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Genetics, Cells, Stem Cells and Embryos: World Genetics and Cell Biology Striding Towards a New Era for Challenges

Jyh-Cherng Ju*

*Graduate Institute of Biomedical Sciences, China Medical University, Taichung, Taiwan.

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Since the appearance of compound microscopes in Europe in the early 1600's and followed by the first discovery of cells by Robert Hooke in 1665, when was first recognized that cells are the fundamental building block of all creatures and life; genetic materials are known as the central element of a functional cell. Along with the development of cell biology and molecular genetics, high performance research tools have been created, which have drastically speeded up the progression of biological sciences, particularly the development in several fields of study. Epigenetics, embryology, cellular reprogramming and stem cell research have been among those most active research fields in the past decades. Some worth mentioning advancements within representative fields of study are summarized below [1].

CELL REPROGRAMMING AND ANIMAL CLONING

With the parallel breakthrough that can reversely turn terminally differentiated somatic cells into the naive pluripotent cells, a.k.a. induced pluripotent stem (iPS) cells; by transfecting some master genes, such as Oct4, Nanog and/or other lineage specific genes. Now almost any types of cells with various degrees of cell potencies, such as pluripotent, multipotent and other cell types, can be produced, although in some cases there are still inefficiencies and achieved stochastically [2,3].

Somatic cell nuclear transfer (SCNT) makes use of ooplasmic factors as the major factor to reprogram terminally differentiated cells back to their omnipotent (totipotent) and/or naïve status. For reproductive cloning in animals, even though an extremely low efficiency is associated with the birth of Dolly the sheep, more than 20 cloned mammals, such as cattle, goats, pigs, horses, mules, mice, rats, ferrets, rabbits, cats, dogs, wolves, buffaloes and many other species, have been produced by the SCNT technology. The successful generation of cloned embryos and animals facilitates potential applications in agriculture (for food-producing animals, reproductive cloning) and human medicine (therapeutic cloning). Purposely expanding specific transgenes in genetically superior animal herds can be more effectively achieved by combining SCNT and other technologies such as stem cell, cellular reprogramming and epigenetics, instead of the traditional breeding program. In humans, no report on the reproductive cloning is currently documented due to the legal, ethical and, most likely, technical issues, which was once considered as one clear boundary to delineate *Homo sapiens sapiens* from animal species by the Mother Nature. This year, however, cloned monkeys by SCNT have just been produced by Chung et al. [4], regardless of its low efficiency due to an insufficient epigenetic reprogramming of the introduced nucleus by the recipient ooplasm during the development of the reconstructed embryos. Apparently, we are now one step closer to the "prohibited" borderline between human beings and animal species [5].

DIRECTED DIFFERENTIATION AND TRANSLATIONAL APPLICATIONS

Recently, several major achievements have linked reproductive cloning to therapeutic cloning and PS cell technologies, shedding light for the treatment of human diseases and injuries. One is the discovery of the major genes for modulation of ES cell pluripotency and cloning induced PS (iPS) cells. Others are successful generation of ES cell lines from SCNT-derived embryos in both humans and non-human primates. Further understanding the biology and mechanisms of cellular differentiation, stem cells can be broadly applied to a variety of cell-related therapies. Many studies have shown that PS cells and differentiated cells and

Corresponding author: Jyh-Cherng Ju, Graduate Institute of Biomedical Sciences, China Medical University, Taichung, Taiwan, E-mail: jcju@dragon.nchu.edu.tw

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and other multipotent cells can be differentiated into almost any cell lineages of the three germ layers. For instance, motor neurons, hepatocytes, cardiamyocytes and their progenitors can be derived from pluripotent stem cells *in vitro* by directed differentiation or transdifferentiated from other cells type by transfection with lineage specific genes. Moreover, with a proper 3D scaffold, PS cells can self-organize and differentiate into optic caps in both human and mouse model [6-15]. Also, a phase I clinical trial has shown that an ES cell-derived retinal pigment epithelium patch is effective in treating age-related macular degeneration of patients [4].

