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Author(s)	PARK, Jong-Im
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Developmental potential of mouse parthenogenetic embryonic stem cells

Jong-Im Park

Laboratory of Theriogenology,
Department of Veterinary Clinical Sciences,
Graduate School of Veterinary Medicine,
Hokkaido University, Sapporo 060-0818, Japan.

For the ability of colonization in chimeric animal as well as the unique properties to form well-differentiated tumors in ectopic site of host animals and *in vitro* via embryoid bodies differentiation, embryonic stem (ES) cells has been used as indispensable tools for research of mammalian embryogenesis and further advances in reproductive biology. Recently, ES cells whose genomes are composed of only maternal or paternal origin have been used as an alternative way of studying developmental events including genomic imprinting. These ES cell lines with a distinguishable marker are invaluable for tracing distribution and differentiation potency of ES cells in chimeras. I initiated this study to analyze the role of genomic imprinting in early embryonic development in mammals making use of parthenogenetic ES cells. Chapter 1 was devoted to isolation of *lacZ*-positive parthenogenetic ES cell lines from TMA-48P and its subsequent characterization. T48PZ4 cell lines isolated after transfection of pENL plasmid were trisomic for chromosome 8, but there were nothing unusual about their behavior in culture including embryoid body formation as parthenogenetic ES cells. In chapter 2, behavior of T48PZ cell lines in chimeric embryoid bodies with fertilized ES cells was studied by means of *in situ* X-gal staining of β -galactosidase. Morphological and histological examination of T48PZ4-derived embryoid bodies revealed that this parthenogene-

tic cell line had considerably restricted differentiative potential compared to fertilized ES cells, particularly in the formation of endodermal layers and cavitation in the core. In contrast to underdevelopment of the outer endodermal layer, T48PZ4 cells were mainly allocated to the endodermal layer in chimeric embryoid bodies formed by T48PZ4 and TMA-24 cell line of a fertilized embryo origin. These findings indicate T48PZ4 cell clone retains principal traits specific to parthenogenetic cells. In chapter 3, differentiative potential of parthenogenetic ES cell lines TMA-47P and TMA-48P was studied by histological examination of tumors produced by transplantation of these cell lines. Undifferentiated parthenogenetic ES cells gave rise to well-differentiated teratomas closely similar to those produced by fertilized ES cell lines. However, restriction of differentiative potential was evident when embryoid bodies were transplanted under the kidney capsule. The longer the embryoid bodies were kept in culture before transplantation, the simpler became the histological profiles of induced tumors.

In summary, it may be stated that parthenogenetic ES cells retain the basic characteristics of undifferentiated embryonic cells of parthenogenetic origin. Hence, these cell lines may be used as convenient resources alternative to parthenogenetic embryos themselves in various fields of biology and medicine.