



The 5th International Andrology Symposium
Cryptorchidism: Molecular Biology meets Endocrinology and Surgery
September 26-27 2025
Valetta Malta

Roles of Temperature and Retinoic Acid in the spermatogenesis defect associated with cryptorchidism



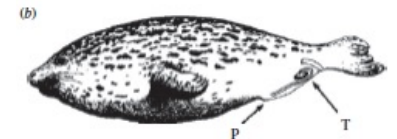
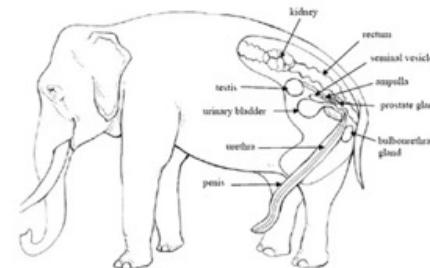
Shosei Yoshida
National Institute for Basic Biology, Okazaki Japan

Testicles are cooled in mammals

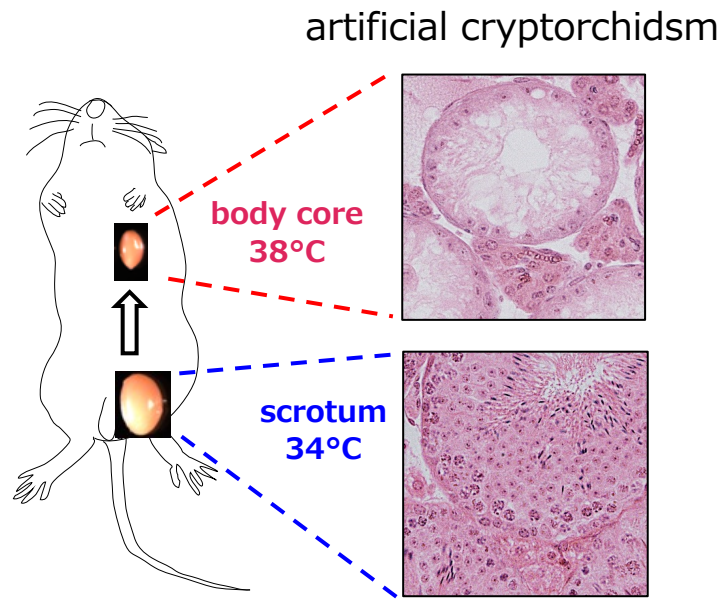
species with scrota



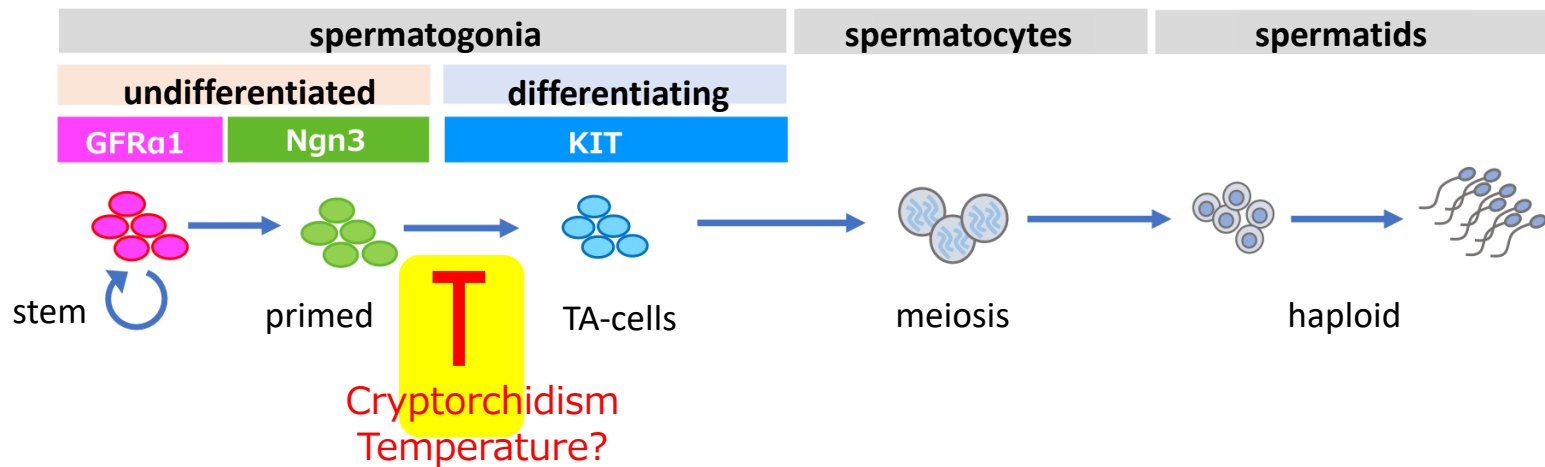
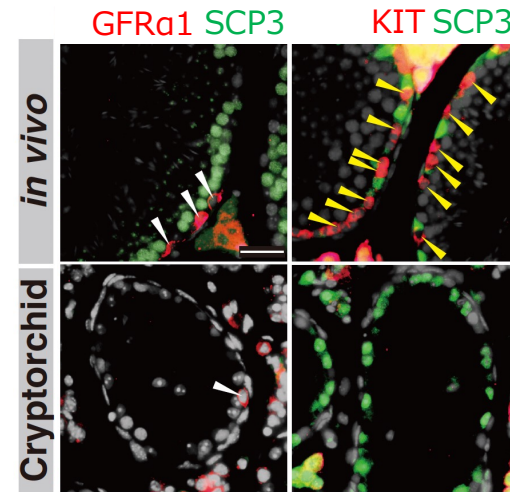
species without scrota



