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Molecular Signature of Various Signaling Pathways in Human Embryonic Stem Cells

Yong-Mahn Han

Laboratory of Development and Differentiation, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon 305-806

Embryonic stem cells (ESC) derived from early embryos are able to maintain indefinitely under the optimal culture conditions by self-renewingand differentiate into all cell types of embryo proper. It is known that JAK/STAT signaling pathway, in which LIF functions as a ligand, is very important for the self-renewal of mouse ESC. Although a variety of signaling pathways are involved in self-renewal of stem cells, little information is available regarding the transcriptional profiles of developmentally important signaling pathways in human ESC. In this study, transcriptional profiles of key genes related tothe developmentally important signaling pathways such as BMP4, TGF-β, FGF4, Wnt, Hh, Notch, and JAK/STAT signaling, were examined to understand self-renewal of human ESC in the molecular level. In BMP4, TGF-β and FGF4 signaling pathways, extracellular molecules, ligands and antagonists, were highly expressed in human ESC as compared to the human embryoid body (EB). In Wnt, Hh and Notch signaling, expression of intracellular molecules was enriched in human ESC. In JAK-STAT signaling pathway, no difference was detected in the expression levels of the genes between human ESC and EB. These results suggest that self-renewal of human ESC is likely to be maintained by the coordinated regulations of signaling specific molecules. In another experiment, we performed transcriptional profiling of key genes involving in the cell-cycle of human ESC. Major factors responsible for G1/S transition including Cyclins, Cyclin-dependent kinases and pRb family were highly expressed in human ESC. The transcripts of INK4 family members were expressed at a low level in human ESC, whereas upregulated in differentiation controls such as hEB, HeLa and HEK cells. Theresults demonstrate that the cell-cycle controlling genes exhibit unique transcriptional signatures in human ESC that may contribute to propelling ES cells from G1 to S-Phase, eventually resulting in short G1 phase. Our findings provide foundationfor further research on human ESC to understand the molecular mechanisms of self-renewal and differentiation.