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Recent advances in assisted reproductive technologies of feline reproduction

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ABSTRACT

Many wildcat species are threatened with extinction, rare or vulnerable due to habitat destruction and poaching. In addition, Ankara and Van domestic cat species originating from Türkiye are in danger of extinction and are under protection. Thus, the requirement for assisted reproductive techniques in b oth domestic and nondomestic cat species has been increasing in recent years. Assisted Reproductive Technologies (ART) such as in vitro maturation, in vitro fertilization, embryo transfer, and cloning in domestic cats (Felis catus) provide a useful and suitable model for the conservation of endangered cat species. Domestic cats can be recipients for embryo transfer and recipient cytoplasm for nuclear transfer from various small wildcat species. Thanks to ART, it is possible to ensure the continuation of the generation by producing in vitro embryos or by making intra or inter-species clones from wild cats that have lost their reproductive functions or even died recently. Many inherited genetic disorders have been identified in cats that are similar to humans. Due to their genetic closeness, they have recently begun to be used as animal models in some therapeutic studies on humans, especially on kidney and nervous system diseases. In the early years, in vitro study results were less successful than in farm animals but in recent years ART's such as in vitro embryo production, embryo transfer, cloning, and transgenesis have made significant progress in domestic of domestic and wild cats. This review includes the assisted reproductive technologies applied in recent years and the results obtained in domestic cat and felines.

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Introduction

Although there is currently no species-specific culture medium, significant advances have been made in assisted reproductive technologies in domestic cats since the birth of the first kitten produced from IVF-derived embryos was born in 1988 (Goodrowe et al., 1988). This review will give information about the estrous cycle in cats, and recent ART's such as in vitro oocyte maturation, in vitro fertilization, embryo transfer, semen storing, cloning, and transgenic studies, which have rapidly developed in recent years.

1. Estrus Cycle of Cat

Free-living female cats show seasonal polyestrus. This season in the northern hemisphere begins in January when the day length begins to increase and melatonin pressure begins to disappear and intensifies in spring. Estrus continues to decrease towards the summer and lasts until autumn. Melatonin hormone has an anti-gonadal effect in cats, and the period of anestrus is between October and December when the dark period becomes longer. Cats living at home may show estrus

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and ovulation can only occur by stimulating endogenous LH secretion through natural/artificial mating reflex or exogenous hormone applications. If there is no mating or any exogenous stimulation or hormone administration, the follicles developed in the ovaries are resorbed after about a week and cats enter interestrus, which is a calm period. After 2-3 weeks of interestrus, cats come into estrus again. This cycle continues throughout the season. Even if a non-fertile mating occurs, rapidly rising progesterone levels decrease to basal levels only after 40-45 days, and this period is called pseudo-pregnancy. After a fertile mating, the resulting embryos descend to the uterus in 4–5 days, and at the morula stage, and implantation occurs in 12–13th days. The number of offspring varies depending on the breed, age, and number of ovulations that will occur in parallel with the number of mating. The gestation period varies depending on some factors such as breed and number of offspring, but it is approximately 62– 67 days (Pope, 2000).

2. In Vitro Technologies

a. Collection and Transport of Ovaries: The ovaries collected after routine ovariohysterectomy are used for in vitro studies of cats. The ovarian transport solution type, temperature, and duration are critical factors in the quality of oocytes to be recovered. Ovaries are usually transported to the laboratory within a few hours in isotonic solutions such as PBS or 0.9 % NaCl are generally preferred as transport solutions (Evecen et al., 2009; Evecen et al., 2003b; Johnston et al., 1989). Recently, a study was conducted with oocytes obtained from ovaries stored in ET-Kyoto solution (ET-K), which is used for the transportation of human organs. It is revealed that in vitro fertilized cat oocytes were more successful than the control group, in terms of cleavage and further embryo development in vitro (Yoshhida et al., 2022). The temperature of the transport solution was preferred by some researchers as warm (22–38 ^{o}C) (Karja et al., 2002; Merlo et al., 2005; Güriş and Birler, 2011; Evecen et al., 2016), and by some researchers as cold (5 ^{o}C) (Johnston et al., 1989; Wolfe and Wildt, 1996; Evecen et al., 2002). The ability of oocytes obtained after storing cat ovaries in cold environments for a long time to mature and be fertilized in vitro provides significant contributions to the protection of wildlife and endangered species (Wolfe and Wildt, 1996; Evecen et al., 2010; Arıcı et al., 2022). We demonstrated in our previous study that the in vitro maturation rates obtained after keeping cat ovaries at 5 ^{o}C for 24 hours, gave similar results (50.7 and 48.2%) to the control group (Evecen et al., 2010). Adding some antioxidants such as Superoxide dismutase (SOD), Catalase (Cocchia et al., 2015). Resveratrol, Melatonin, and Lycopene, in the transport solution (Swelum et al., 2022) help prevent oxidation that may occur during transport, improving oocyte yield and viability. It can make positive contributions to the quality of the embryos to be produced.

