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APPENDICES

APPENDIX A

All media were prepared using MilliQ water, otherwise indicated. The pH of all media was adjusted to 7.2-7.4; the osmolality was 300 to 310 mOsm for the fusion medium. All media were sterilized by filtration immediately after preparation then aliquot and stored at –20° C.

Stock solutions

FSH	1 mg pFSH-P1/ml 0.9% NaCl
pLH	1 mg/ml 0.9% NaCl
Estradiol (water soluble)	0.1 mg/ml 0.9% NaCl
Penicillin-streptomycin	5,000 IU/ml
Hyaluronidase	0.5% (w/v) in M199 with HEPES
Cycloheximide	1 mg/ml M199 with $NaHCO_3$
Cytochalasin B	1 mg/ml DMSO
6-DMAP	1 mg/ml M199 with $NaHCO_3$
Ionomycin	1 mg/ml DMSO
Hoechst 33342	1 mg/ml FCS

Oocyte collection medium

For bovine oocytes; M199 (Earle's salts) with HEPES	25 mM
For goat oocyte collection; aspiration	
M199 (Earle's salts) with HEPES	25 mM
FCS	2% (v/v)
Penicillin-streptomycin	1% (v/v)
Heparin	50 IU/ml

Maturation medium	
For bovine; M199 (Earle's salts) with $NaHCO_3$, L-glutamine	
FCS	10 % (v/v)
FSH stock	1% (v/v)
pLH stock	1% (v/v)
Estradiol stock	1% (v/v)

Enucleation medium	
M199 (Earle's salts) with HEPES	25 mM
FCS	10% (v/v)
Cytochalasin B	5 µg/ml
Hoechst 33342	0.5 µg /ml

Fusion medium		Cell culture medium	
Mannitol	0.3 M	DMEM high glucose	
$MgSO_4.7H_2O$	0.1 mM	FCS	10% (v/v)
$CaCl_2.2H_2O$	0.1 mM	Penicillin-streptomycin	1% (v/v)

APPENDIX B

Fixation of NT embryos and parthenogenetic embryos

According to Adenot et al. (1994)

At the end of the culture period:

- Incubate embryos in a medium for 30 min; medium: M199 $NaHCO_3$ + 10% FCS containing BrdU.

- Rinse in PBS for 15 min.

-Fix in fixative solution for 15 min. Fixative solution contains: 2.5% paraformaldehyde and 0.5 N NaOH in PBS.

- Rinse in PBS (2 % FCS. PBS) for 3 X 5 min.

- Store in PBS (or PBS + 2 % FCS) at 4° C for Immunocytochemistry.

Immunocytochemistry

1. Incubate the fixed embryos in PBS + 10% FCS + 0.1% Triton X100 for 30 min at 39° C.
2. Incubate in anti-BrdU 1/50 in PBS + 2% FCS for 1 h at 39° C (tarasaki plate).
3. Rinse in PBS + 2% FCS for 1 X 5 min, 1 X 30 min and 1 X 5 min.
4. Incubate in goat anti-mouse FITC 1/300 in PBS + 2% FCS for 1 h at 39° C.
5. Wash with PBS + 2% FCS for 2 X 5 min.
6. Counterstain with 1/100 Propidium Iodide (PI) in 2% FCS. PBS for 5-10 min.
7. Rinse in PBS + 2% FCS for 3 X 5 min.
8. Mount with vectashield then cover with a coverslip.
9. Keep in refrigerator and protect from light then observe within 2 weeks.