Another example among those of the most impressive translations, for instance, such technology knowledge is to produce bundles of muscle fibers and hence finally harvested them into slices of hamburger meat by differentiation of stem cells into muscle cells. Development of such stem cell technology highly impacts agriculture, food technologies and biomedicine through directed differentiation into various adult cell types [16].

IN VITRO EMBRYOGENESIS AND ES CELL-DERIVED EMBRYOS

Scientists have been working for decades to produce embryos *in vitro*; however, only the early stage embryo prior to the implantation stage can be successfully cultured and produced in both animal species and humans. One of the most recent progress is that both human and mouse embryos can be continuously cultured across implantation stage [1,2] which offers a sophisticated tool for studying post-implantation development without animal sacrificing.

The other way around, an intriguing and relevant breakthrough in pluripotent stem cell research has been done by UK and Dutch scientists, who have successfully "synthesized" mouse [14] and human [8] blastocyst-like embryos, designated as blastoids, by a combination of ES cells with trophectoderm stem cells in a 3D culture condition. Some of these artificial mouse embryos are even capable of initiating implantation *in vivo* by inducing decidualization of the endometrium. These technologies would help to dissect the complicate mechanisms underlying cell-cell interactions and developmental abnormality during embryogenesis. Also, it could circumvent, or at least, minimize the ethical issues in procuring human embryos and potentially lay a solid foundation for the treatment of infertility.

Disclosure of those underlying mechanisms would also benefit regulating self-renewal, stem ness and differentiation of PS cells. Although much remains unclear and controversial issues exist, scientists are gaining more insights into nuclear and cellular reprogramming of the cloned embryos and stem cell biology during embryogenesis.

Regardless of the legal and/or ethical issues in various societies, generation of human embryos for pluripotent stem (PS) cell research by SCNT would have relatively less concerns or hustles than retrieving embryos directly from consented patients.

FROM THE VACANTI MOUSE TO INTERSPECIFIC ORGANOGENESIS

For centuries, humans are in need of transplantable organs for extending lives. Two decades ago, the ear-mouse idea first reported by Dr. Charles Vacanti in 1994 has inspired many subsequent studies and efforts. One of the brilliant and promising ideas is to experiment on how to create human organs directly from animal species, i.e., xeno-organ production or interspecific organogenesis [10,12,17].

Along with these continuous developments in genetics, epigenetics and genome editing tools, organoid culture such as generation of stomach and other tissues from embryonic or pluripotent stem cells [13] and interspecies SCNT has offered promising perspectives for biomedical translation in the near future.

A scheme in **Figure 1** is to illustrate the focuses of this journal, namely, the advanced Genetics and Cell Biology are mainly centered by technologies in Embryogenesis, cellular reprogramming, stem cells, epigenetics and many other extended fields of study.

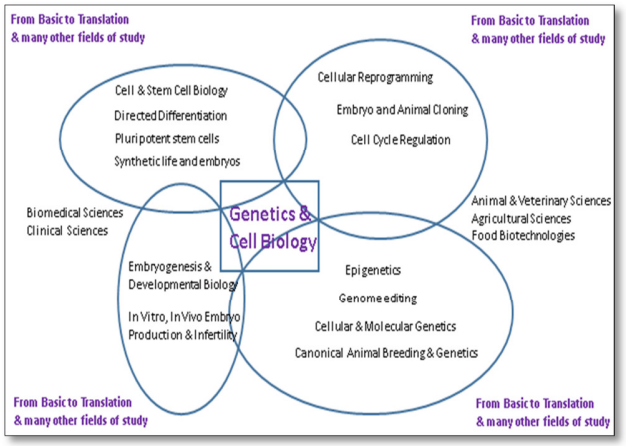

Figure 1. Scopes and waterfronts of cell research are schematically illustrated with some representative fields of studies that center Genetics and Cell Biology.

With the full support from all the editorial members and staff of this Journal, we are launching our inaugural issue and other follow-up issues of this journal to cover all the waterfronts in Genetics and Cell Biology, such as canonical genetics, epigenetics, cellular reprogramming, stem cell biology, cell cycle regulation, regenerative medicine, embryo and animal cloning, embryology, genome editing, and so forth, in agriculture, food biotechnology and biomedicine, for both basic and translational research [18].

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