b. Harvesting of Oocytes: Oocytes from both domestic and wild felines can either obtained by stimulation of follicles with exogenous hormones or by collection from ovaries obtained after neutering (Pope 2000).
Stimulation of Ovaries: Oocytes are collected according to the principle of starting hormone therapy when female cats are in their interestrus period. The estrus period of a female cat is easily determined by vaginal cytology. To stimulate the ovaries, either a single dose of PMSG (50-100 IU) or FSH (1.5–4 mg) is applied for 4 days. For the maturation of follicles and oocytes, a single dose of hCG (100-150 IU) or 3 IU LH is administered 80-84 hours after PMSG. Then, matured oocytes are collected by aspiration of preovulatory follicles with the help of a laparoscope or laparotomy Hormone doses are calculated and applied in the same way for wild felines, calculated on a live weight basis (Pope 2000).
Slicing of Ovaries: If the ovaries have been transported at a cold temperature, they are kept at room temperature for 30–60 minutes before the processing begins. After cutting sections on the surface of the ovaries with the help of a scalpel (slicing), they are washed and rinsed with a suitable washing medium (Oocyte washing medium, M2 medium, TCM–199 with Hepes buffer) at 32–38 °C (Uchikura et al., 2011; Evecen et al., 2003a; Evecen et al., 2004).

c. Selection of Oocytes: The recovered oocytes are rinsed and evaluated under a stereo-microscope and only oocytes with Grade A quality are selected for in vitro maturation. The selection of Grade A oocytes to be matured in vitro is made according to the following criteria: A complete and intact zona pellucida, surrounded by at least four cumulus oophorous/ corona radiata cell layers, having large, homogeneous, and darkly pigmented vitellus structure filling the inside of the zona pellucida. Approximately 5–20 Grade A oocytes canbe obtained from each ovary, depending on the cat's age, weight, nutritional status, season, and estrus cycle stage (Evecen et al., 2003a; Evecen et al., 2004).

d. In Vitro Maturation: In the cat, the oocyte ovulates in the metaphase II stage (MII) and is ready for fertilization. However, the oocytes obtained by slicing the ovaries are still in the primary oocyte stage and are not yet mature. Thus, they must be matured in vitro

is generally carried out between 32–48 hours (Evecen et al., 2009; Karja et al., 2002; Evecen et al., 2002; Evecen et al., 201et al., 2009; Evecen et al., 2003a). In vitro maturation period 0; Pichardo et al., 2021). In vitro, maturation of oocytes is one of the most critical points of the in vitro embryo production process. Therefore, several researchers reported very different (2–82%) in vitro maturation results in cat (Pope 2000). Becausethe process can be affected by many variables such as season, nutritional status, and cyclic period of donor cats, the selected oocyte quality, the type of medium used, different substances added to the medium (proteins, hormones antioxidants, and growth factors), the gas ratios, the temperature and humidity of the incubator (Evecen et al., 2004).

The Season and The Cyclic Period of Donor Cats: Different studies on this subject have obtained either supporting or contradictory results in cats (Pope 2000). Some researchers declare that they did not find a difference between the in vitro maturation rates of oocytes obtained in different estrus cycle stages or seasons (Karja et al., 2002; Uchikura et al., 2011; Pichardo et al., 2021). In our previous study, we found that although not statistically significant, there were differences in in vitro maturation rates between different estrus cycle stages of queens and that the follicular stage was superior to other stages (Evecen et al., 2004).

In Vitro Maturation Chamber: The ambient temperature is regulated according to the body temperature of the animal species, and the gas composition varies depending on the type of environment used. Cat oocytes are matured in an incubator with a temperature of 38°C, containing 5% CO2 or a gas mixture (5% CO_2, 5% O_2, and 90% N_2) and approximately 100% humidified atmosphere (Pope 2000; Evecen et al., 2003a).