Spermatogenesis defect at a high temperatures in the body core



Spermatogenesis defect leaving undifferentiated spermatogonia only



Temperature and cryptorchidism

Question

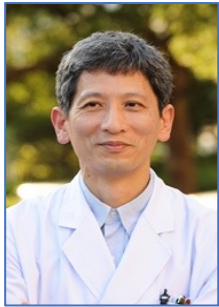
Which steps of spermatogenesis is impaired in high temperatures, and how?

Limits

In previous studies, testis temperature cannot be measured or controlled.

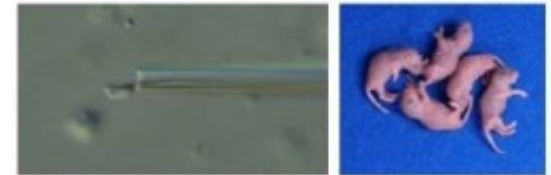
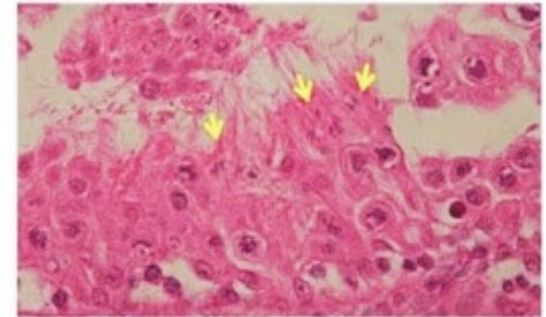
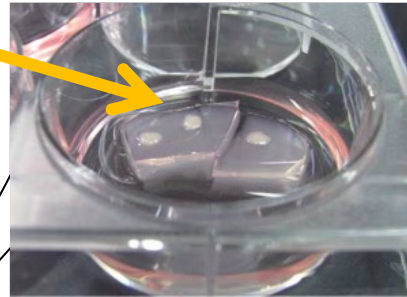
Extratesticular factors cannot be excluded

