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Induction of pluripotency in human endothelial cells resets epigenetic profile on genome scale

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Abstract

Reprogramming of a limited number of human cell types has been achieved through ectopic expression of four transcription factors to yield induced pluripotent stem (iPS) cells that closely resemble human embryonic stem cells (ESCs). Here, we determined functional and epigenetic properties of iPS cells generated from human umbilical vein endothelial cells (HUVEC) by conventional method of direct reprogramming. Retroviral overexpression of four transcription factors resets HUVEC to the pluripotency. Human endothelial cell-derived iPS (endo-iPS) cells were similar to human ESCs in morphology, gene expression, in vitro and in vivo differentiation capacity. Endo-iPS cells were efficiently differentiated in vitro into endothelial cells. Using genome-wide methylation profiling we show that promoter elements of endothelial specific genes were methylated following reprogramming whereas pluripotency-related gene promoters were hypomethylated similar to levels observed in ESCs. Genome-wide methylation analysis of CpG sites located in the functional regions of over than 14,000 genes indicated that human endo-ipS cells were highly similar to human ES cells, although differences in methylation levels of 46 genes were found. overall CpG methylation of promoter regions in the pluripotent cells was higher than in somatic. We also show that during reprogramming female human endo-iPS cells exhibited reactivation of the somatically silenced X chromosome. Our findings demonstrate that iPS cells can be generated from human endothelial cells and reprogramming resets epigenetic status of endothelial cells to pluripotency. © 2010 Landes Bioscience.

Keywords

Endothelial, Induced pluripotent stem cells, Methylation, Reprogramming, X chromosome