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Editorial

Influence of Parent Cell Types on Pluripotency Induction and Applications of Such Induced Pluripotent Stem Cells (iPSCs)

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Editorial

Era of Embryonic Stem Cells

The days were thought to be revolutionary when human ES cells were derived for the first time from the 5-6 day old human embryos called blastocysts [1,2]. Prof. James Thomson's group in the University of Wisconsin, Madison, USA, pioneered this derivation of ESC. People all over the globe got involved in deriving new hESC lines, both research and clinical grade [3-7]. Also, ESCs were differentiated into various lineages [6,8] aiming at feasibility for cell therapy applications. Human ethics critiqued this method of deriving hESCs because of the involvement of destruction of human embryos [9,10] Consequently, questions were raised regarding the use of the differentiated lineages for cell therapy applications. Suddenly, within a decade of the pioneering of hESC derivation, the Nobel Prize-winning discovery of the close cousin of embryonic stem cells, Induced Pluripotent Stem Cells (iPSC) by Prof. Shinya Yamanaka of Japan was made [11]. This time, it was a somatic cell giving rise to ES-like/pluripotent stem cells. Also, because of the pluripotency of such a cell, no ethical issues were involved, and it appeared much simpler to use reprogrammed somatic cells for cell therapy applications.

Era of Induced Pluripotent Stem Cells

Researchers started using this iPSC technology for deriving iPSCs from various cell types, such as fibroblasts [11] , adult and fetal neuronal stem cells [12,13] adult and fetal hepatocytes [14] myogenic cells [15] blood cells [16], dental pulp cells [17]. Interestingly, iPSCs were not only derived from humans and mouse, but also from large farm animals [18] and other large animals such as bovine [19], domesticated goats [20] equine [21] and canine [22]. In-vitro human disease modeling has been facilitated in the recent times by the derivation of iPSCs from various cell types taken from diseased individuals. Diseases from which iPSC have been derived are familial cancers such as Li-Fraumeni Syndrome (LFS [23], Hutchinson-Gilford Progeria [24-27] Diabetes [28,29] and so forth.

Recommended Applications of iPSCs Depending on the Parent Cell Type

Although the iPSC derived from a wide variety of parent cell types are still called the pluripotent cells, there remains a slight difference amongst such iPSCs. The difference is not obvious when characterizations are done, on the assessment of pluripotency such as expression of key pluripotency genes, Oct4, Nanog, Sox2, Rex1; ability to form teratomas showing all three germ layers in immunocompromised mice and embryoid body formation in suspension cultures. Interestingly, the parent cell type of the respective iPSCs has a strong influence on the differentiation propensity of that particular iPSC line [30]. For example, in iPSCS where the parent cell types are cardiomyocytes, exhibit higher propensity towards cardiac lineage, as compared to the iPSCs derived from fibroblast parent.[31,32] This difference in differentiation propensity is attributed to the epigenetic memory of the iPSC line that comes from the parental cell type [33,30]. However, this epigenetic memory reportedly erases over extended passaging in mouse iPSC lines [34]. More recently, standardized gene expression selection criteria for iPSCs has been able to minimize the effect of parental cell line on the differentiation propensity of iPSC [35].

As the use of iPSCs have been for modeling various diseases in the areas of research, the epigenetic memory, and enhanced differentiation towards the parent cell type works as an added advantage for modeling the specific disease. Since the epigenetic memory reportedly erases with time in long-term cultures in mouse iPSC, and the iPSCs do not show a preferred differentiation towards parental cell type, such cell types might be useful for modeling multiple diseases from a single iPS cell line. As the clinical uses of iPSCs are applications in regenerative medicine, large

scale iPSCs generations with uniform differentiation potentials are desirable. Indeed, uniform differentiation propensity can be achieved via extended culture of human iPSCs that still need to be validated. However, standardized gene expression selection criteria [35], to achieve a uniform differentiation amongst iPSCs originated from various cell types can be recommended.

Conclusion

Hence, from the perspective of application of iPSCs, the parent cell types have a lot of influence to decide the respective differentiation propensities. However, ES cells also have variable differentiation propensities that are yet to be explained. Most important, based on the parent cell type, it is easy to assess beforehand the differentiation propensity of a particular iPSC line, however, for an ESC line; it becomes difficult to estimate the differentiation propensity unless experimentally validated.

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