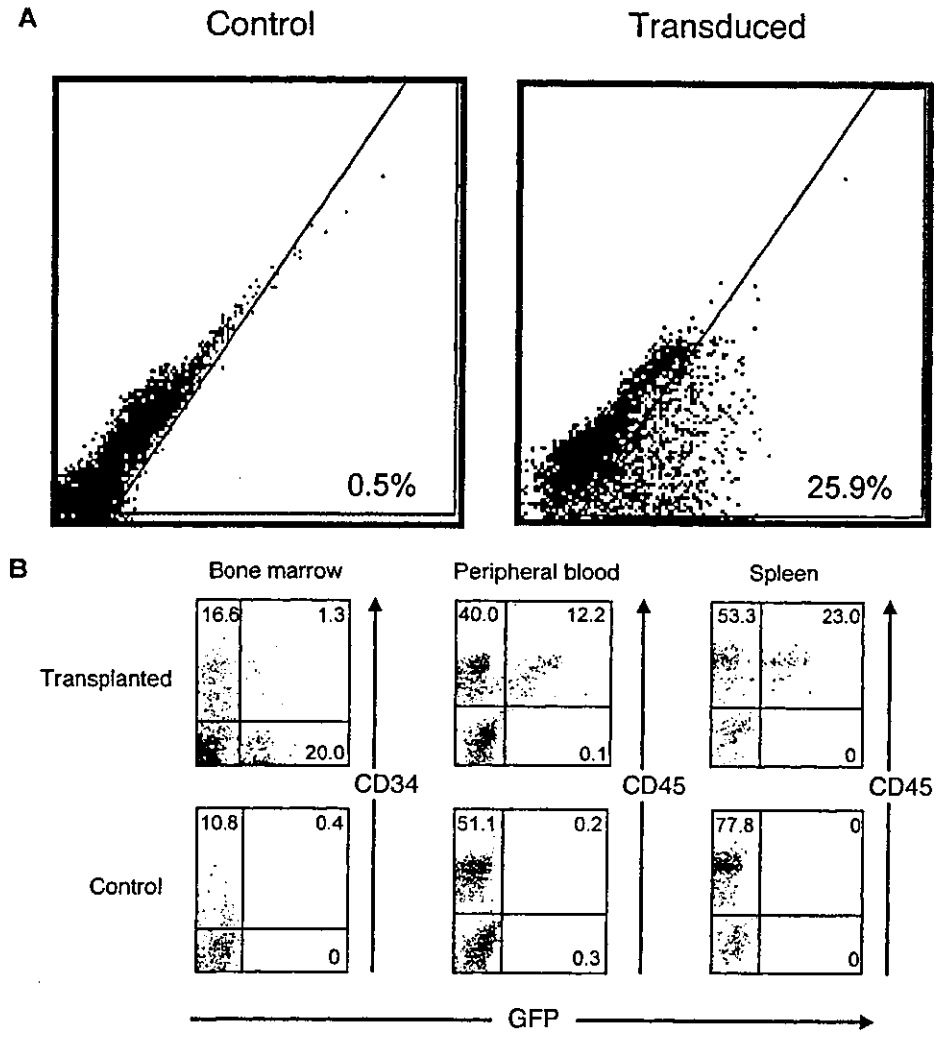

Figure 3. Gene transfer into human CD34$^+$ cells by simian immunodeficiency virus (SIV) vector and transplantation into sublethally irradiated nonobese diabetic/severe combined immunodeficiency (NOD/SCID) mice. **(A)** Human CD34$^+$ cells were transduced with a green fluorescent protein (GFP)-expressing SIV vector and 25.9% of the cells fluoresced. After transduction, the CD34$^+$ cells were transplanted into sublethally irradiated NOD/SCID mice. **(B)** Six weeks after transplantation, bone marrow, peripheral blood, and spleen cells were harvested and examined for human CD34 or CD45 expression (*vertical axes*) and GFP expression (*horizontal axes*). Fluorescent human cells were detected (*right upper quadrants*), clearly indicating that the progeny of engrafted human cells expressed the GFP gene.

deficient, human HSCs can engraft and generate their progeny in these animals (Bhatia et al. 1998). As shown in Figure 3, the progeny of engrafted cells also fluoresced, suggesting that transcriptional silencing did not occur.

• Discussion

We have shown that primate ES cells and HSCs can be transduced efficiently with SIV vectors and that the transgene expression persists without transcriptional silencing. Recently, two groups (Lois et al. 2002. Pfeifer et al. 2002) revealed that trangenes delivered into mouse ES cells by HIV-1-based lentiviral vectors, in contrast to retroviral vectors, were expressed without transcriptional silencing during in vivo embryogenesis, resulting in the generation of transgenic mice. Retroviral and lentiviral vectors might have very different intrinsic susceptibilities to silencing, presumably as a consequence of their contrasting lifestyles. Whereas retroviruses rely on germline transmission as one form of spreading, lentiviruses rely on horizontal and nongermline vertical transfer. Thus, organisms might have evolved mechanisms to suppress the activity of endogenous retroviruses that would otherwise lead to their parasitic expansion in the genome (Yoder et al. 1997). In contrast, such mechanisms might not target lentiviral sequences, because endogenous lentiviruses have not been found in any mammalian genome. The highly efficient gene transfer method using lentiviral vectors without transgene silencing allows for faithful gene delivery to primate ES cells and HSCs with the potential for research and therapeutic application.

• Acknowledgments

The authors thank Dr. Norio Nakatsuji (Kyoto University, Kyoto, Japan) and Tanabe Seiyaku Co. Ltd. (Osaka, Japan) for providing the cynomolgus ES cells.

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PII S1050-1738(02)00253-0 **TCM**