ex vivo organ culture of the testis



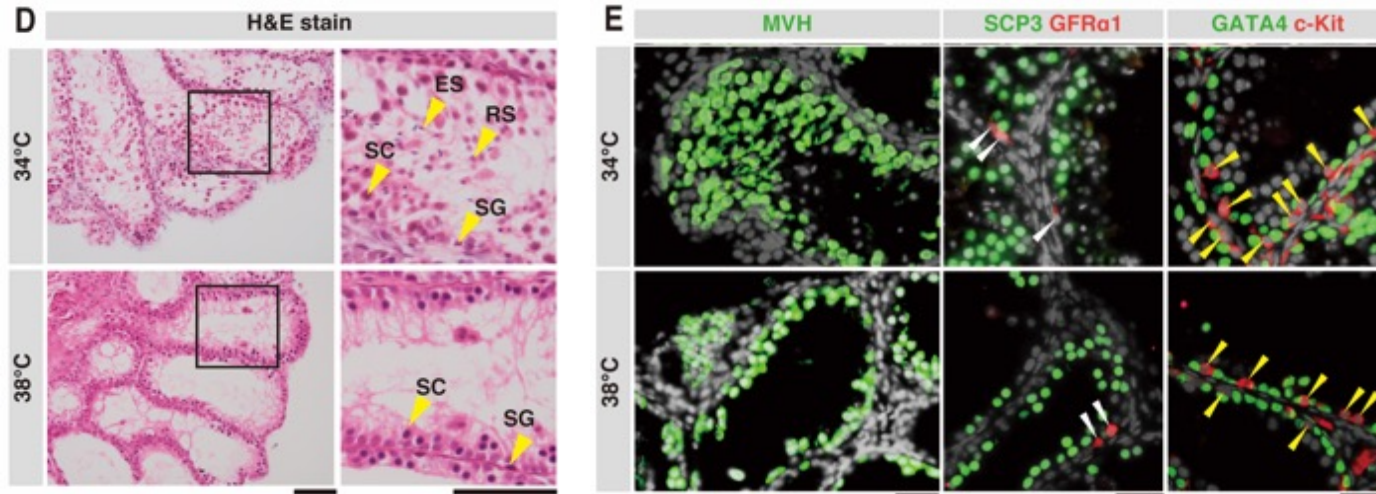
Takehiko Ogawa

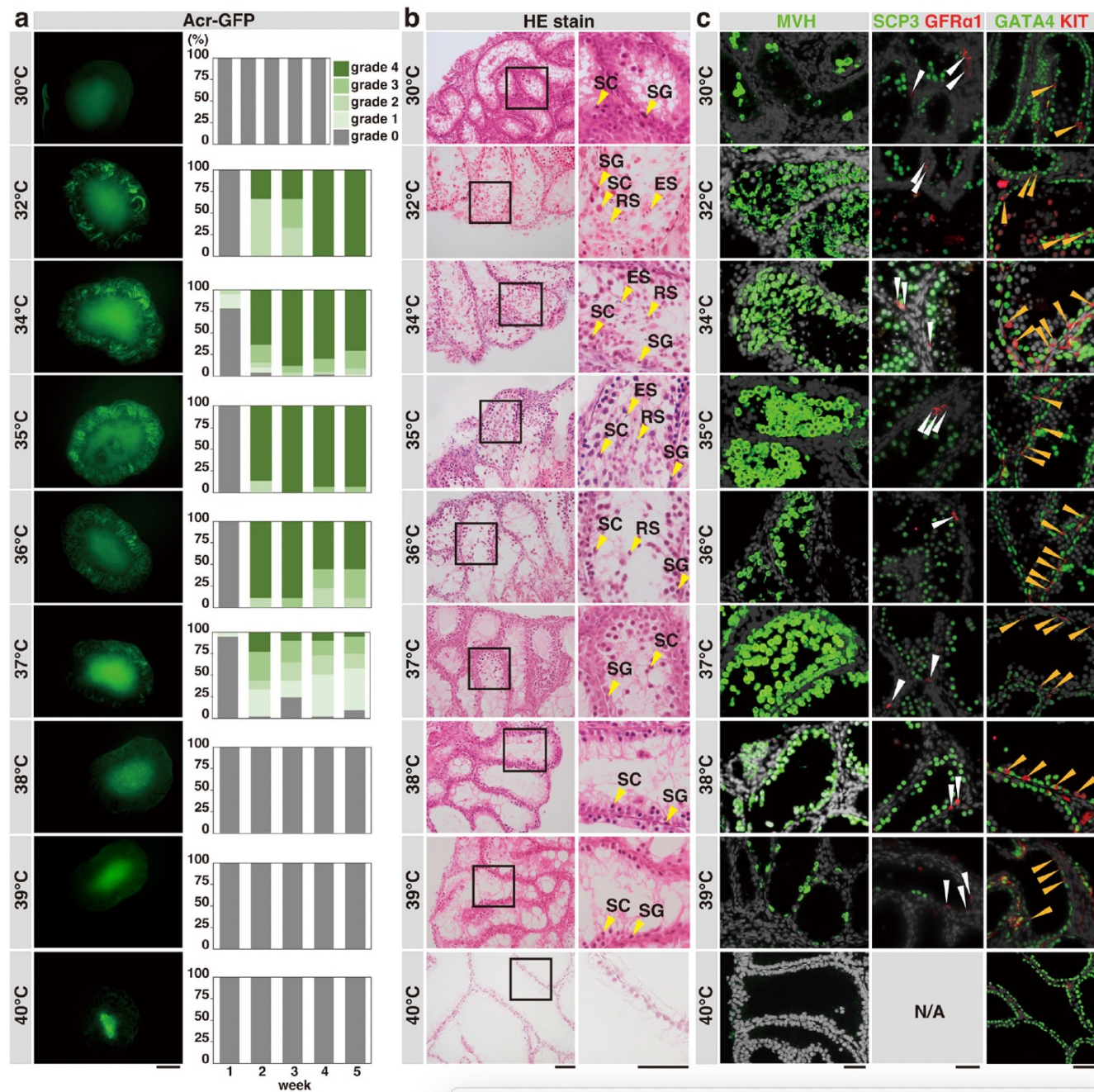
testicular explant
in air-liquid
interface



