2022.11.24
Award lecture of Kei-ichiro Maeda Memorial Ise Award 2022

Basic and clinical approach to improving bovine fertility

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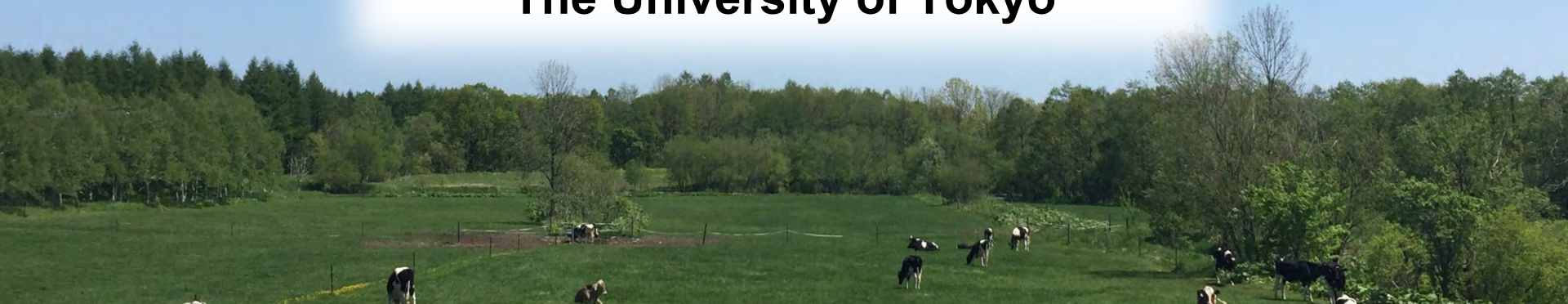
The University of Tokyo



The mission for sustainable Dairy production

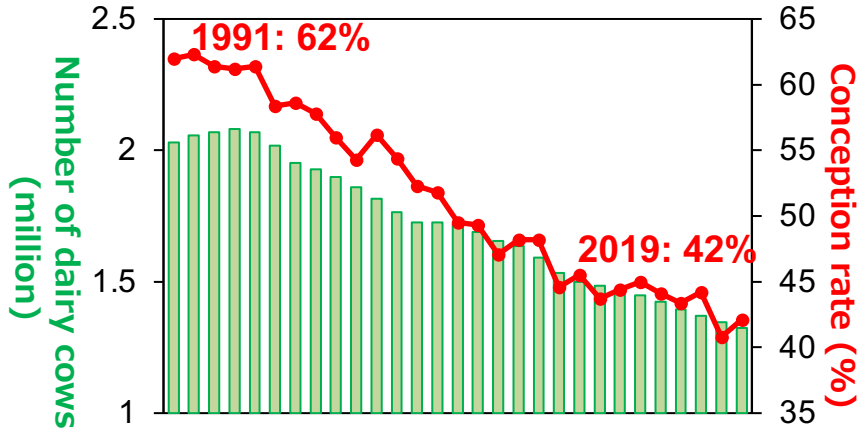
Parturition

Pregnancy

Reproduction

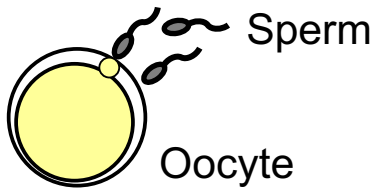
Milking

The declining bovine fertility in Japan



What causes declining fertility?

e. g. **Impaired oocyte quality**



Uterine inflammatory diseases

Impact of uterine inflammation

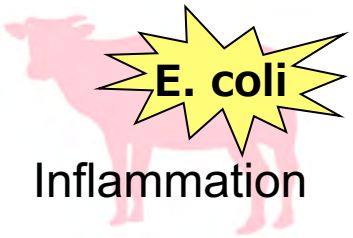
Incidence ⇒ 30 to 50%
Conception rate ⇒ 20% decrease
Economic loss/year ⇒ € 1.4 billion (EU)
$ 650 million (USA)

(Sheldon et al., 2009)

Escherichia coli

Endotoxin

Lipopolysaccharide (LPS)