In Vitro Maturation Media: Because there is no medium specifically designed for the in vitro maturation of cat oocytes, researchers use media that is used for other mammalian oocytes. The most commonly used media are; TCM 199 (Karja et al., 2002; Evecen et al., 2016; Evecen et al., 2002; Evecen et al., 2003a), Ham's F-10 (Evecen et al., 2016; Evecen et al., 2003a). Synthetic Oviduct Fluid (Evecen et al., 2010; Evecen et al., 2009; Evecen et al., 2004), and Eagle's Minimal Essential Medium (Wolfe and Wildt, 1996). Several scientists used different media for in vitro maturation of cat oocytes and different results have been obtained (2–82 %) (Pope, 2000).

Supplements to In Vitro Maturation Media: In vitro maturation of immature oocytes is an attempt to mimic the in vivo environment (Pope et al., 2006). For this purpose, the temperature, humidity, and gas components of the incubator, there are also other important supplements such as Hormones, Proteins, Growth factors, and sometimes Antioxidants that need to be added to the medium (Pope 2000).

Hormones: Gonadotropic hormones such as FSH and LH are essential to support the maturation of cat oocytes in vitro (Pope et al., 2006). Additionally, in studies where steroids were used, it was reported that better in vitro maturation (Wolfe and Wildt, 1996; Wood et al., 1995; Pope et al., 2006) and in vitro fertilization (IVF) results were obtained compared to control groups (Wood et al., 1995).

Most researchers add FSH and LH to the maturation medium at 1-10 µg/ml (Evecen et al., 2009; Evecen et al., 2016; Wolfe and Wildt, 1996; Evecen et al., 2002; Pope et al., 2006) and estradiol-17b at 1 µg/ml (Wolfe and Wildt, 1996; Uchikura et al., 2011).

Protein Sources: Proteins are crucial molecules for the integrity of the zona pellucida, survival, and development of oocytes/embryos in vitro. Complex biological macromolecules with different structures are used as protein sources in many in vitro culture systems (Pope et al., 2006). Different homologous and heterologous protein sources such as Bovine Serum albumin (BSA), Fetal Calf Serum (FCS), Estrus Cat Serum (ECS), and Polyvinyl Alcohol (PVA) are generally used in various doses in cat studies in vitro and various results obtained (Pope et al., 2006). Researchers generally used BSA 3–6% mg/ml, FBS 5-10%, Polyvinyl Alcohol 1–3%, and OCS 5% in culture medium (Karja et al., 2002; Güriş and Birler, 2011; Wood et al., 1995; Pope et al., 2006; Nestle et al., 2012). Although some researchers claimed that the protein sources do not affect the quality of blastocysts produced during in vitro in cats (Nestle et al., 2012), many others have reported different results (Karja et al., 2002; Güriş and Birler, 2011; Wood et al., 1995; Pope et al., 2006; Nestle et al., 2012). It has been reported that the use of BSA was superior to Fetal Calf Serum (FCS) for oocytes reaching the M II stage (16,5 vs 5.4%) in cat oocytes in vitro (Güriş and Birler, 2011). It has been reported that BSA supports in vitro maturation rates more than FCS, whereas FCS is more successful in in vitro fertilization in cats (Wood et al., 1995). It has been also reported that FCS is more successful than BSA in terms of both reaching the embryo stage and the number of embryonic cells (Karja et al., 2002).

Growth Factors: Epidermal growth factor, which is thought to play an important role in folliculogenesis in cats, has been reported to be present in the theca interna cells of cats, smaller cells of the ovarian cortex, and corpus luteum (Göritz et al., 1996). EGF is known

to promote nuclear and cytoplasmic maturation in human, bovine, and porcine oocytes. Additionally, beneficial effects of EGF on oocyte maturation were found in rats, rabbits, buffalo, sheep, and horses (Merlo et al., 2005). It is reported that the addition of epidermal growth factor (EGF) to in vitro maturation of domestic cat oocytes in 10 ng/mL, enhances fertilization frequency and blastocyst development in vitro (Gomez et al., 2001). Another study comparing 10, 25, and 50 ng/ml EGF doses in cats, found that EGF did not contribute to in vitro maturation rates but at 25 ng/ml better supported in vitro fertilization and blastocyst rates (Merlo et al., 2005).