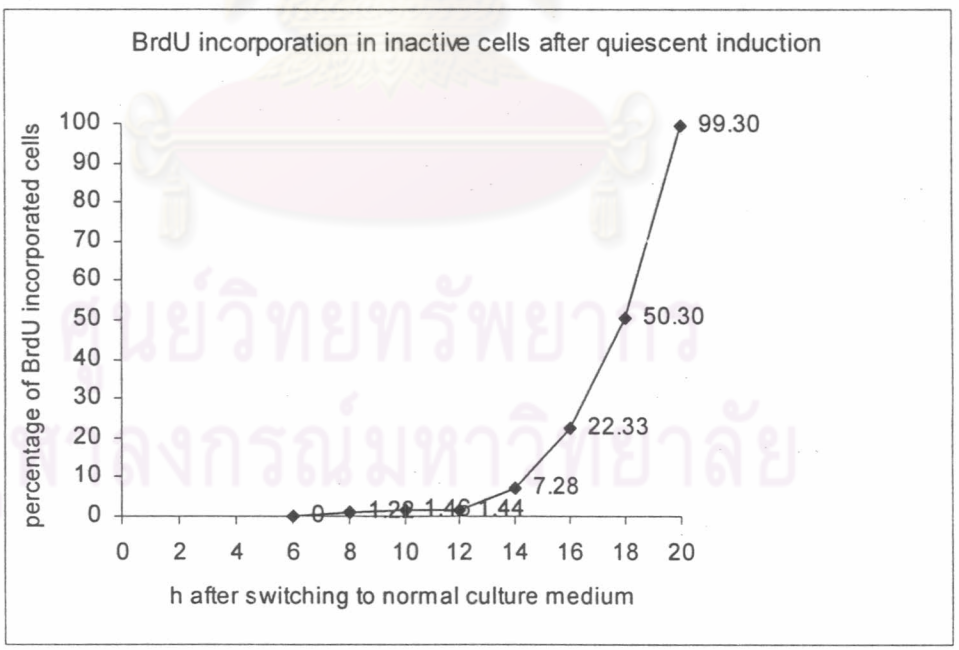
APPENDIX C

BrdU incorporation in inactive cells after induction of quiescence

Normal fibroblast cells (The same cell line as was used in CHAPTER III)

Culture time with BrdU (h)	No.cells green	No.cells red	% green/red
6	0	109	0.00
8	3	246	1.22
10	3	205	1.46
12	3	208	1.44
14	27	371	7.28
16	46	206	22.33
18	83	165	50.30
20	141	142	99.30

green: BrdU positive, red: propidium iodide



BrdU incorporation in nuclei of 1-cell stage NT embryos at various times after fusion when used non-activated oocyte as recipient cytoplast (NT-MII group, CHAPTER III)

Time post fusion (h)	Replicates	Fused	Embryos incorporated to BrdU (% mean ± SEM)
5	2	25	0 (0)
6	6	53	10 (12.6 ± 8.2)
7	6	52	16 (46.5 ± 11.6)
8	3	31	30 (97.6 ± 2.4)
9	3	24	23 (95.8 ± 4.2)
10	3	26	22 (85.0 ± 1.7)
11	2	33	28 (84.1 ± 2.3)
12	3	37	25 (68.5 ± 2.0)
13	3	48	21 (38.9 ± 10.5)
14	4	27	11 (32.5 ± 5.1)
15	4	29	10 (28.6 ± 20.2)
16	3	61	15 (31.9 ± 8.4)
17	2	46	5 (12.8 ± 3.9)
18	2	55	2 (3.5 ± 3.5)

In this experiment, a total of 46 replicates were performed, 1,267 *in vitro* matured bovine oocytes were enucleated, 1,164 enucleated oocytes were reconstructed and 547 reconstructed oocytes were fused.

BrdU incorporation in nuclei of 1-cell stage NT embryos at various times after fusion when used activated oocyte as recipient cytoplast (NT-ACT group, CHAPTER III)

Time post fusion (h)	Replicates	Fused	Embryos incorporated to BrdU (% mean ± SEM)
4	2	14	0 (0)
5	2	27	10 (37.6 ± 2.4)
6	2	19	15 (79.3 ± 0.7)
8	1	7	5 (71.4)
10	2	22	19 (89.3 ± 10.7)
12	2	24	17 (71.0 ± 1.8)
16	2	23	12 (49.6 ± 19.6)
18	2	25	9 (35.9 ± 2.6)
20	2	19	7 (36.7 ± 3.3)
22	2	21	11 (50.0 ± 7.1)

In this experiment, a total of 19 replicates were performed, 444 *in vitro* matured bovine oocytes were enucleated then activated, 365 enucleated-activated oocytes were reconstructed and 201 reconstructed oocytes were fused.

