FEATURES

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Dopaminergic Differentiation Using Pluripotent Stem Cells

Olga Momčilović, Justine Montoya-Sack, and Xianmin Zeng

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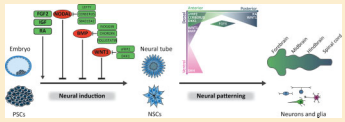

Parkinson's disease (PD) is the second most common neurodegenerative disorder. The motor symptoms of PD are caused by the loss of dopaminergic (DA) neurons in the substantia nigra pars compacta of mesencephalon. The causes for death of DA neurons are not well understood, but the strongest risk factor is increasing age. There is no cure currently available for PD, and treatment is limited to management of PD symptoms in patients. Primary DA neurons are virtually unobtainable from living patients and animal studies have proven inadequate for studying the mechanism of PD development. Pluripotent stem cells (PSC) are primary self-renewing cells capable of differentiating into allcell types of an organism, including DA neurons. PSCs represent an abundant source of cells that can be genetically modified or isolated from patients with complex diseases, enabling the production of large quantities of DA neurons for disease modeling, drug screening, and gene function studies. Furthermore, since PD arises as a result of deterioration of DA neurons in a specific brain region, it has been suggested that a relatively small number of cells could restore normal function. PSCs could provide a source of DA neurons for cell replacement therapy. The focus of this Prospect is on the development and *in vitro* derivation of DA neurons from PSCs, as well as current applications of the technological advances, with the emphasis on future directions and efforts in the field.

Quiescence and Attenuated DNA Damage Response Promote Survival of Esophageal Cancer Stem Cells

Yulin Chen, Dan Li, Dapeng Wang, Xuefeng Liu, Ning Yin, Yongmei Song, Shih Hsin Lu, Zhenyu Ju, and Qimin Zhan

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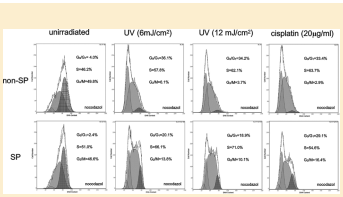

Accumulating evidence indicates cancer stem cells (CSCs) possess the capability to resist DNA-damage induced cell death, whereas the mechanism is largely unknown. It is shown here that cell cycle status and DNA damage response (DDR) in CSCs probably contribute to their survival in genotoxic insults. In this study, esophageal cancer stem cells (ECSCs) are isolated from esophageal cancer cell line EC9706 by side population (SP) phenotype through flow cytometry and it is found that ECSCs preferentially stay quiescent as compared to the non-ECSCs and are more resistant to DNA damage agents. Further study revealed that ECSCs express a lower level of EGFR, phosphoralated Stat3, and c-Myc, yet abnormally upregulated p27. More interestingly, different from non-ECSCs, when suffering DNA damage agents, ECSCs showed attenuated DDR, as well as declined DNA repair potential. These data indicated ECSCs probably employed an impaired DDR to handle severe genomic insults. Conclusively, it is inferred that the damage-resistance ability of ECSCs is likely attributed to their slow-cycling status and avoidance of apoptosis or senescence triggered by an excessive DDR.

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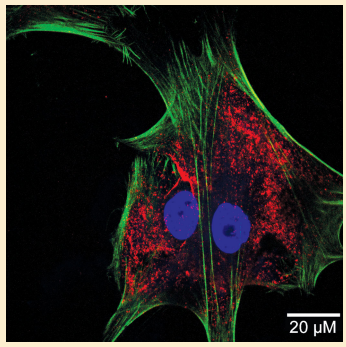

Caveolin-1 is a scaffolding protein of cholesterol-rich caveolae lipid rafts in the plasma membrane. In addition to regulating cholesterol transport, caveolin-1 has the ability to bind a diverse array of cell signaling molecules and regulate cell signal transduction in caveolae. Currently, there is little known about the role of caveolin-1 in stem cells. It has been reported that the caveolin-1 null mouse has an expandedpopulation of cells expressing stem cell markers in the gut, mammary gland, and brain, suggestive of a role for caveolin-1 in stem cell regulation. The caveolin-1 null mouse also has increased bone mass and an increased bone formation rate, and its bone marrow-derived mesenchymal stem cells (MSCs) have enhanced osteogenic potential. However, the role of caveolin-1 in human MSC osteogenic differentiation remains unexplored. In this study the expression of caveolin-1 in human bone marrow derived MSCs is characterized. It is shown that caveolin-1 protein is enriched in density gradient-fractionated MSC plasma membrane, consisting of _100nm diameter membrane-bound vesicles, and is distributed in a punctate pattern by immunofluoresence localization. Expression of caveolin-1 increases in MSCs induced to undergo osteogenic differentiation, and siRNA-mediated knockdown of caveolin-1 expression enhances MSC proliferation and osteogenic differentiation. Taken together, these findings suggest that caveolin-1 normally acts to regulate the differentiation and renewal of MSCs, and increased caveolin-1 expression during MSC osteogenesis likely acts as a negative feedback to stabilize the cellphenotype.

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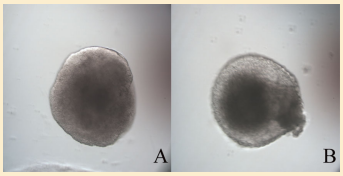

In recent years, applications of stem cells have already involved in all domains of life science and biomedicine. People try to establish human embryonic stem cell lines (hESCs) in order to carry out hESC-related studies. In this study, it is explored what embryos are conducive to the establishment of hESCs. The discarded embryos from in vitro fertilization–embryo transfer (IVF–ET) cycles were sequentially incubated into blastocysts, and then the inner cell mass (ICM) was isolated and incubated in the mixed feeder layer. The cell lines which underwent serial passage were identified. After a total of 1,725 discarded embryos from 754 patients were incubated, 448 blastocysts were formed with 123 high-quality blastocysts. The blastulation rate was significantly higher in the discarded embryos with non-pronucleus (0PN) or 1PN than in the discarded embryos with 2PN or _3PN. The blastulation rate of the D3 embryos with 7–9 blastomeres was higher. Among the originally incubated 389 ICMs, 22 hESCs with normal karyotype were established, and identified to be ESCs. Therefore, in establishing hESCs with discarded embryos, D3 0PN or 1PN embryos with 7–9 blastomeres should be first selected, because they can improve high-quality blastulation rate which can increase the efficiency of hESC establishment.