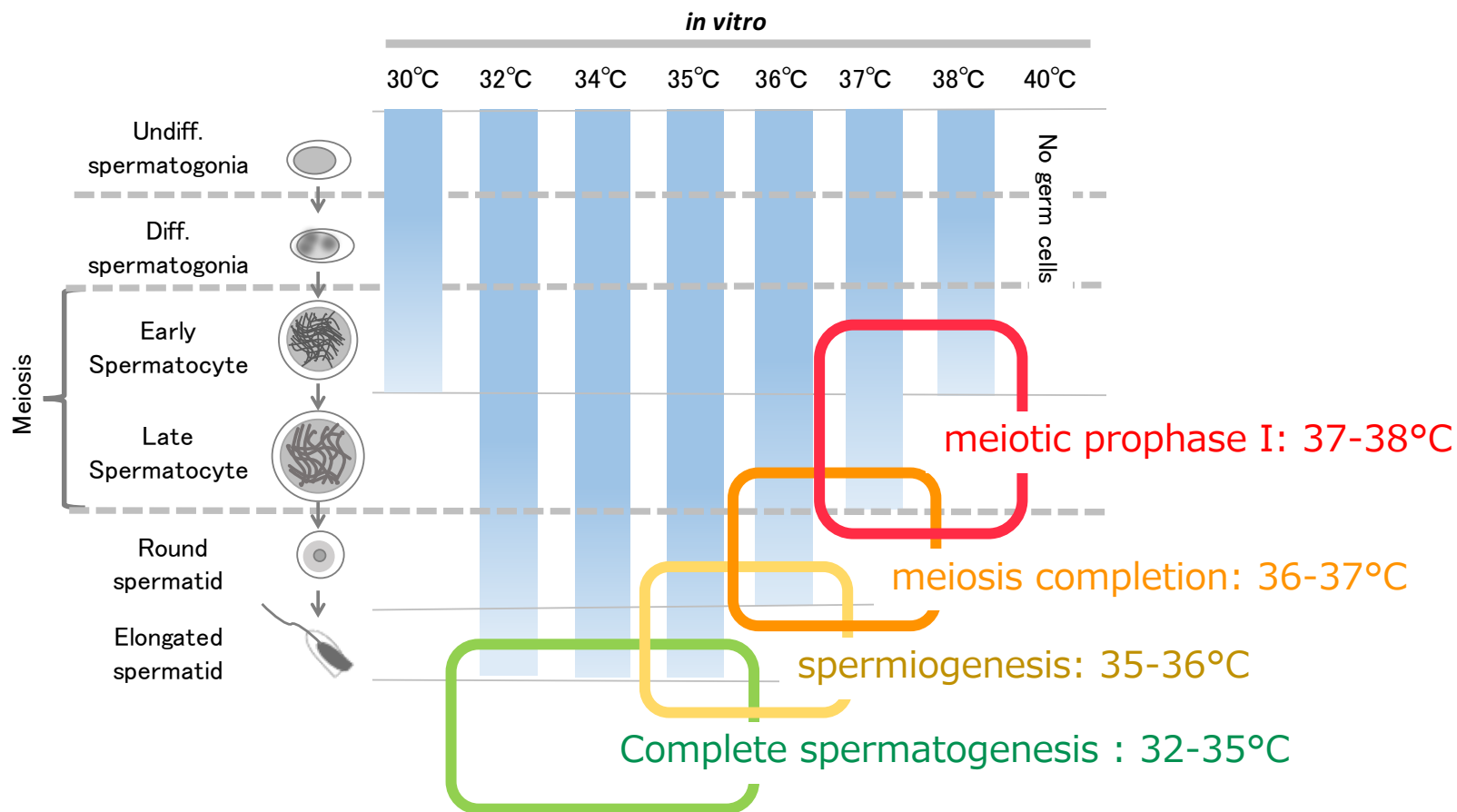
Sato et al. *Nature* 2011

