SL 104 Current Research Trends and Knowledges in Mammalian Somatic Cell Cloning

Hee-Tae Cheong
Department of Veterinary Medicine
Kangwon National University

Somatic cell nuclear transfer is an efficient technique for the multiplication of elite livestock, engineering of transgenic animals and analyzing the interactions between nucleus and cytoplasm, for various agricultural, biomedical and research purposes.

Since the first somatic cell clone lamb was born(Wilmut et al., 1997), tremendous progress has been made toward developing technology for animal cloning. Viable lambs(Wilmut et al., 1997; Schnieke et al., 1998), calves(Cibelli et al., 1998; Kato et al., 1998; Wells et al., 1998, 1999; Vignon et al., 1999; Zakhartchenko et al., 1999), goats(Baguisi et al., 1999) and mice(Wakayama et al., 1998, 1999) have now been produced by nuclear transfer using fetal and adult somatic cells as nuclei donors.

Somatic cell cloning is different from the embryonic cell cloning in a view of the nucleus from a differentiated donor cell to direct development to term. In this procedure, it has been suggested that the quiescent state of donor cells is a very important factor for the reprogramming of donor cell in the oocyte cytoplasm (Campbell et al., 1996; Wilmut et al., 1997). In the majority of somatic cell cloning reports, primary cell populations have been established in culture and induced to enter quiescence prior to use as nuclear donors(Wilmut et al., 1997; Kato et al., 1998; Wells et al., 1999). Naturally quiescent cells also used for nuclear donor. Mouse brain neural cells and Sertoli cells were transferred into enucleated recipients, but could not develop to term. Only cumulus cells that were mostly arrested in G0/G1 developed to term after cytoplasmic injection(Wakayama et al., 1998). On the other hand, nonquiescent proliferating bovine fetal fibroblast cells could develop to term(Cibelli et al., 1998), which suggesting that intentionally induced quiescence is not essential for term development.

Variety of fetal and adult somatic cell types were used as nuclei donors to investigate their totipotencies. At present, it was confirmed that fetal fibroblast, fetal skin and muscle cells, adult mammary gland, skin, muscle, cumulus, granulosa and oviduct cells have totipotencies in sheep, bovine, mouse or goat. In sheep, clones were produced from fetal fibroblast cells and adult mammary gland cell(Wilmut et al., 1997). In bovine, clones were obtained from more various cells, such as fetal cells(Zakhartchenko et al., 1999), cumulus cells(Kato et al., 1998), granulosa cells(Wells et al., 1999), oviduct cells(Kato et al., 1998), skin and muscle cells(Vignon et al., 1999). Developmental potentials in vitro varied according to the cell types and researchers. It was suggested that the fetal derived-cells had higher developmental potential than adult cells, However, some kinds of adult cells such as cumulus cells(Kato et al., 1999) and granulosa cells(Wells et al., 1999) more reliably results in blastocyst development and live offspring than fetal cells after nuclear transfer.

Somatic cells nuclear transfer can provide advantages for making transgenic animals.

Schnieke et al.(1997) produced transgenic lambs by introducing a foreign gene into fibroblast subsequently used for nuclear transfer, which requires fewer embryos than direct DNA microinjection into zygotes. Transgenic bovine clones also produced by the same approach (Cibelli et al., 1998). Another approach was attempted to make transgenic clone goats, in which the cells derived from transgenic fetus were transferred into enucleated oocytes, and obtained three offsprings(Baguisi et al., 1999).

Interspecies nuclear transfers were attempted to investigate the interaction between nuclear and cytoplasm derived from different species, and the possibilities of using for salvaging endangered species or human cell therapies(Dominko et al., 1999; White et al., 1999).

In the future, somatic cell nuclear transfer will provide more numerous opportunities, both in basic and appled research as well as immediate uses in the generations of superior clone and transgenic animals.

Baguisi et al., 1999. *Nature Biotech.* 17: 456-461
Campbell et al., 1996. *Nature* 380: 64-66
Cibelli et al., 1998. *Science* 280: 1256-1258
Dominko et al., 1999. *Biol. Reprod.* 60: 1496-1502
Kato et al., 1998. *Science* 282: 2095-2098
Schnieke et al., 1997. *Science* 278: 2130-2133
Vignon et al., 1999. *Theriogenology* 51: 216(abstract)
Wakayama et al., 1998. *Nature* 394: 369-374
Wakayama et al., 1999. *Nature Genetic* 22: 127-128
Wells et al., 1998. *Reprod. Fertil. Dev.* 10: 369-378
Wells et al., 1999. *Biol. Reprod.* 60: 996-1005
White et al., 1999. *Cloning* 1: 47-54
Wilmut et al., 1997. *Nature* 385: 810-813
Zakhartchenko et al., *J. Reprod. Fertil.* 115: 325-331