APPENDIX D

General anesthesia procedure:

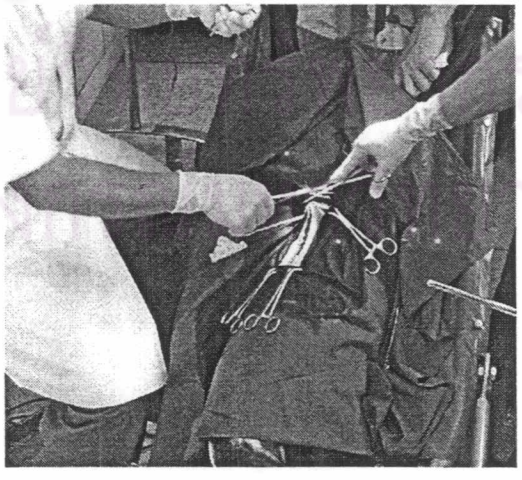
According to Sumretprasong et al. (1995)

1. Injection of 0.22 mg/kg of xylazine (0.1 ml/10 kg Rompun®, Bayer, S.Korea) intramuscularly
2. Ten to 15 min later inject 6.6 mg/kg of ketamine intravenous
3. Administration of 6.6 mg/kg of ketamine at 10 min-intervals after the first injection.

Laparotomy procedure:

Following general anesthesia, the doe was placed in dorsal recumbency on a surgical table for a midventral laparotomy procedure.

Midventral laparotomy



Postoperative care:

After surgery, a dose of 5 ml/doe of penicillin-streptomycin (20,000 IU-20 mg/kg) was injected intramuscularly. It was repeatedly given 24 h later, and then every 48 h. The does were rested for at least two months before being used for oocyte collection again.

APPENDIX E

List of publications and conferences

1. Apimeteetumrong, M., Laloy, E., Lavergne, Y., Chesné, P., Techakumphu, M., Kunawongkrit, A., Renard, J.P. and Vignon, X. 2002. DNA replication during the first cell cycle of bovine nuclear transfer embryos. **The 18th Annual Meeting of Association Europeenne de Transfert Embryonnaire**, 6-7 September 2002, The Netherlands, p. 34.

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5. Apimeteetumrong, M., Thuangsanthia, A., Leingcharoen, N., Yiengvisavakul, V., Harintharanon, A, Kunavongkrit, A., Sumretprasong, J., Vignon, X., and Techakumphu, M. 2004. The effect of activation protocols on the development of cloned goat embryos. **J. Vet. Med. Sci.** 66 (12): 1529-1534.

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7. Apimeteetumrong, M., Thuangsanthia, A., Leingcharoen, N., Yiengvisavakul, V., Sumretprasong, J., Kunavongkrit, A., and Techakumphu, M. 2005. Repeated surgical oocyte collection and its effect on pregnancy in goats. *In*: **Proceedings of 43nd Kasetsart University Annual Conference,** 1-4 February 2005, Bangkok, Thailand.

8. Apimeteetumrong, M., Thuangsanthia, A., Leingcharoen, N., Yiengvisavakul, V., Sumretprasong, J., Kunavongkrit, A., and Techakumphu, M. 2005. Repeated oocyte collection and its influence on fertility in goats. **Thai J. Vet. Med.** (in press).

CURRICULUM VITAE

Miss Malee Apimeteetumrong was born in Nakhonratchasima province, Thailand, on July 3rd, 1960. She graduated with B.Sc. (Chemistry) from Khon Kaen University, Faculty of Science, in 1983 and M.Sc. (Biotechnology) from King Mongkut's Institute of Technology in 1996. In 1984, after graduation, she became a scientist at the Artificial Insemination Division (the Bureau of Biotechnology for Animal Production; since 2003), Department of Livestock Development, Minister of Agriculture and Cooperatives. Her responsibility was in the area of the research and development on reproductive biotechnologies for animal production. She is still working for the department. In 2000, she attended her Ph.D. study under the Royal Golden Jubilee Program, Thailand Research Fund, at the Department of Obstetrics Gynaecology and Reproduction, Faculty of Veterinary Science, Chulalongkorn University.