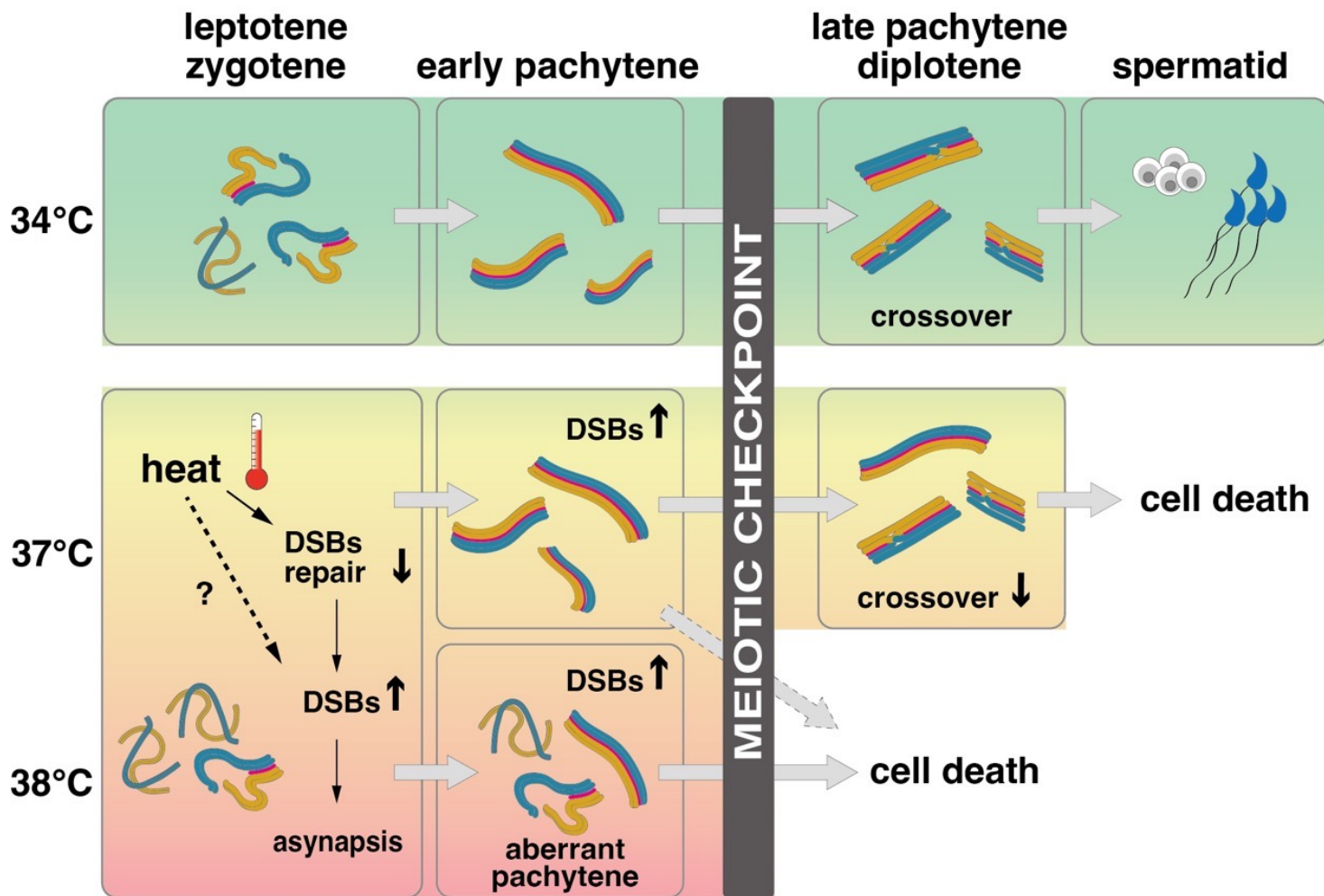
Heat-induced spermatogenesis failure *ex vivo*



