

Gene Expression Profiling of Differentiating Mouse Embryonic Stem Cells Predicts Global Oscillation of Gene Expression during Differentiation

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Embryonic stem (ES) cells are pluripotent cells directly derived from early stage embryos that retain the ability to differentiate into all cell types. This unique feature is the basis of various applications of ES cell technology such as *in vitro* models of mammalian development, germline transgenesis to make knockout mice, and a generic source for cell therapy in regenerative medicine. To achieve success in these applications, the molecular mechanisms for pluripotency and differentiation processes of ES cells have to be determined. To delineate the pathways involved in pluripotency and differentiation of mouse ESCs as a long term goal, we examined global changes of gene expression patterns in differentiating ES cells *in vitro* and also compared with those of early embryos (morulas and blastocysts) as well as adult progenitor cells (Sca+ blood cells and mesenchymal stem cells). According to their expression patterns, genes were sorted into several groups and some of them were confirmed their expression by RT-PCR and *in situ* hybridization. We also identified groups of genes differentially expressed in specific time points of differentiation using the Chen-test. Finally, we could found several unexpected findings. First, ES cells were closer to mesenchymal stem cells than blastocysts, although they derived from blastocysts. Second, dramatic oscillations of gene expression were observed during the random differentiation of ES Cells, such that expression profiles were similar among 12, 48, 72, and 120 hrs after differentiation, whereas those of 24, 36, and 96 hrs were alike. This pattern of expression was not different when separately analyzed the known and unknown genes. Thus, our data may provide fundamental information for research of pluripotency and mammalian early embryogenesis, and it also suggests that the oscillation of gene expression may occur intrinsically during normal development although further study is required.