Antioxidants: Aerobic metabolism is associated with the production of pro-oxidant molecules called free radicals or reactive oxygen species (ROS). A state of oxidative stress begins when there is an imbalance between pro-oxidants and antioxidants. When free radicals begin to increase in the environment, it negatively affects gametes. Oxidative stress affects both embryonic implantation and early embryo development by interacting with cytokines and hormones (Agarwal et al., 2006). To protect oocytes and embryos from oxidative stress in the in vitro culture environment, some researchers sometimes prefer to add antioxidant substances. In studies conducted in different animal species, various antioxidants such as cysteamine cysteine, taurine and hypotaurine, βmercaptoethanol, vitamins E and C, superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) have been used to reduce ROS and supports developing embryos in vitro (Cocchia et al., 2015; Agarwal et al., 2006). It reported that superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) added to the medium provided significant benefits and while supplementing IVM media with SOD and CAT did not improve the oocyte maturation rate but it accelerated progression to the blastocyst stage on in vitro maturation and in vitro fertilization of cat oocytes (Cocchia et al., 2015). Another recent study showed that SOD and taurine supplementation promoted blastocyst development in low-quality cat oocytes (Ochota et al., 2016).

e. In Vitro Fertilization and Embryo Development: In vitro fertilization can be performed either by using in vivo matured (MII stage) oocytes (collected from female ovaries by aspiration) or in vitro matured oocytes. Thereafter, the mature oocytes and capacitated sperm are placed in the same environment, or sperm cells can be injected into the oocyte's cytoplasm (intracytoplasmic sperm injection: ICSI) (Johnstonet al.,1989). Various IVF protocols have also been developed for domestic cats and have been adapted to the wild cat species. However, in most studies the proportions of offspring surviving after ET have been highly irregular. Due to this inconsistency, IVF/ET is not currently used as a genetic management tool for the reliable production of offspring in any cat breed, but studies on this subject are ongoing (Pelican et al., 2006).

Sperm Capacitation: Ejaculated or epididymal collected cat semen can be used. Semen is diluted 1:1 with capacitation medium (Hams F-10, Synthetic Oviduct Fluid, TCM-199, Brackett Oliphant Medium, or others) including heparin, which improves the capacitation process and centrifuged at 300 g for 8 minutes. Then the supernatant is discarded, the remaining pellet is added to 100 µl of a medium, and the sample is kept at room temperature (swim up) for 1 hour. Later, about 50 µl of the upper layer containing active spermatozoa swimming upwards is taken and evaluated in terms of sperm motility, motility, and concentration (Evecen et al., 2003a).

In Vitro Fertilization (IVF) and Embryo Culture: The selected motile sperm concentration was adjusted to 2 –4x10^6/ml for fertilization. The prepared semen sample was left next to groups of 10–20 oocytes in fertilization medium drops under mineral oil. The gametes co-incubated for 20–24 hours, then transferred to the embryo culture medium. The embryo formation and development were checked every two days and eliminated those oocytes that had not divided. Also on the third and fifth days, the culture medium renewed, and in vitro culture continued for up to seven days (Johnstonet al.,1989; Karja et al., 2002; Evecen et al., 2003a). Although much lower rates were initially achieved (2–10 %), with the improvement of in vitro culture systems in recent years approximately 30 - 50 % of cat embryos produced in IVM/IVF developed into blastocysts on Day 7 of IVC (Pope 2000; Evecen et al., 2003a).

f. Embryo Cryopreservation and Transfer: Although both vitrification and slow freezing methods can be used to freeze cat embryos, the slow freezing method was found more successful (Pope 2000). Since the birth of live kittens from the transfer of in vitro derived and frozen embryos in 1994 (Pope et al., 1994), several pregnancies and births have occurred in both domestic and wild cat species (Pope 2000; Pope et al., 2006). In the first successful transfer of fresh cat embryos, 47 embryos from nine females were transferred to the uteri of nine recipients, and four live kittens were born (Pope et al., 2006). The first kittens after transfer of IVM/IVF-derived embryos were born in 1997 and three litters were produced (Pope 2000).

