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INDUCTION OF FUNCTIONAL NEURONS FROM EMBRYONIC STEM CELLS

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Embryonic stem (ES) cells can continuously proliferate in an undifferentiated state and differentiate into a desired cell lineage under certain conditions. These abilities make ES cells an appealing source for cell replacement therapies, the study of developmental biology, and drug/toxin screening studies. We are very interested in the efficient generation of various neuronal phenotypes from human/mouse ES cells. In this presentation, I will focus on methods for efficiently generating neurons from ES cells and then give a general introduction for application of ES cell-derived cells to central nervous system (CNS) disorders such as Parkinson's disease.

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ES CELL CULTURE FOR GENE DISCOVERY

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While ES cell has a potential to give rise to all differentiated somatic cells, in vitro control of their differentiation is still difficult goal requiring extensive efforts from various directions. Such efforts include 1) specification of intermediate stages during differentiation of each cell lineage, 2) development of markers to define intermediate stages, 3) specification of molecular signaling regulating cell specification, and 4) use of obtained results for establishment of defined culture conditions to attain guided ES cell differentiation. All these are indeed nothing but major issues of developmental biology. This is the reason for increasing expectation that in vitro ES cell differentiation can serve as a model for studying embryonic development at cell level. For this purpose, DNA microarray that enables comprehensive analysis of changes of gene expression profile should be a useful method particularly for ES cell culture that has basically no limitation in available cell number. Thus, we have spent some years for preparing a data base of gene expression during ES cell differentiation and use it for uncovering molecular networks that regulate cell specification during embryogenesis. To this end, we have developed surface and knock-in markers to define and purify intermediate stages appearingES cell differentiation culture. Those intermediate populations have been collected and subjected to DNA microarray analysis, that have developed to a continuously expanding database of transcription based on Affymetrix oligonucleotide arrays. This database currently contains ca. 200 purified samples including various distinct early intermediates purified from ES cell differentiation and also a similar number of samples derived from embryonic and adult tissues which provide a powerful transcriptional context aiding the meaningful analysis of the differentiation data. In parallel, we have prepared a user-friendly data managing systems that allow easy dialogue of users with accumulated data. The Value of this data base increase when combined with a reliable and rapid functional assay mediated by siRNA gene knock down method. In this symposium, we will present a couple of genes that we isolated from this data-base, which turned out to be essential for oncogenesis as well as embryogenesis.
Key Words: ES cell, Stem cell, DNA microarray, siRNA