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Stem Cell Therapy is a Promising Tool in Reproductive Veterinary Medicine

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Abstract

Stem cell therapy is the main focus of regenerative medicine. Both scientifically and practically, the stem cell field in veterinary medicine is still developing quickly. Several animal reproductive problems can currently be treated with stem cell therapy, according to scholarly literature. A subspecialty of medicine known as "regenerative medicine" researches ways to create, fix, or replace harmed or diseased cells, organs, or tissues. The sources of pluripotent and progenitor cell lineages include embryonic stem cells (ES), adult stem cells, induced pluripotent stem cells (iPSCs), fetal stem cells, and umbilical cord blood stem cells. Which are used to treat the various syndromes and complications of animal reproduction gynecology and obstetrics.

Keywords: Infertility; Pluripotent; Regenerative medicine; Stem cells; Testis xenografting.

INTRODUCTION

Regenerative medicine is a discipline of medicine that studies how to create, repair, or replace cells, organs, and tissues that have been damaged or diseased. Just few years in the past, it has gained considerable traction (***Voga*** et al.,2020). In multicellular organisms, stem cells are specialized cells. They have the unusual capacity to separate and diversify themselves into a range of various types. A collection of specialized cells Stem cells have a unique property that allows them to perform a variety of functions, one of which is to repair damaged tissue. As an internal repair system, you can help. They can divide indefinitely since they have the power to divide. They can restore certain cell types and tissues due to their limitless ability to divide (***Shihadeh H.*** 2015). In translational regenerative medicine research, stem cells are increasingly being examined as possible alternative therapies. The biology and function of stem cells have made huge strides in recent years. Mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs) are the subjects of extensive investigation for their potential use in reproductive medicine, particularly in cases of infertility brought on by azoospermia and early ovarian insufficiency. These studies are being undertaken with the utmost ethical concern and with readily available, enough resources (***Saha*** et al., 2021). The field of stem cells in veterinary medicine is constantly developing, both theoretically and practically. The most common therapeutic use of

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stem cells in clinical veterinary medicine is to treat musculoskeletal injuries in horses and dogs. To use the potential of spermatogonial stem cells to help endangered animal species survive, new assisted reproductive technologies are being created (***Fortier*** et al., 2011).

Where are we now and where can we go with stem cells in reproductive medicine?

Animals have been used as models for human challenges rather than humans in the bulk of research on stem cell use in reproductive medicine (***Vassena*** et al., 2015). For disorders associated to the endometrium, such as endometriosis, MSCs have been employed in addition to conventional therapies.(***Pieri et al.***, 2019). IPSCs, on the other hand, have a lot of potential since they could help researchers understand disease pathways and develop drugs in the same manner that ESCs do, with the added benefit of allowing autologous transplantation (***Singh*** et al., 2015) and avoiding ethical issues. Several research has been conducted on both people and animals to causemultipotentcells, ESCs or iPSCs differentiate into germ cells capable of producing gametes, which are the most specialized cells in an organism and are necessary for the species continuance and evolution. The creation of germ cells from somatic cells is still an uncommon and complicated process, with no evident similarities between in vitro and in vivo induction (***Pieri*** et al., 2019). The same group reported the in vitro restoration of the whole female germ line through the in vitro differentiation of PGCLs into primary oocytes in 2016, which needed co-culture with gonadal somatic cells (***Hikabe*** et al., 2016).

Stem Cell

What are the adult stem cells whenever there is injury or change that takes place in the animal body? To restore optimum health injured tissue or organ release messenger compound. Which travel through blood circulation to reach the bone marrow. These messenger compounds activate the stem cell present in the bone marrow. After that stem cells multiply and migrate into the bloodstream. So the number of stem cells in blood circulation increases at the same time injured tissue releases a specific compound called stromal-derived factor or SDF-1. SDF attracts the stem cells from blood circulation. so migration of stem cells from blood circulation to near the affected or injured tissue takes place. At that place stem cells amplify to become normal tissue cells and restore the tissue function (***Kucia*** et al., 2013).

