bone marrow and blood cells, respectively. Depicted in the following figure is a FACS analysis (Left) of CD45- cells from the blood in which double CD133+/KDR+ cells (EPCs)shown in the upper right quadrant; and IHC (Right) of expanded cells FITC-stained with CD133 antibody.



Depicted below is a FACS analysis of CD45- bone marrow cells (left) showing double CD44/CD117 cells (MPCs) in the upper right quadrant and IHC (right) of expanded cells PE-stained with CD44.



Depicted below are expaned EPCs FITC stained with KDR (A) and expanded MPCs from bone marrow labeled with Vybrant® CM-dil (B).



Conclusions

While both bone marrow and blood yielded EPCs, only bone marrow yielded MPCs. Both cell types can be collected, phenotyped and expanded. Labeled cells may be used for seeding of bioengineered vessels, cell-based therapy of unstable atherosclerotic plaques, or genetically engineered and used as a vector to deliver recombinant proteins in vivo.