Embryos are transferred via laparotomy depending on the day of development, into the cornu uteri or oviduct of recipient females in domestic or wild cats whose estrus cycles are similarly synchronized (at varying doses) by exogenous gonadotropic hormones. After the first domestic kittens were born after transferring cryopreserved embryos derived from in vitro matured oocytes, several additional pregnancies and births have been reported by using the slow cryopreservation method in both domestic and non-domestic cats (African wildcat (Felis silvestris lybica), Ocelot (Leopardus), Pardalis, and Caracal (Caracal caracal) (Pope et al., 2006). Pregnancy success in both domestic and wild felines ranges from 0-50% (Pelican et al., 2006).

g. Semen Storage and Cryopreservation: The main purpose of storing and cryopreserving cats of domestic cat sperm is to preserve the gamet for future use and thus to apply the freezing techniques to wild felines that are in danger of extinction and vulnerable. Semen from domestic cats can be collected by the following methods: Artificial vagina (AV), Electroejaculation (EE), sperm collection from the epididymis or testicles, and a newly developed technique named "urethral catheterization after pharmacologically induced sedation". The cat embryo development rates in vitro, after IVF using ejaculated spermatozoa that had been stored in Tes-Tris egg yolk extender at cold temperature (4–8 ^{o}C) to 21 days were found similar to that obtained when fresh spermatozoa were used (Harris et al., 2002). Cat semen canbe successfully frozenby the paiette or pellet method in Tris (hydroxymethyl-aminomethane), TesT (N Trishydroxymethyl-methyl-2-aminomethane-sulfonic acid + Tris), and Tris-Fructose-Citric acid extenders, which contain 3–8% glycerol (Axner and Linde-Forsberg, 2002). There is no diluent specifically developed for cryopreservation of cat sperm. Therefore, diluents formulated for other species are used. Although many extenders such as; Skim milk-glucose-taurine (SMGT), egg yolk sodium citrate (EYC), and lactose egg yolk-based extenders have achieved similar success in freezing cat semen, Tris-egg yolk-based (TEY) extender, which contains glucose and was developed to freeze dog sperm, is the most commonly used extender in the cryopreservation of cat sperm. Besides, successful results are also obtained in studies in which lactose and fructose are added to the same diluent instead of glucose. If cat semen is cryopreserved as a pellet, a warm Tris-buffered solution that does not contain glycerol and egg yolk is generally used. However, if the semen has been cryopreserved in straws, it can be thawed by placing the straws in warm water for 30 sec. (37–38 ^{o}C) (Buranaamnuay 2017). In our previous study, we found that the post-thaw motility and morphologic defect rates in 3% and 4% glycerol-containing Tris extenders (including fructose instead of glucose) were similar and cat semen could be frozen with both glycerol levels successfully (Baran et al., 2010).

h. Artificial Insemination: Artificial insemination in domestic cats does not have widespread clinical application as it does in dogs. Many factors limit AI in cats. The main ones are; aggression, difficulty in semen collection techniques, very low semen volume, insemination method, ovulation induction, and sedation. Although intravaginal AI has been achieved in domestic cats and tigers, very high concentrations of sperm (107–108) were required to achieve pregnancy (Chagas e Silva et al., 2000). Although artificial insemination studies in cats have been tried for fifty years, the results are still very different and not at the expected level (Buranaamnuay 2017). However, recently some researchers announced that two healthy kittens were born from artificial insemination of domestic cats with fresh semen (Daşkın et al., 2022). It is known that the anesthesia applied during this procedure has a negative effect on both sperm transport and ovulation in domestic cats through mechanisms that reduce uterine contractions (Howard 1992). Freezing procedures reduce the potential fertility of semen (Buranaamnuay 2017). This necessitated the development of intrauterine AI procedures. While AI with fresh spermatozoa is applied successfully in domestic cats and cheetahs, this success rate is much less in other wild felines, mostly for unknown reasons (Pelican et al., 2006).