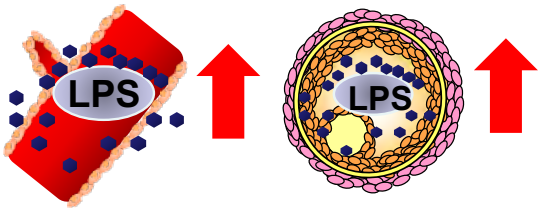


Inflammation

Recovery

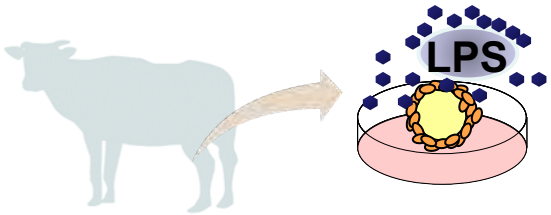
Accumulation of LPS after recovery

<Blood> <Follicles>



(Magata et al., *Anim Reprod Sci*, 2014)
(Magata et al., *Anim Sci J*, 2017)
(Magata et al., *J Vet Med Sci*, 2019)

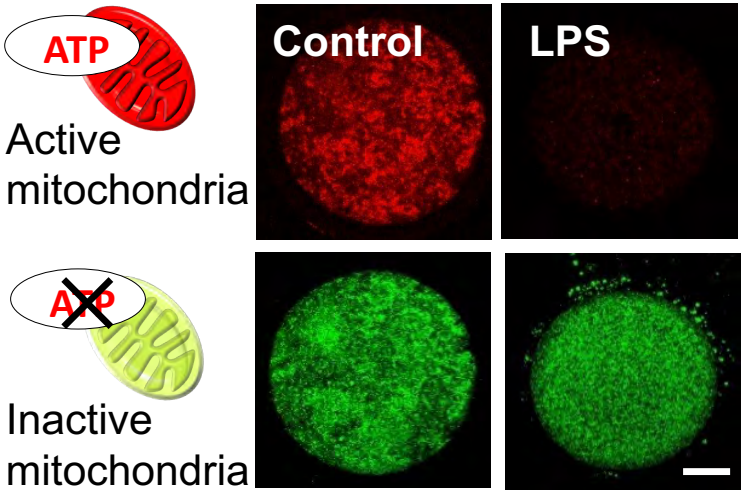
LPS reduces developmental ability of bovine oocytes



In vitro maturation
with LPS

Oocyte maturation ↓

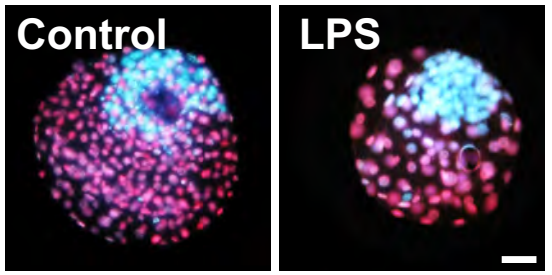
(Low mitochondrial activity)



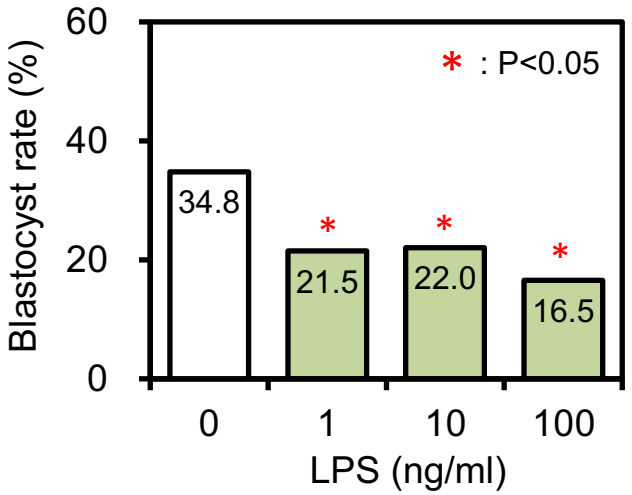
JC-1 staining (bar = 25 μm)

Embryo development ↓

(Developmental failure of embryos)



Hoechst & PI
staining
(bar = 50 μm)



(Magata et al., *Toxicol in vitro*, 2017)
(Magata et al., *J Reprid Dev*, 2020)

