Generation of induced pluripotent stem cells from cynomolgus monkey and the differentiation towards functional

S. Wunderlich\textsuperscript{1}, A. Haase\textsuperscript{1}, S. Merkert\textsuperscript{1}, J. Beier\textsuperscript{1}, A. Schambach\textsuperscript{2}, S. Glage\textsuperscript{3}, G. Göhring\textsuperscript{4}, E.C. Curnow\textsuperscript{5}, U. Martin\textsuperscript{1}

Abstract

Induced pluripotent stem cells (iPSCs) may represent an ideal cell source for future regenerative therapies. Clearly, the development of iPSC-based therapeutic concepts requires suitable animal models. Nonhuman primates show the highest similarities to humans concerning the physiological, cellular and molecular level and macaques are frequently used in preclinical research and pharmacology. Considering the establishment of allogeneic / autologous cell transplantation models, we have generated iPSCs from cynomolgus monkeys (M. fascicularis, cyiPSC). Instead of the commonly human immunodeficiency virus (HIV) based reprogramming vectors that show poor transduction of simian cells, cynomolgus skin fibroblasts were reprogrammed using simian immunodeficiency virus (SIV) based vectors encoding OCT4, SOX2, KLF4, and c-myc. Resulting cyiPSCs show all typical characteristics of primate embryonic stem cells (ESCs). Culture characteristics and cell / colony morphology is almost identical to cynomolgus ESCs and cyiPSCs stain positive for typical pluripotency markers such as OCT4, NANOG, and TRA-1-60. CyiPSCs differentiate in vivo and in vitro into derivatives of all three germlayers. Furthermore, differentiation into functional cardiomyocytes could be demonstrated. Our data indicate that the generated cyiPSCs are highly similar to human iPSCs and should therefore represent an excellent cell source for allogeneic / autologous preclinical cell transplantation models.