Available online at www.sciencedirect.com
ScienceDirect
Theriogenology 75 (2011) 1400–1415
Theriogenology
www.theriojournal.com

Biology and Therapeutic Use of Domestic Animal Stem Cells

Fetal adnexa derived stem cells from domestic animal: progress and perspectives

F. Cremonesi[a], B. Corradetti[b], A. Lange Consiglio[a,*]

[a] *Università degli Studi di Milano, Reproduction Unit, Large Animal Hospital, Faculty of Veterinary Medicine, Via dell'Università 6,-26900 Lodi, Italy*

[b] *Università Politecnica delle Marche, Department of Biochemistry, Biology and Genetics, Via Brecce Bianche, 60131 Ancona, Italy*

Received 6 August 2010; received in revised form 20 December 2010; accepted 31 December 2010

Abstract

The fetal adnexa such as umbilical cord, amnion and amniotic fluid have been proposed as ideal sources of different stem cell lineages. Use of adnexal tissue has many potential advantages, including the noninvasive nature of the isolation procedure, the large tissue mass from which cells can be harvested with high efficiency and the potential of these cells to differentiate. Moreover, particularly in human medicine, the harvesting of these tissues is more ethically acceptable making these sources of stem cells very attractive for regenerative therapies and biotechnological applications. The adnexal tissue cells preserve some of the characteristics of the primitive embryonic layers from which they originate. Indeed, many studies indicate that these stem cells exhibit some features of embryonic stem cells as expression of embryonic markers and proliferation capability, without showing immunogenicity. However, the differentiation potential of these cells, either *in vivo* or *in vitro*, is intermediate between the pluripotent embryonic stem cells and the multipotent adult stem cells. Non-embryonic extra-fetal derived stem cells have opened new perspectives for developmental biology and for regenerative medicine, not only in humans but also in animals. In this update, we report the state of the art of fetal adnexa-derived stem cells from domestic animals and analyze their applications and potential uses in veterinary medicine.

Keywords: Stem cells; Amnion; Wharton's Jelly; Umbilical cord blood; Amniotic fluid; Domestic animal

Contents

* Corresponding author. Tel.: +390250331150; fax: +390250311115.
E-mail address: anna.langeconsiglio@unimi.it (A. Lange Consiglio).

0093-691X/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.theriogenology.2010.12.032

1. Introduction

The ability to collect large numbers of cells, in an inexpensive and noninvasive way without risk to the donor, and the ability to cryogenically bank and expand the cells *in vitro*, are important considerations to facilitate stem cell use in veterinary medicine [1].

Multipotent autologous bone marrow-derived mesenchymal stem cells (MSCs) are used in regenerative veterinary medicine for their potential to treat equine musculoskeletal injuries including tendon [2–6] and cartilage [7] damages. Bone marrow-derived MSCs have a more limited potential for *in vitro* proliferation (about 32 d for expansion from isolation to implantation) and target differentiation than embryonic stem cells. In addition, bone marrow-derived MSCs are reported to be more difficult to extract from the marrow cavity, show reduced plasticity and growth with increasing donor age and number of *in vitro* passages [8–10], and do not appear to improve long-term functional repair [11].

Stem cells derived from the fetal adnexa could overcome many of the limitations of bone marrow-derived MSCs and open new possibilities for developmental biology and regenerative veterinary medicine. The fetal adnexal tissues of particularly importance as sources of stem cells are the umbilical cord (for isolation of MSCs from cord blood and Wharton's Jelly), amnion and amniotic fluid. With regard to amnion, it is noteworthy that in placental mammals the epithelial layer of amnion originates from the trophectoderm and it is continuous with the epiblast [12]. It is therefore reasonable to speculate that some amniotic epithelial cells may escape the specification that accompanies gastrulation, and that these cells may retain some (or all) of the characteristics of epiblastic cells, such as pluripotency [13].

Moreover, the fact that the placenta is fundamental for maintaining fetomaternal tolerance during pregnancy suggests that cells present in placental tissue may have immunomodulatory characteristics [14] that could decrease the risk of the recipient rejecting transplanted stem cells immunologically.

This review illustrates the advances in isolation and characterization of fetal adnexa-derived stem cells from domestic animals and analyzes their impact on stem cell therapy in veterinary medicine.

2. Definition and sources of stem cells

Stem cells have been isolated from virtually all life stages, from preimplantation embryos through to adulthood. Presently, three types of stem cells have been described: embryonic stem cells, found in the inner cell mass (ICM) of the early embryo, extra-embryonic stem cells isolated from extra-embryonic tissues (amnion, placenta, umbilical cord matrix) and adult stem cells [15,16].

The best known stem cell is the zygote. It has the ability to give rise to an entire living organism and therefore is considered to be totipotent. Once the blastocyst stage is reached, embryonic stem cells isolated from the inner cell mass lose the totipotency of the zygote but are still able to differentiate into the three germ layers. These embryonic stem cells are considered to be pluripotent [17]. Based on their self-renewal and differentiation abilities, embryonic stem cells are hierarchically higher than other cell types that have more restricted properties, but it is important to take into account potential problems in clinical applications posed by embryonic stem cells because of their high tumorigenic rate after transplantation [18].

MSCs represent a population of stem cells with more restricted differentiation potential. They are characterized by three defining properties. Firstly, MSCs are plastic-adherent when maintained in standard culture conditions. Secondly, MSCs express the cell surface markers CD105, CD73, and CD90 and lack expression of CD45, CD34, CD14 or CD11b, CD79 or CD19, and human leukocyte antigen (HLA)-DR. Thirdly, MSCs differentiate to osteoblasts, adipocytes, and chondroblasts *in vitro* [19]. These cells are considered to be multipotent [19].

In veterinary medicine, MSCs have been harvested successfully from a variety of tissues including, but not limited to, bone marrow [6,20–26], skin [27], adipose tissue [22,26] and peripheral blood [28,29].

Tissues that contain unique and primitive cells whose potential is as yet undefined, but which represent attractive candidates as a resource for stem cell biotechnology and biomedicine, are gestational tissues and amniotic fluid. In these context, umbilical cord blood [22,30–36], umbilical cord tissues [1,37–41], amniotic tissue and amniotic fluid [42,43] have been isolated and characterized for the first time in veterinary medicine.