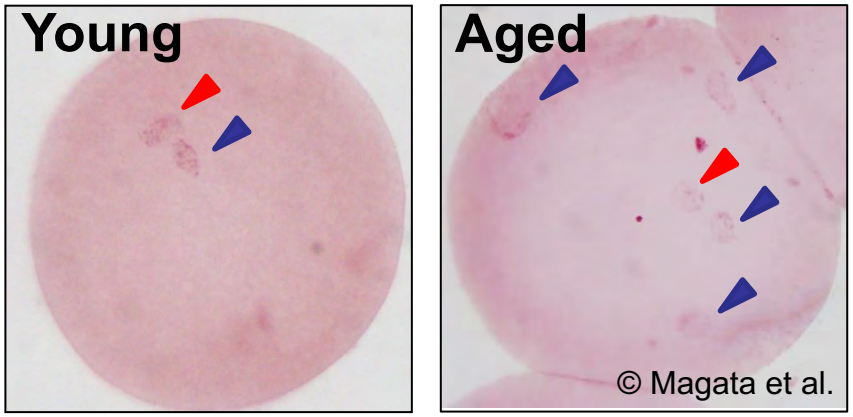
Maternal aging causes abnormal fertilization

Young cows
(< 10 years old)

vs.

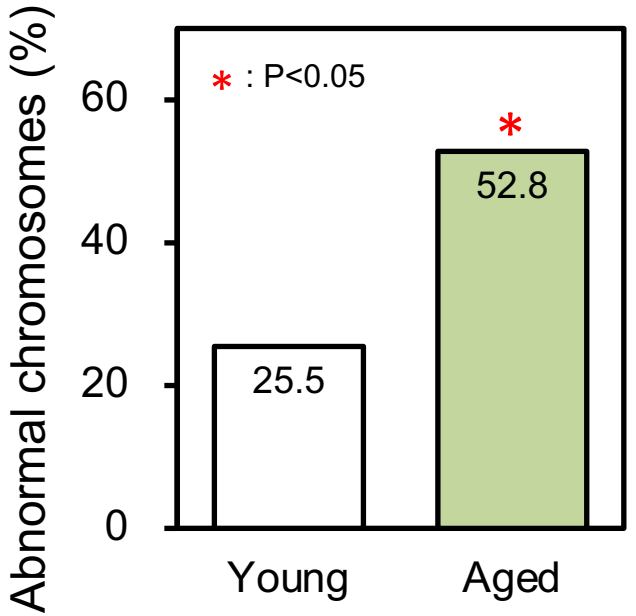
Aged cows
(≥ 10 years old)

Abnormal fertilization ↑
(high incidence of polyspermy)



Female pronucleus
Male pronucleus

Chromosome abnormality in developed embryos ↑



(Magata et al., *J Vet Med Sci*, 2019)

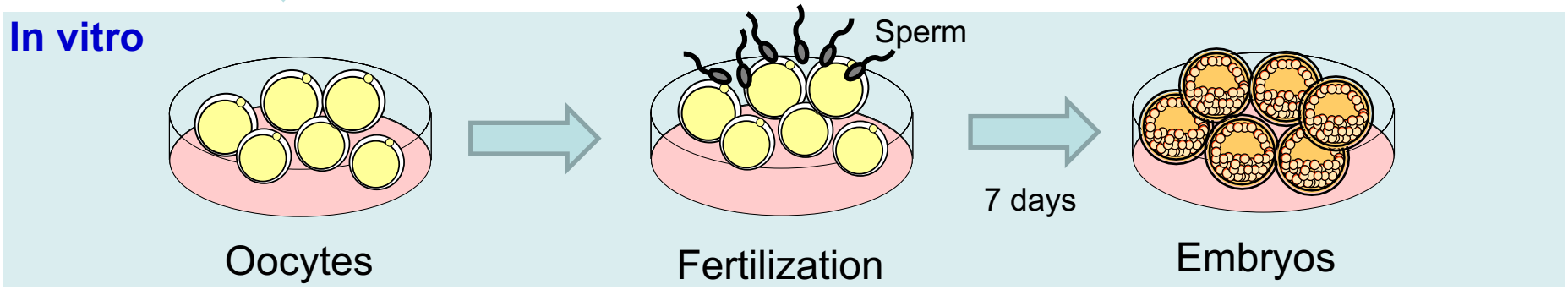
In vitro fertilization – embryo transfer

