



A Short Review: Research progress of bovine stem cells

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Abstract

All bodies rely on stem cells to grow from a single cell into an adult. Stem cells allow our bodies to build new tissue, such as new muscle when we exercise. Domestic livestock stem cells offer a unique opportunity to study developmental biology, serve as a resource to screen for harmful toxins or lifesaving drugs or even regenerative therapies for a number of diseases. This review provides information on bovine stem cells, emphasizing different sources of stem cells and current methods for isolation and culture of pluripotent stem cells from cattle. We also review the application of bovine stem cell in future.

Key words: Bovine, Stem Cell, Application.

Introduction

Small experimental animals can be used to research the principles of stem cell transplantation therapy, but prior to transferring this technology to the therapy it is important to introduce it to a large-animal model, which is biomechanically more relevant to humans. The bovine is a domestic species of important economic interest.

The generation of pluripotent stem cell lines may allow for complex genetic manipulations, opening new venues for biomedical and agronomical applications (1).

Bovine embryos will be powerful model to study developmental and stem cell biology. They offer several advantages as an animal model for studying stem cell biology and animal model for human disease including their gestation period similar to human and as a mammalian animal model to focus on stem cell research are avoid faces serious ethical concerns.

Sources of bovine stem cells

Bovine embryonic stem cells

Embryonic stem cells (ESC) were first established from explant cultures of in vivo day (d) 3.5 mouse embryos almost three decades ago. Rang of work in the stem cell field is done using human and mouse; the big mammalian system from which pluripotent embryonic stem cell lines can be established is the bovine system. In bovine, bESCs (2), bPGCs (3), bSSCs (4) and iPSCs (5), pluripotent cells have been isolated from several sources (Tables 1).

Isolation, culture and characterization of bESCs in vitro

Most attempts to isolate and culture bESCs have been done with day 7–9 bovine blastocysts (6) (7). Although ESC-like cells have also being isolated from day 12–14 embryos. Yet, the best time of bovine pre-implantation development to isolate ESCs is still unknown (8).

Another source of pluripotent stem cells is the trans-

formation of primordial germ cells (PGC). Murine PGC-ES (EG) cell lines have been established and chimeric mice have been produced (9). An important discovery was that basic fibroblast growth factor (bFGF) helped to transform PG cells into permanent EG cell lines (10). The firstly isolated from of bovine ovaries (11). PGCs cultured medium containing growth factors and cytokines including bFGF, SCF. Like mESCs, bPGCs can be maintained in an undifferentiated state in the presence of LIF (9).

Several characterizations have been shown to be shared between bESCs and other species ESCs counterparts. Firstly, alkaline phosphatase (AP) activity is conveyed by bESCs (12).

Several immunological markers are also expressed, including stage-specific embryonic antigens (SSEA) SSEA1, SSEA3 and SSEA4 (13) (14). Expression of homologues of Oct3/4 (14), Nanog and Sox2 (16).

Bovine somatic and adult stem cells

Neural Stem cells

First time report of culturing bovine neural stem/progenitor cells (NSCs) by the neurosphere method NSCs are multipotent cells with the self-renew and to differentiate into various cells the nervous system such as glia. The floating cell aggregates expressed nestin, an intermediate filament of neural stem/progenitor cells and, under the differentiation condition, nestin-expressing cells decreased and the proportions of the three types of neural differentiated cells increased (17)(18).

Mesenchymal stem /progenitor cells

Mesenchymal stem cells (MSCs) were first reported in bone marrow cultures displaying shuttle-like, colony capacity and adherent to dish(18)(19).MSCs are multipotent, self-renewing cells that can be found in almost all postnatal organs and tissues. The main functional characteristics of MSCs are their immunomodulatory ability, capacity for self-renewal and to differentiate in to variety of cell types such as adipocytes(21)(22)(23),

Table 1. Pluripotent stem cell types from bovine.

Cell type	Source	Identified methods
ESCs	7-9 days embryos	EB formation, in vitro differentiation
PGCs	18 – 39 days embryos	Alkaline phosphatase staining in vitro differentiation
spermatogonial stem cells	adult male bovine	in vitro differentiation
iPSCs	Fibroblasts cells	in vitro differentiation, germline chimaera

myoblasts(24) (25), and neurogenic cells (26).

Several makers have been proposed to characterize MSCs including CD73 (27) (28), and CD105n Development of a human adipocyte model derived from human mesenchymal stem cells (29) (30). Other commonly used indicators include absence of expression of hematopoietic (CD34 and CD45) and endothelial (CD31) markers, co-expression of CD29, CD44, CD73, CD90, CD105, CD166 (19) and CD146 (31).MSC are isolated from various tissues fat (32), liver (33), skin (34), umbilical cord (35) (36) and bone marrow (37).

Like their mammalian counterparts, bovine MSCs have been isolated from different organs including liver (38), bone marrow (39) (40), umbilical cord blood (41) umbilical cord Wharton's jelly (42), adipose, (43), lung (44), skin (45). Cattle MSCs from different organs can be differentiated into ectoderm cells, endoderm cells and mesoderm cells.

Muscle stem cell

The growth of adult skeletal muscle depends on the self-renewal and differentiation of muscle stem/progenitor cells derived from specialized muscle stem cells. Satellite cells are committed myogenic cells. Besides satellite cells, multipotent progenitor cells, such as pericytes, are able to differentiate into myogenic cells, thereby contributing to postnatal muscle growth (46).