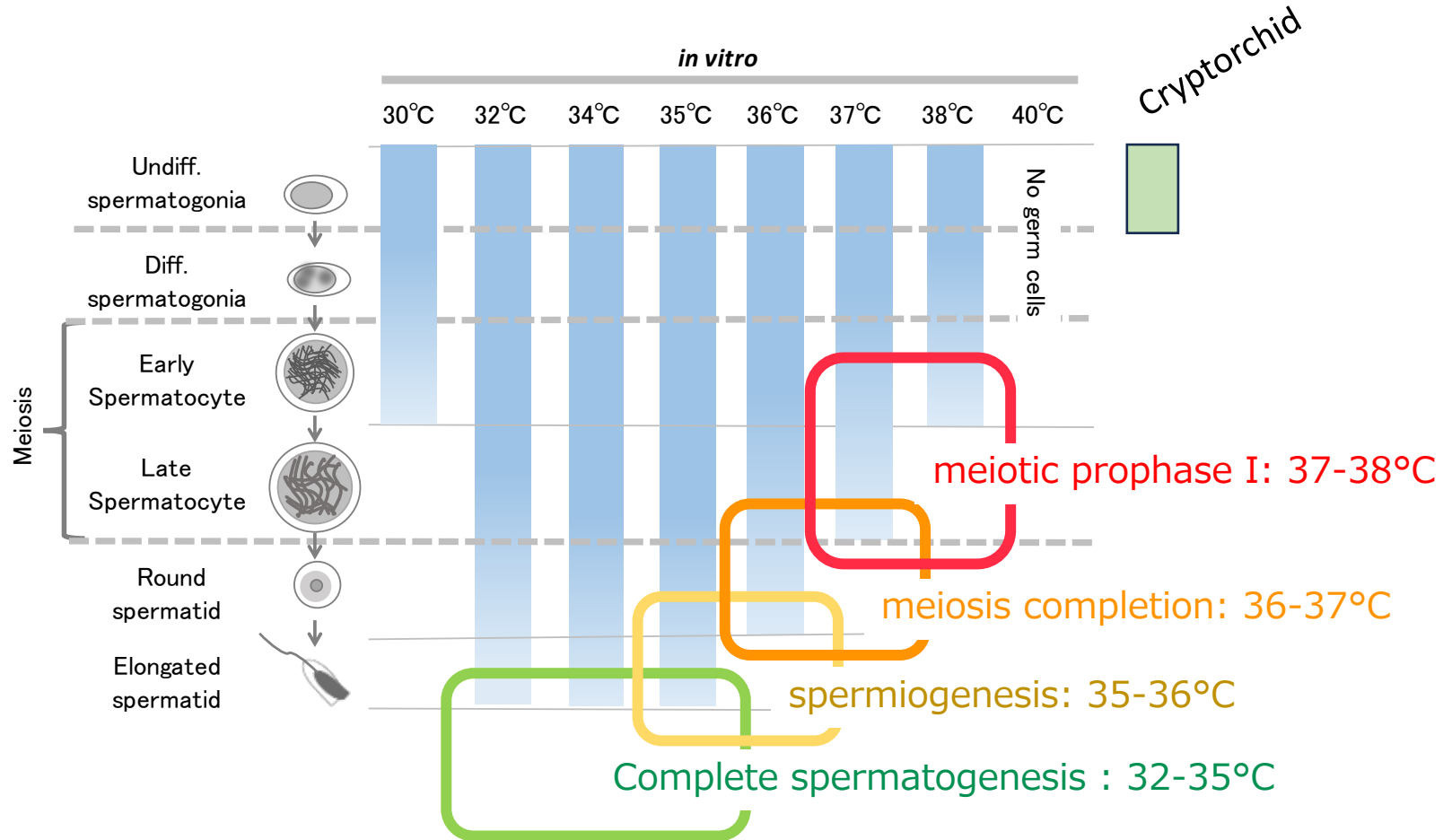


Temperature dependence of spermatogenesis defects





Temperature dependence of spermatogenesis defects

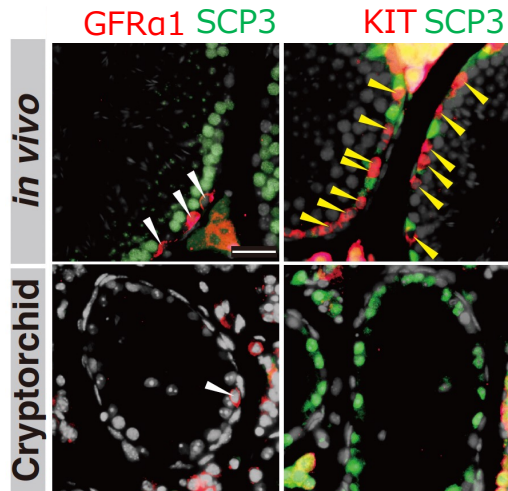


No temperature ex vivo mimics the defect in cryptorchidism.