Stem Cell Characteristics

In addition to being unspecialized, all stem cells also possess the traits of self-renewal and potency. The capacity of cells to regenerate themselves is known as self-renewal, and it prevents them from ageing or losing their ability to differentiate. (***McCulloch, E. A., & Till, J. E.*** 2005). Both symmetrical (when both daughter cells are stem cells or developed cells) and asymmetrical stem cell division theories exist (in which one stem cell and one more differentiated cell are produced). Potency describes a stem cell's ability to develop into many cell types. totipotent, pluripotent, multipotent, Oligopotent and unipotent stem cells are the five types of stem cells (***Ivanova*** et al., 2002).

1. All types of cells in a developing organism, including embryonic and extraembryonic (placental) tissues, can be produced by totipotent cells (S. M. Morganietal.,2013).
2. Pluripotent cells are the only embryonic cells can be produced by pluripotent cells, but they are capable of producing all other embryonic cells, including germ cells and cells from any of the germ layers. This enables them to produce any type of cell in the body(A. Cumano & I.Godin 2001).
3. Multipotent cells cannot develop more than one germ layer's worth of cells at once. All blood cells can be produced by multipotent stem cells from a mesodermal tissue, such as blood, but not cells from a different germ layer, such as brain or liver cells (ectoderm) (endoderm) (S.Fujita 2003).
4. Oligopotent stem cells compared to multipotent cells, have a limited range of diversity. Myeloid cells, for instance, can develop into WBC but not into RBC (Rao, M. S. 2004).
5. Unipotent cells produce only one type of cell. A germ cell stem cell, for example, produces cells that mature into egg or sperm but not other cell types (Rao, M. S. 2004).

Sources of Stem Cells

1. **Embryonic Stem Cells (ES)**

   The embryo is used to create embryonic

stem cells. They are obtained from the pre-implantation blastocyst 7-10 days after conception. ES cells are pluripotent, as previously stated. Other stem cell sources are being investigated due to ethical concerns. Because the blastocyst is disrupted when ES cells are derived (***Nichols*** et al., 2011).

2. **Adult Stem Cells**

The majority of tissues include adult stem cells, commonly referred to as somatic stem cells, albeit not all tissues do. They are mostly multipotent, however, there are a few pluripotent adult stem cells. They live for the rest of their lives and play a part in maintaining and healing the tissue in which they are found in the event of an injury. They've been found in a variety of tissues, including the brain, bone marrow, blood vessels, heart, and liver. They live in a stem cell niche, which is a specific location of each tissue (***White*** et al., 2015).

3. **iPSCs (Induced Pluripotent Stem Cells)**

By co-expressing pluripotency associated proteins, are synthetic stem cells created from somatic cells? Similar to embryonic stem cells, they may multiply and renew themselves endlessly in vitro and grow into derivatives of all three fundamental germ layers (i.e., ectoderm, mesoderm, and endoderm) as well as germ cells that give birth to gametes. (***Zhao*** et al., 2013). iPSCs can be made from a wide range of domestic and farm animals (***Polo*** et al., 2013). Economically advantageous and essential for the development of disease models and the production of medically useful substances, such as enzymes and growth hormones, which are absent or insufficient in patients with particular genetic diseases, the production of iPSCs from companion animals and domesticated species, such as dogs, cattle, chickens, and pigs, includes domesticated species like dogs, cows, chickens, and pigs.

4. **Fetal stem cell**

The development of induced pluripotent stem cells, regenerative medicine, and assisted reproduction are just a few of the uses for fetal cells, which are available in large quantities. Fetal stem cells offer compelling evidence that they are biological homologs of ES cells since they exhibit pluripotency markers and have comparable growth dynamics. (***Yadav*** et al., 2012).

5. **Umbilical Cord Blood Stem Cells**

Mesenchymal stem cells can be found in abundance in the umbilical cord. The ordinarily discarded umbilical cord blood (UCB) can be conveniently recovered at the time of delivery (***Harris*** et al., 2007). The placenta's umbilical vein can be venipuncture while the baby is still inside the womb, or after the placenta has been expelled. The benefits of UCB stem cells include their high proliferative potential, minimal danger of viral contamination in response to alloantigen, accessibility, and donor safety (***Bongso*** et al., 2008). However, there aren't many reports on cow cord blood.The biggest stumbling block in collecting cord blood from livestock, particularly equines, is umbilical cord breaking after parturition. After the placenta has been expelled, a tiny amount of cord blood (5–6 ml) can be recovered in normal calving. According to the morphology of buffalo umbilical cord blood, newborn calf blood, and adult buffalo blood, cord blood parameters were very different from each other.