Healthy cows
with good oocytes

Oocyte collection

Cows with impaired
oocyte quality

Embryo transfer



However…

Pregnancy rate after embryo transfer

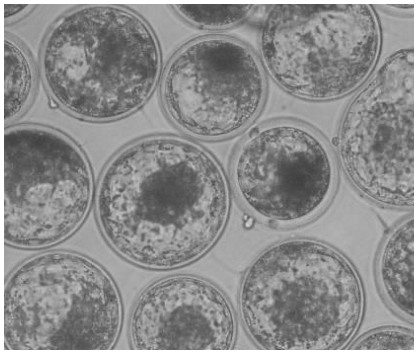
in vivo > in vitro 10 to 20% difference

Selecting embryos with high implantation potential is critical

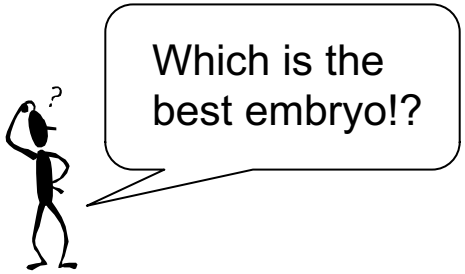
Time-lapse monitoring: Novel embryo selection method

Conventional method

Morphological evaluation after embryo culture



© Magata et al.

