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Titel des Beitrags: Sustained expansion and transgene expression of coagulation factor VIII-transduced cord blood-derived endothelial progenitor cells.

Abstract: OBJECTIVE: Although hemophilia A seems particularly suitable for gene therapy because even low amounts of plasma coagulation factor VIII (FVIII) provide a significant clinical benefit to the patients, the ideal target cell for recombinant FVIII expression and gene therapy approaches remains to be identified. In this study, we tested the capacity of cord blood-derived endothelial progenitor cells (CBECs) for FVIII expression on stable lentiviral transduction. METHODS AND RESULTS: CD34+ endothelial progenitor cells (EPCs) from cord blood were differentiated into CBECs. Endothelial phenotype was characterized, and lentiviral transduction of early-passage CBECs with a vector encoding FVIII and EGFP did not alter their functional properties and proliferative potential. CBEC could be expanded by 5 to 9 orders of magnitude, thus allowing the expansion of up to 10(15) FVIII-secreting CBECs, starting from as little as 10(6) CD34+ cells. CBECs proved to be highly suitable for FVIII secretion, with 0.35 to 0.39 IU FVIII:C/5x10(4) cells per 48 hours (7.0 to 7.8 IU FVIII:C/10(6) cells per 48 hours), which remained stable over the expansion period. CONCLUSIONS: Our data indicate that CBECs are attractive target cells for inherited coagulation disorders such as hemophilia A, which on lentiviral transduction can be readily expanded to large numbers of
transplantable gene-modified cells in vitro.

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