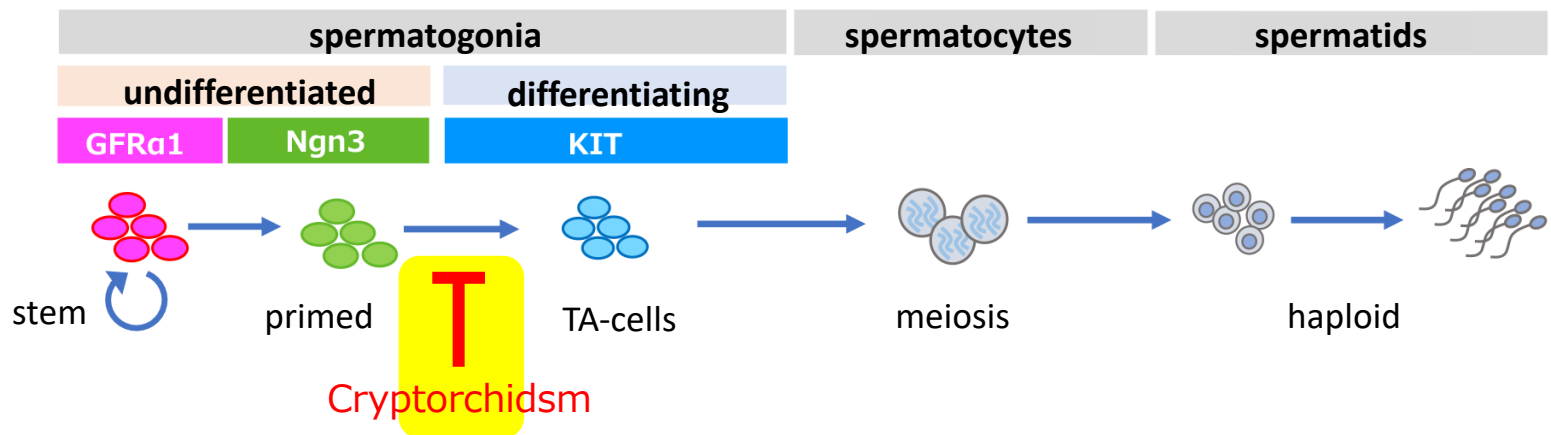
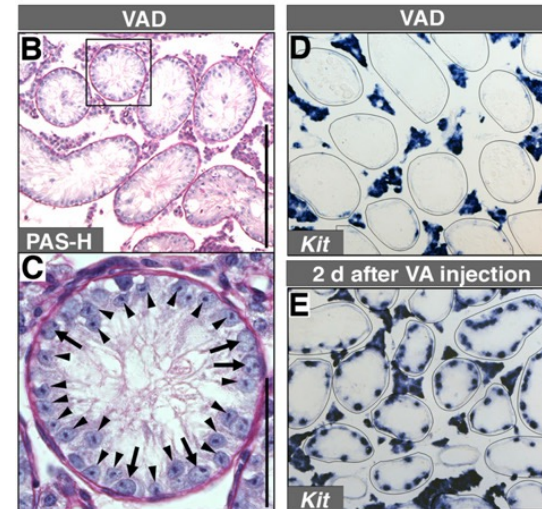
Other mechanisms in addition to high temperature?