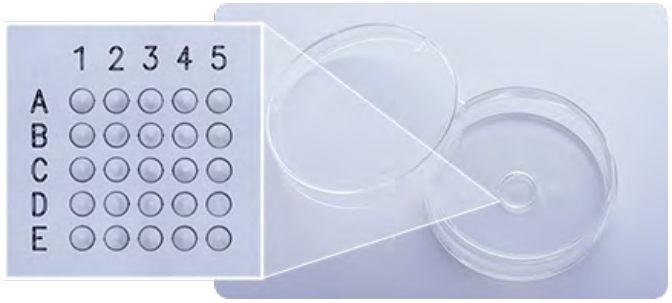


- ✓ Invasive
- ✓ Inadequate
- ✓ Subjective

- ✓ Non-invasive
- ✓ Accurate
- ✓ Objective

Time-lapse monitoring

Images of individual bovine embryos are acquired every 20 minutes



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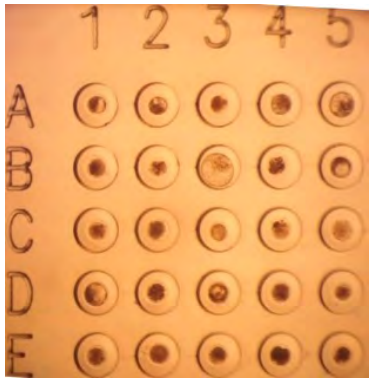
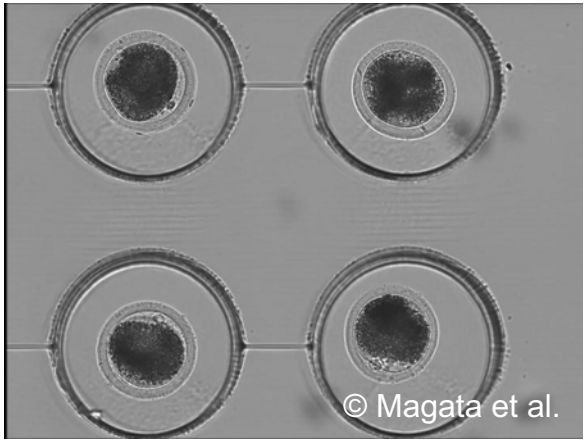
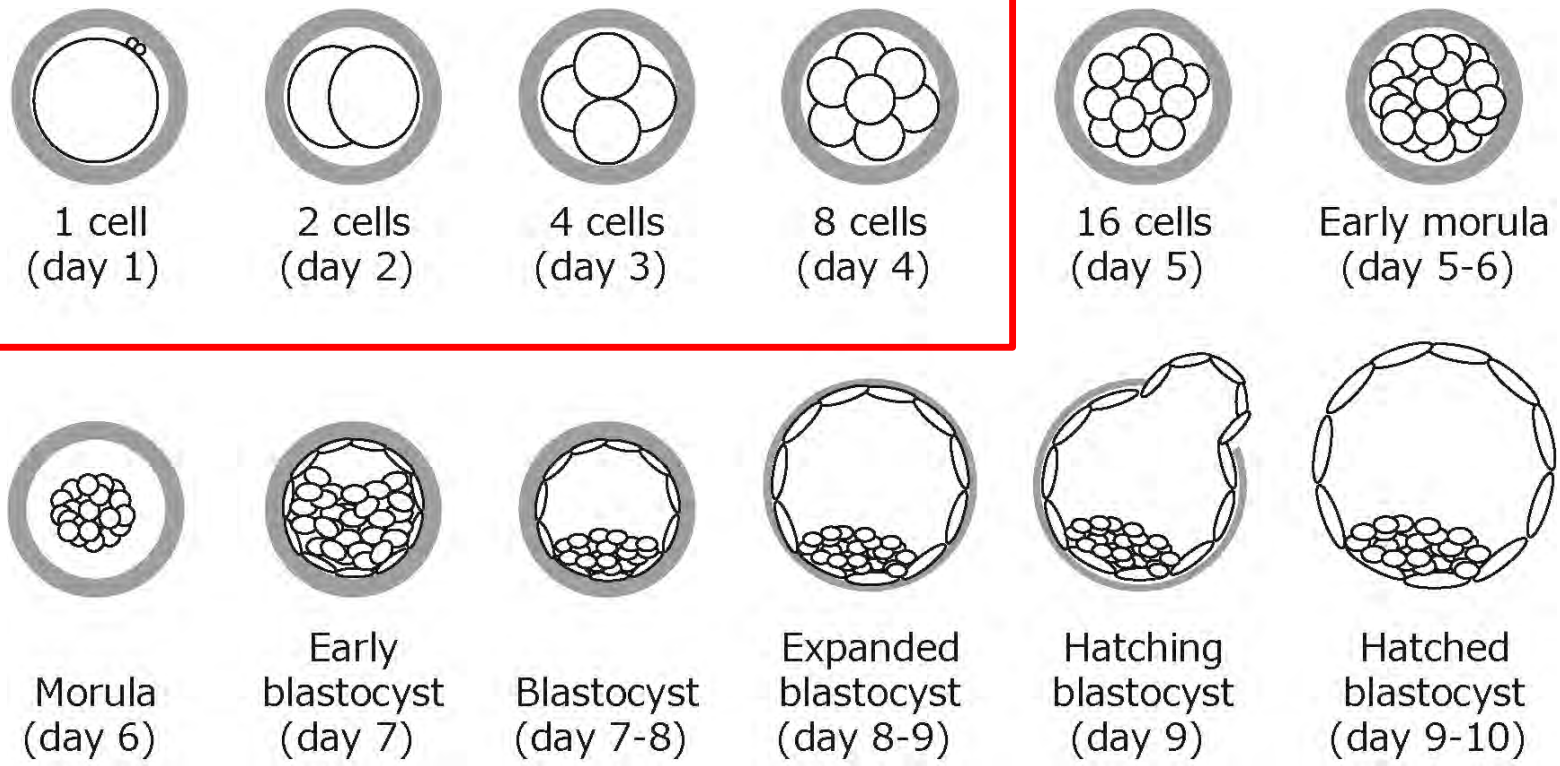