Skeletal muscle satellite cells were first described in frog muscle by Mauro based on their morphology and position relative to mature myofibers and was later identified in adult avian and mammalian muscle. Satellite cells adhere to the surface of myotubes prior to the formation of the basal lamina, such that the basal lamina surrounding the myofiber and satellite cells is continuous (47) (48). Satellite cells mediate the postnatal growth of muscle and are the primary means by which the mass of adult muscle is formed (49).

In the bovine, satellite cells have been isolated from Luxi cattle. This is consistent with other animals of muscle homeostasis during development (50).These cells were characterized molecularly using MyoD, Pax7 and Desmin as myogenic markers and were found to differentiate into osteocytes and adipocytes after exposure to bone morphogenetic (BMPs) and adipogenic factors, respectively (51).

Amniotic stem cells

Like others mammals, bovine embryos contain extra-embryonic membranes including allantois, yolk sac, chorion and amnion. The cavity enclosed by the amnion contains fluid, the amniotic fluid stem cell originated from it. Amnion and amniotic fluid (AF) are inexhaustible sources of mesenchymal stem cells (MSCs) (52). Amniotic epithelial cells (AECs) display a polygonal morphology, whereas AF-MSCs exhibit a fibroblastic-

like morphology. AECs express MSC-specific markers CD29, CD44, CD166, CD105 and CD73. In AF-MSCs, only CD29, CD44, and CD166 are detected; CD73 is expressed and ENG has not been found. AF-MSCs and AECs are positive for the pluripotent markers Oct4 and c-Myc and lack of the hematopoietic markers (52). When appropriately induced, AECs and AF-MSCs are capable of differentiating into ectodermal and mesodermal lineages, suggesting that AECs and AF-MSCs are multipotent (53).

Germline stem cells

Germline stem cells (GSCs) can generate haploid gametes, sperms or oocyte, which are responsible for transmitting genetic information from generation to generation. Since the previous report of isolation of germline stem cell from cattle which were contained testes (4) and ovaries. The male germline stem cells, also called spermatogonial stem cells (SSCs). SSCs can be differentiated into osteoblasts *in vitro* (54).

Bovine induced pluripotent stem cells (iPSCs)

Direct reprogramming has been established recently for converting differentiated somatic cells into pluripotent cells. As a new type of pluripotent stem cells, reprogrammed by ectopic expression of defined factors Oct4, Sox2, Klf4 and c-Myc from differentiated somatic cells (55), iPSCs have unlimited self-renewal capacity, maintain pluripotency, and are very similar to embryonic stem (ES) cells in morphology, proliferation, pluripotent gene expression, promoter methylation, teratoma formation and the capacity to differentiate into all of the cell types *in vivo* or *in vitro* under appropriate induction conditions (56)(57).

The first iPSCs were generated from bovine using embryonic fibroblasts transfected with lentiviral vectors containing bovine 6 factors (Oct4, Sox2, Klf4, Myc, Lin28, Nanog). The biPS cells exhibit a mouse ES-like morphology. They are alkaline phosphatase positive, and express pluripotent markers such as SSEA1, Sox2, and Nanog, which can differentiate to three basic germ layers *in vitro* and *in vivo* (58). In another study a lentiviral expression vector for human POU5F1 and porcine SOX2, C-MYC, and KLF4 fused with EGFP was transduced into fetal fibroblasts obtaining a reprogramming efficiency of 0.0002–0.0007% in the presence of LIF and bFGF. The derived colonies resembled human ESCs rather than mouse ESCs, but the transgenes were only partially silenced, indicating incomplete reprogramming (59).

For practical applications, bovine iPSC cells are artificially derived from adult somatic cell without the use of rare and excellent embryos, so bovine iPSC cells and their derivatives especially germ cells will enable the precise genetic engineering of livestock for improved

production traits, are also powerful reproductive tools and can be used as somatic cell nuclear transferred donor cells to produce genetically modified breed.

The future in bovine stem cell

Bovine Stem cell for Biology genetic diversity

Biodiversity is facing unprecedented challenges, and one of the causes is that high-yielding breeds of domestic livestock are being spread actively throughout the world. Vulnerable animals are threatened by the introduction of foreign species and by industrial pollution. Unless these genomic resources are conserved in some form before they are lost, we will not only lose the genes peculiar to rare breeds but will also find it impossible to explore the cytological and molecular biological mechanisms that are required to reproduce these breeds by somatic cell cloning. The conservation of endangered species and breeds is therefore an urgent requirement.

Currently, many strategies are used to conserve the genetic resources of domestic animals. Generative cells, somatic cells, zygotes and embryos can all be cryopreserved in cell banks.

We are exploring establishment of stem cells line is a new and effective approach to conservation and maintenance of the diversity of livestock. Not only does this technique preserve precious genetic material, but it also provides an excellent resource for biological research.

Animal model for human medical research

The typical experiment animal model included rat, mice, rabbit, zebrafish and money et al. but more and more animal model have been joined to research various human disease for animal model. The chicken is a classic model of vertebrate developmental biology and medicine that has been used for many decades (60) Swine as an animal model has occupied an important position, especially play important role in in heart disease (61) (62), sudden infant death syndrome Development of a swine animal model for the study of sudden infant death syndrome (63) Cattle are considered large-animal experimental models, and as such give numerous advantages for making progress in clinical application of stem cells to human medicine (39). They offer several advantages as a model for studying stem cell biology including their average length of gestation (pregnancy) in cattle is about 280 days just like humans (64).

Conclusions

Bovine stem cells can be isolated from embryos and maintained in culture. They can be originated from different sources at various stages of embryonic development. They have been illustrated to be pluripotent because they can form embryonic bodies, differentiate into various cell types from all three embryonic germ layers and contribute to somatic and germline lineages in chimaeras. They can offer a model for studying stem cell biology as well as being a tool for many applications.

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