Application of stem cells in animal reproduction

1. Spermatogonia stem cells advance the restoration of infertility in Breeding Bull.

Spermatogonial stem cells are the germ stem cells of the seminiferous epithelium of the testis (SSCs). Spermatogenesis is the process through which they create sperm while also maintaining their cellular pool through self-renewal. SSC biology has profound implications for animal reproduction and the development of regenerative therapeutics for human disease (***Aponte*** 2015). Since the 1994 publication of the first successful spermatogonial stem cell transplant, several advancements been created to improve the technique's efficiency. In addition, the approach has been useful in the research of testicular stem cells and spermatogenesis in fundamental science. The ability to separate the problematic cell type within sterile research animals ensures that this technique will be used

more often than, and its enormous possible applications to endangered species, invaluable zoological and agricultural animals, and human medicine will continue to sure the development of spermatogonial stem cell technology. The current problems centre on developing strategies for producing pure populations of stem cells, incorporating stable foreign DNA into these populations, and comprehending and overcoming potential immunological obstacles (***Johnston*** et al., 2000). The most effective strategy to boost production quality in domestic animal populations is to selectively employ the gametes from animals considered to be elite, and this idea has been the cornerstone of selective breeding techniques used by humans for thousands of years. In contemporary animal agriculture, artificial insemination (AI) has long been a mainstay of selective breeding programmes, yet it has inherent limitations in the production of pigs and beef cattle. This study discusses the potential and existing state of the Surrogate Sires idea as a next generation breeding tool for cattle production (***Giassetti*** et al., 2019). These animal models are useful for studying SSCs, testis tissue morphogenesis and development, germ somatic cell interactions, and spermatogenetic processes. Importantly, these animal models may be applied in a range of experimental and therapeutic situations, such as the genetic preservation of threatened species and the maintenance of fertility in prepubertal cancer patients. Furthermore, these models make it feasible to do investigations that would be challenging or impossible to perform on the target species directly (***Ibtisham*** et al., 2020).

2. Endometrial repair by using Stem Cells in Farm Animals

   Mesenchymal stem cells can be obtained from the endometrium. In response to the estrous cycle, pregnancy, involution, as well as uterine disorders, the endometrium undergoes a range of cell proliferation, growth, and death cycles. In most mammals, the endometrium goes through stages of cell proliferation, apoptosis, and endometrial atrophy without bleeding during the estrous cycle ***Lara Evelyn*** et. al., (2018). In highly regenerative tissues like the endometrium, adult stromal mesenchymal stem cells (MSCs) have been hypothesised as the source of cell renewal. With tremendous success, Cabezas et al. (2018) discovered and characterised endometrial MSCs (eMSCs) from mares. These cells exhibited characteristics that are typical of horse MSCs, including fibroblast like shape, flexible growth, population doubling times, tri-lineage differentiation (osteo, chondro, and adipogenic), migration toward foetal calf serum attraction, and a pattern of surface indicators. Mesenchymal stem cells (MSCs) have the potential to treat a variety of diseases due to their immunomodulatory and trophic effects, as well as their capacity to repair damaged tissues. The cell transport mechanism, which should enable extensive cell dispersion and homing into injured regions, plays a role in the effectiveness of stem cell treatments (***Mambelli*** et al. 2012) investigated the creation of a new MSC delivery method for endometriosis-ridden mares' uteri (degenerative alteration of uterine glands and surrounding stroma). Endometriosis was present in all of the mares used in this study (N = 6). To identify multipotent equine adipose tissue-derived MSCs (eAT-MSCs) in endometrial tissue prior to transplantation, cells were labelled with a fluorescent dye. A straightforward procedure comparable to artificial insemination (AI) was used to inject the eAT-MSCs (2 107 diluted in 20 mL sodium chloride 0.9 percent) into the uterus of mares during synchronised estrus. Confocal microscopy of uterine biopsies taken at 7 and 21 days after transplanted from the uterine body and both uterine horns, including the glandular and periglandular areas, indicated homing of fluorescently tagged eAT-MSCs in three of four treated mares. In the paper published by (***Mambelli*** et al. 2012) shows a new approach for delivering MSCs into the uterus of mares with endometriosis that is both minimally invasive and technically straight forward.