Stages of embryo development

Morphokinetic evaluation during the early growth stage

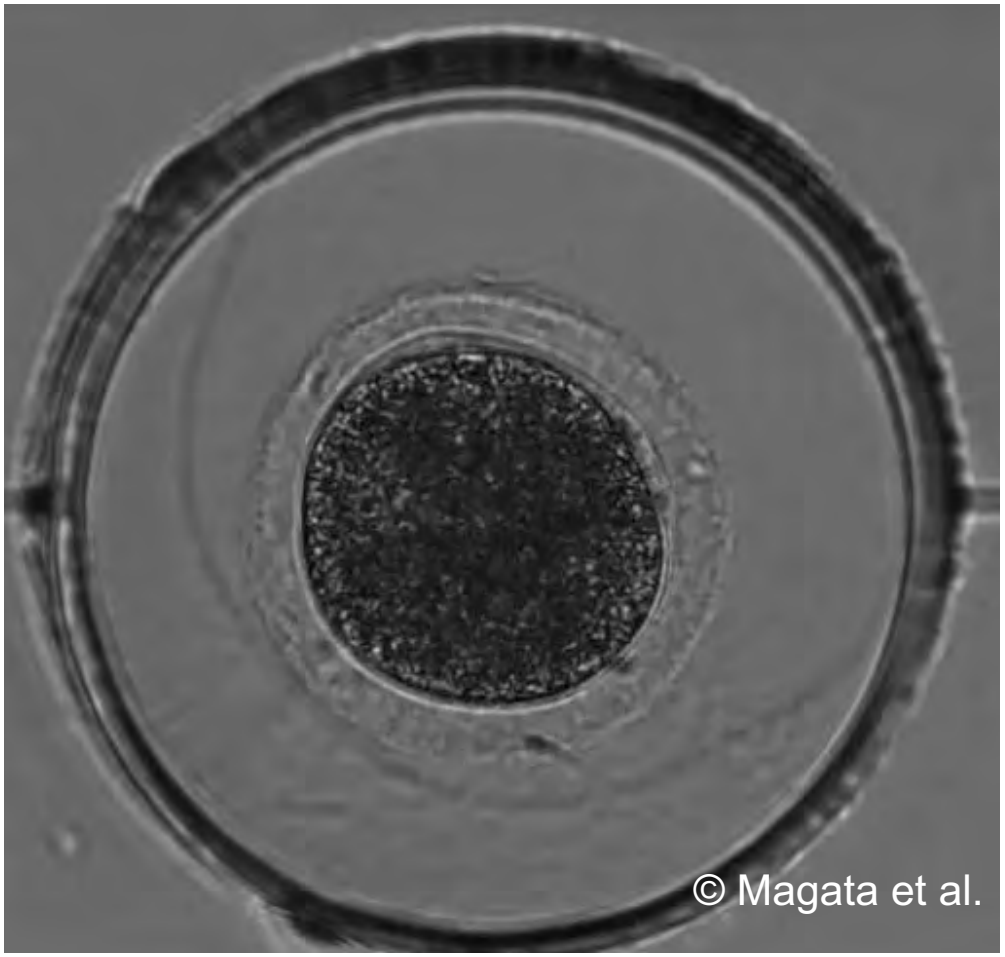


Normal cleavage

Cell divided to two daughter cells of the same size

(Magata et al., *Theriogenology*, 2019)

Reverse cleavage



The fusion of several cells after cell division

(Magata et al., *Theriogenology*, 2019)

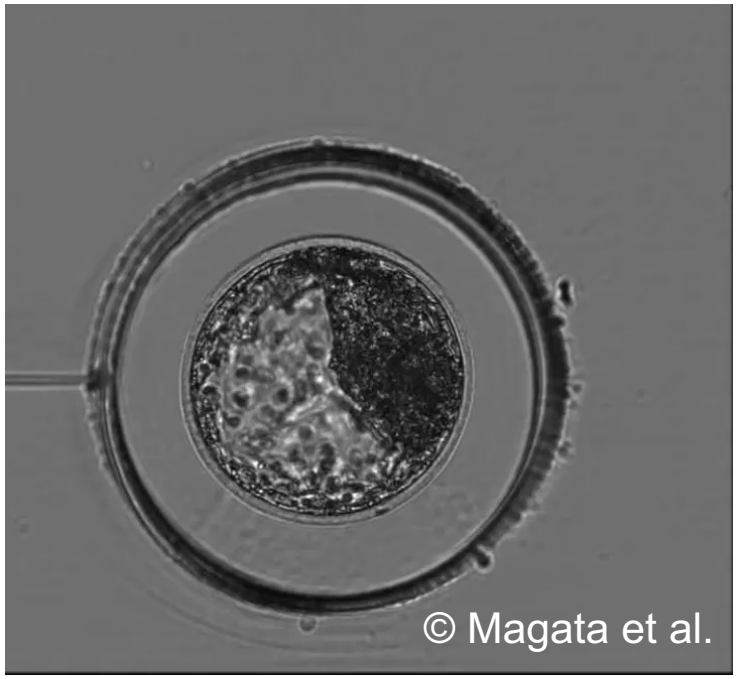
Direct cleavage

Cell division from the one-cell to three or four daughter cells

(Magata et al., *Theriogenology*, 2019)