3. Somatic Cell Nuclear Transfer (Cloning)

Animal breeding through Somatic Cell Nuclear Transfer (SCNT) is a valuable tool for the conservation of vulnerable and endangered species and the production of transgenic animals. In recent years, great advances have been made in assisted reproductive technologies for the protection of endangered felines, as in other animal species. SCNT also known as cloning, is a very valuable technology in preserving genetic diversity. Although Nuclear transfer (NT) technology is used for producing identical individuals, it is also an important tool for understanding the cellular and molecular aspects of nuclear reprogramming (Gomez et al., 2004). Following the birth of the first cloned domestic cat kittens in 2002 (Shin et al., 2022), the first wild cat (African wildcat) was born in 2004 after SCNT and intra -species transfer (to the domestic cat) (Gomez et al.,

2004). Since endangered cat oocytes are very scarce, the ooplasm of a domestic cat oocyte can be used as a somatic cell nucleus recipient of an endangered cat. At the same time, collecting tissue samples (such as a piece of skin) from wild animals is easier, less costly and harmless than collecting gametes or embryos. The possibility of obtaining somatic resources from fetal cells offers the advantage of obtaining genetic material from animals even in cases of stillbirth and abortion. This provides great convenience in protecting wild felines with the help of domestic cats. Despite the common belief that cloned animals have the same cellular structure, telomere length in cats is independent of telomere length in donor cells (Imsoonthornruksa et al., 2012). Although offspring can be produced via SCNT in different mammalian species, success rates are still very low (1–11%). Different somatic cell types have been tried as sources of genetic material for SCNT. These; are fibroblasts, cumulus cells, and preadipocytes from adults and fetuses. However, fetal cells were generally found to be better than those obtained from adults. In our previous study, where we used cumulus cells as a source of somatic cells, we produced in vitro cat embryos with SCNT (Evecen et al., 2016). Howeveralthough cytoplasts were cleaved (15.75 %) and some of them (9.58%) reached the morula cell stage, none of them could reach the blastocyst stage. While some authors prefer to transfer early-stage embryos to the oviduct (Goodrowe et al., 1988), others have chosen to transfer more developed embryos (morula/ blastocyst) into the uterus (Pope et al., 2006). Both methods have resulted in pregnancy and the production of live kittens in both domestic and wild cats. The first cloned cat (a female named Copy Cat) reproduced naturally and gave birth to three healthy kittens (Shin et al., 2002). Thus, the view that cloned animals are normal is confirmed and that SCNT is therefore a valuable method to preserve endangered felines. Recently, the use of endoscopy for transcervical artificial insemination in cats has created excitement for the application of this method in embryo transfer (Zambelli et al., 2015).

4. Transgenesis

Studies in domestic cats have discovered that cats have 18 pairs of autosomal chromosomes and XY sex chromosome pairs. Gene mapping studies in cats have shown that the genome organization of cats is more similar to humans than that of dogs or mice (Muldoon et al., 1994). Recently it has been demonstrated that 90 % of the genes discovered in the cat carry homologues of human genes (Gomez et al., 2009). Sandhoff disease is a genetic disorder characterized by the deposition of GM2-gangliosides and other related asialoglycolipids in the brain and other tissues. Children with the infantile form of this disease usually die by the age of four. In 1985, researchers detected a disorder in Korat cats that is analogous to human type II GM2-gangliosidosis (Neuwelt 1985). Studies are being carried out to examine the mutations that cause diseases in cats to develop a cat model for similar diseases in humans. The Korat cat provides an animal model that may be suitable for testing gene replacement therapy in, Sandhoff disease in humans (Muldoon et al., 1994). Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic diseases in humans and affects approximately five million people in the world. Polycystic kidney disease is a disease seen in longhaired Persian cats and is similar to autosomal dominant polycystic kidney disease (ADPKD) in humans. Cats are also a valuable animal model for studies on the treatment of this disease in humans (Biller et al., 1996). Recently, different researchers have conducted successful transgenic studies in domestic cats, proving that green and red fluorescence genes are expressed in the born kittens (Gomez et al., 2009; Yin et al., 2008). Transgenic studies such as these offer great opportunities to create desired disease models and cure individuals with genetic diseases with gene therapy (Gomez et al., 2009).

Conclusion

Since the first successful embryo transfer, significant advances have been made in assisted reproductive technologies in cats. These advances have encouraged researchers to adapt these techniques to wild cat species, mostly in the last two decades. Thanks to these technologies, domestic cats are now successfully cloned commercially and provide great happiness to their owners whose pets have aged or died by giving them new ones. Thus it becomes much easier to protect endangered wild cat species, with domestic cats becoming good model animals for wild cats or serving as interspecies embryo carriers. Additionally, due to their genetic similarity cats are helpful as animal models in the study of many genetic diseases found in humans that are similar to their feline counterparts. ARTs also make great contributions to the development of future treatment methods by helping to investigate and understand the mechanisms of many genetic diseases that are similar to their counterparts in humans and cats.

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