3. **Recent advancements in testis tissue xenografting to help genetically valuable animals regain their reproductive potential**

To better understand and control mammalian spermatogenesis, Jose R. Rodriguez-Sosa and Ina Dobrinski offered two novel discoveries:i) When transplanted ectopically into immunocompromised mice, testis tissue from immature animals can react to mouse gonadotropins and commence and complete differentiation to the point where fertilization competent sperm can be produced. ii) Isolated testicle cells can arrange themselves into seminiferous cords, new directive complete full development, including the generation of healthy sperm. The current work summarises recent developments in these methods that open up new research directions for understanding testis development and spermatogenesis in a number of mammalian species. It is possible to stimulate the development of immature germ cells in mammalian gonads by xenografting testicular tissue into immunodeficient mice. The capacity of xenogeneic sperm-infused oocytes to develop in vivo was evaluated by (***Nakali*** et al., 2010). Neonatal pig testicular tissues with seminiferous cords that only contained gonocytes and spermatogonia were implanted beneath the skin of castrated nude mice. A single spermatozoon was then implanted into an in vitro produced pig egg using morphologically normal sperm that had been obtained between 133 and 280 days after xenografting.After ICSI, the oocytes were electrostimulated and implanted into recipients who had their estrus timed. Two of the 23 recipient gilts gave birth to six piglets (***Abbasi, S., & Honaramooz, A.*** 2012). After a 2-month-old white tailed deer fawn (Odocoileus virginianus) was removed post-mortem, tiny fragments of testis tissue were implanted under the back skin of immunodeficient recipient mice. Every two months for up to 14 months following grafting, single xenograft samples were taken from representative recipient mice. The recovered xenografts were evaluated for seminiferous tube density (per mm^2), tubular diameter, seminiferous tubular form, and identification of the most advanced germ cell type found in each tubule cross section. 63 percent of the transplanted testis parts yielded xenografts. Testicular growth in testis tissue xenografts was constant, starting with tubular extension at two months, followed by spermatocyte presence at six months, spherical and elongated spermatids at eight months, and fully mature sperm at twelve months. Complete spermatogenesis happened at the same time as sexual maturation in white tailed deer, according to the researchers. This research proved for the first time that transplanting immature deer testis tissue into recipient mice may cause testicular maturation and spermatogenesis in the grafts up to the point of sperm production. These results may lead to the development of a paradigm for genetic material recovery from young male white tailed deer who pass away before reaching sexual maturity ***Abbasi, S., & Honaramooz, A.*** (2012).

4. **Stem Cells and Vaginal Reconstruction**

   Zhang et al., 2002, studied that vaginal MSC transplantation may enhance the biomechanical properties of the vaginal tissue and offer a novel possible therapy for pelvic organ prolapsing. Muscle derived stem cells and SIS implants promote vaginal tissue regeneration in rats, indicating that autologous MDSC on scaffolds may be a potential therapeutic alternative for the repair of damaged vaginal tissue (***Heydarkhan*** et al., 2009). By encouraging vaginal epithelial cell regeneration, vaginal tissue repair, and vaginal tissue repair, the complexes reduced vaginal stenosis and contracture (***Ye*** et al., 2020). Complexes implanted into rats produced better therapeutic outcomes than ADSCs placed into rats. Protein scaffold ADSC complexes showed a positive therapeutic effect on radiation induced vaginal damage in rats and may serve as the foundation for a novel radiation dermatitis therapy.

CONCLUSION

The animal body is strengthened with specialized cells known as stem cells that have the capacity to self renew and differentiate into diverse body cell types. These cells are the best tool for the restoration of fertility and preservation of endangered species in captive breeding management because they are simple to isolate, can be safely transplanted to injured tissue,

and can be grafted from donor to recipient. They also have excellent immune regulatory properties. The promise of stem cells for treating a variety of reproductive illnesses has been effectively proven in several in vitro and in vivo experiments in animal models; nevertheless, the clinical results are not particularly encouraging. Based on research in the field of stem cells, several disorders, including azoospermia, vaginal prolapse, vaginal fistula, and endometrial repair, have potential uses for stem cells.

Competing interest

Author declares none

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