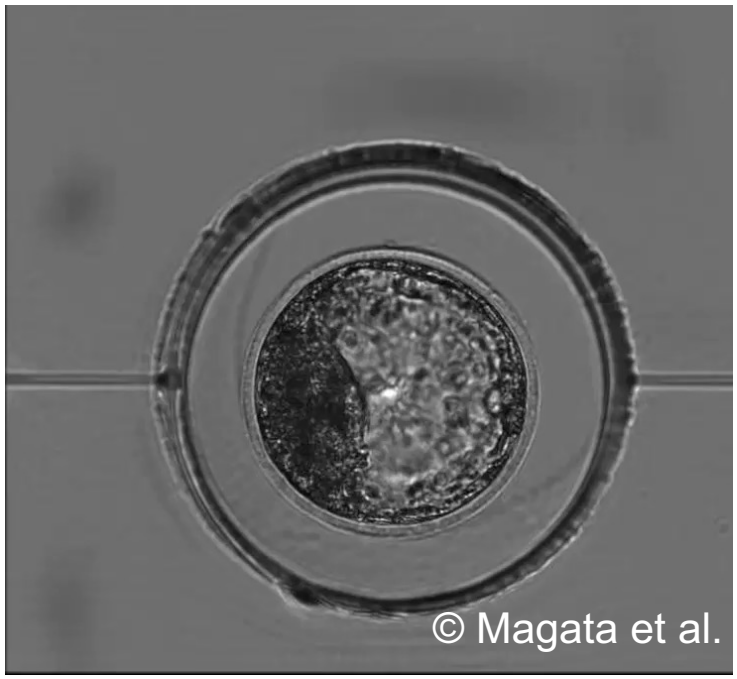
Abnormal cleavage may result in implantation failure

Normal cleavage



Conception rate: **59%**

Reverse cleavage

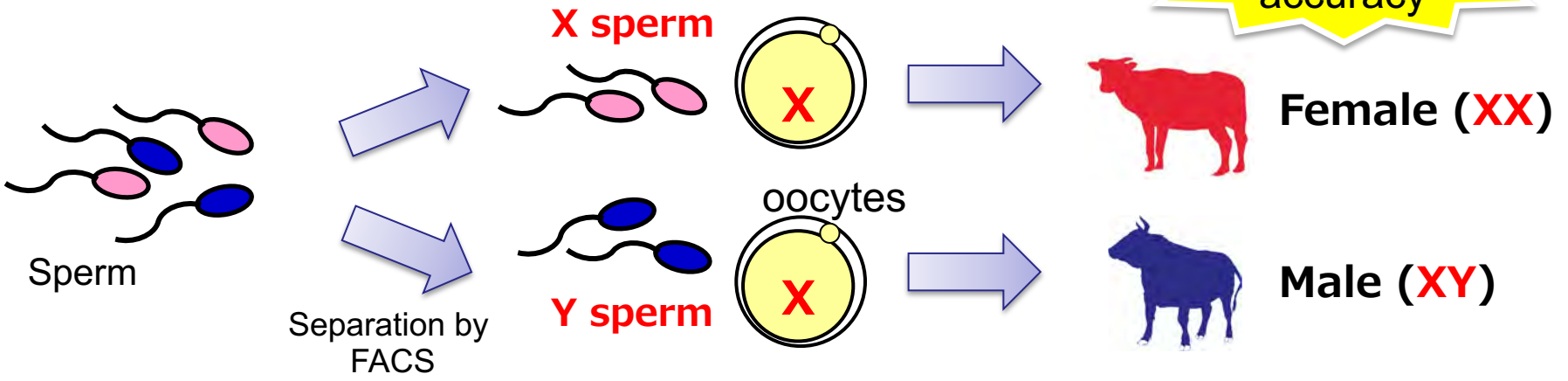


Conception rate: **25%**

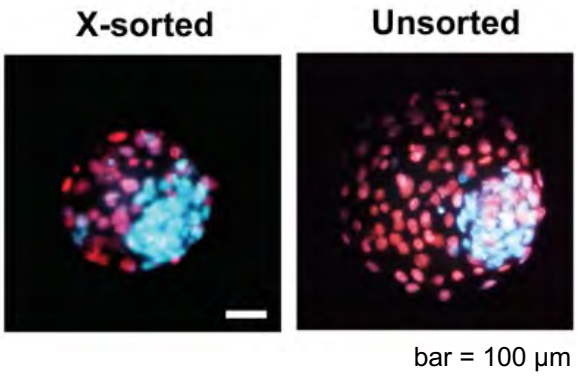
Problems of embryo production using sex-sorted semen

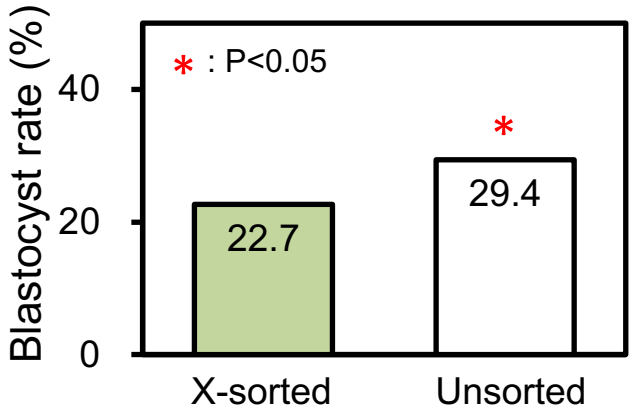
<Sex-sorted semen>

Over 90% accuracy



However…

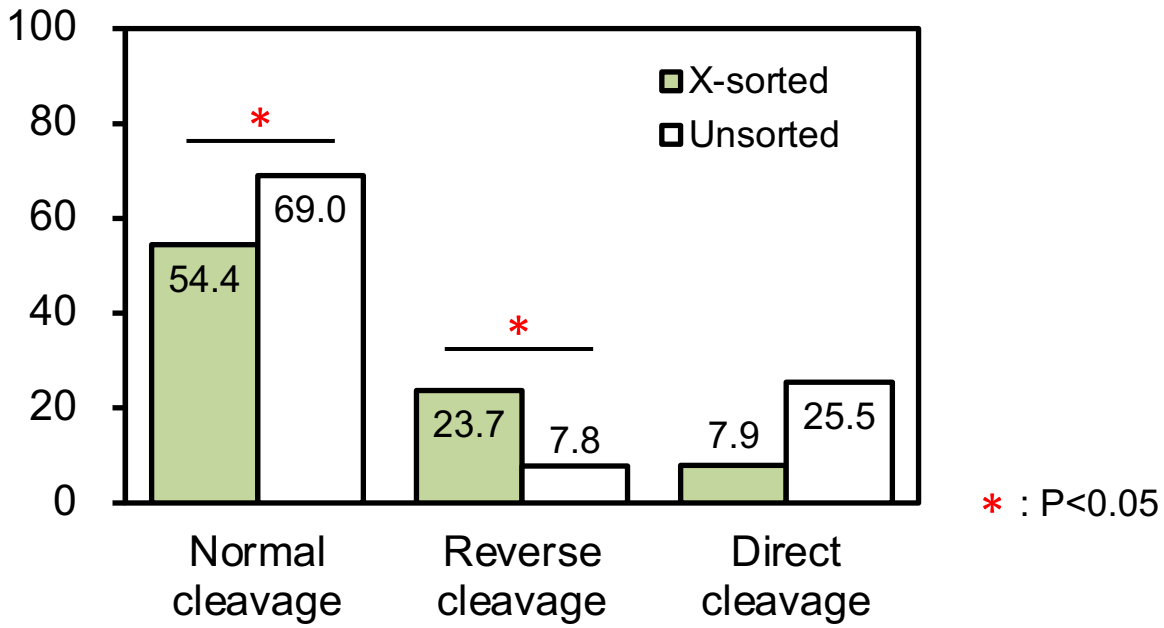




X-sorting of sperm decreased the developmental ability of embryos

(Magata et al., *Theriogenology*, 2021)

High incidence of abnormal cleavage in embryo produced with X-sorted sperm



(Magata et al., *Theriogenology*, 2021)

De-selection of embryos with abnormal cleavage

Production of sexed embryos with high implantation potential

Conclusion:

Basic and clinical approach to improving bovine fertility

■ Problems

Declining fertility

■ Basic approach

What causes poor oocyte quality that reduces fertility?

- ✓ **Uterine inflammation**
- ✓ **Maternal aging**

■ Clinical approach

Technologies to produce high-quality embryos

- ✓ **Time-lapse monitoring**
- ✓ **Embryo sexing**

■ Improve fertility

Sustainable milk & meat production

Final goal:

Contributing to solving the global food crisis

Acknowledgement

<The University of Tokyo>

Dr. Kei-ichiro Maeda
Dr. Fuko Matsuda

<Zennoh Embryo Transfer Center>

Dr. Yoshio Oono
Dr. Manami Urakawa
Dr. Atsushi Ideta

<Obihiro University of Agriculture and Veterinary Medicine>

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