Cryptorchidism and Vitamin A deficiency

Cryptorchid testis

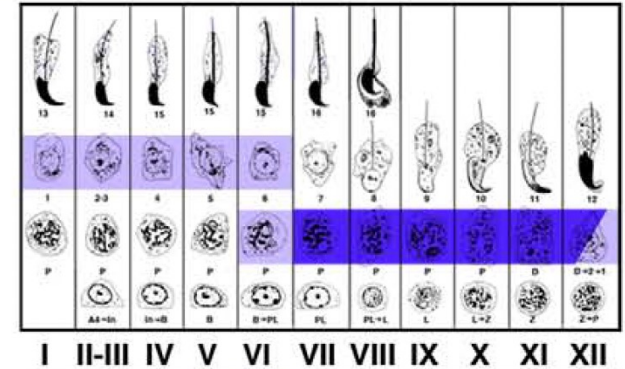
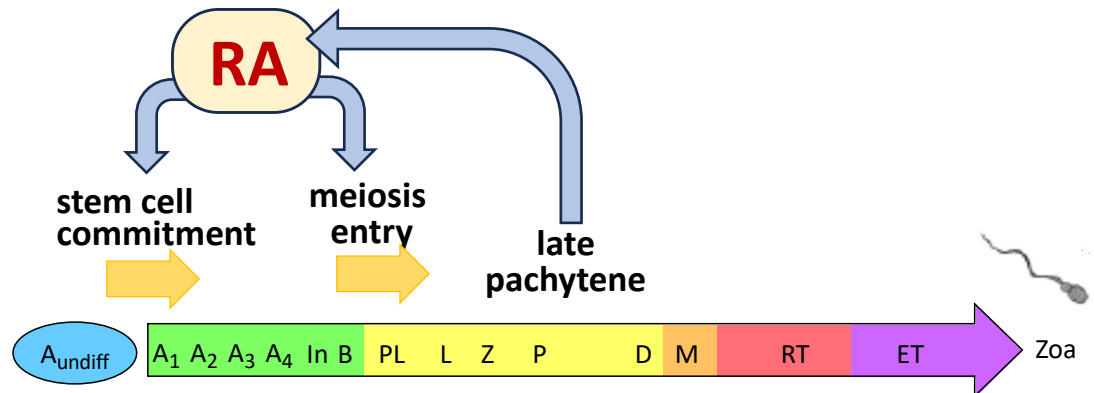
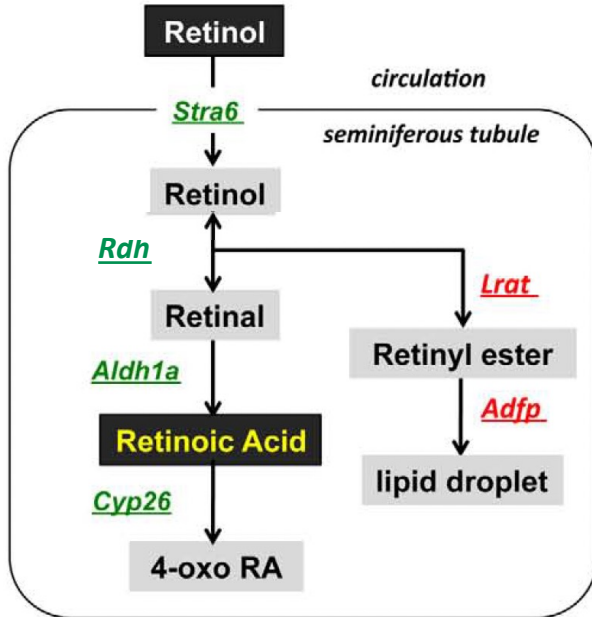


Vitamin A deficiency

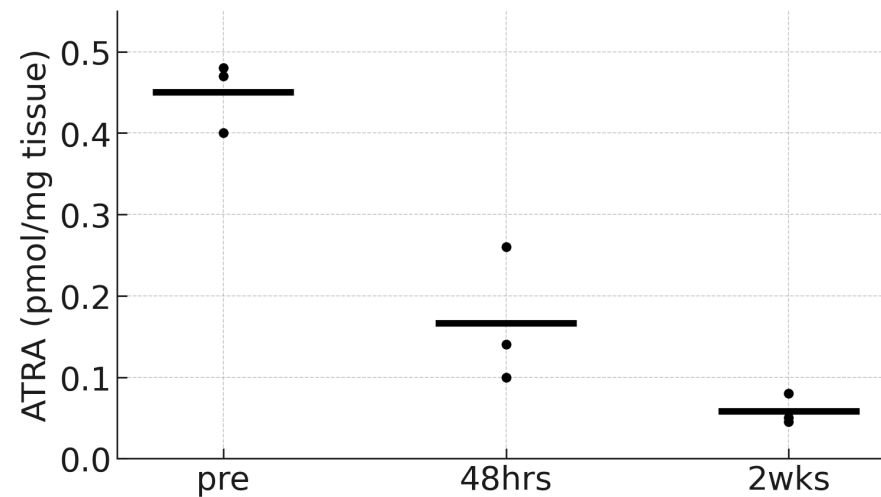
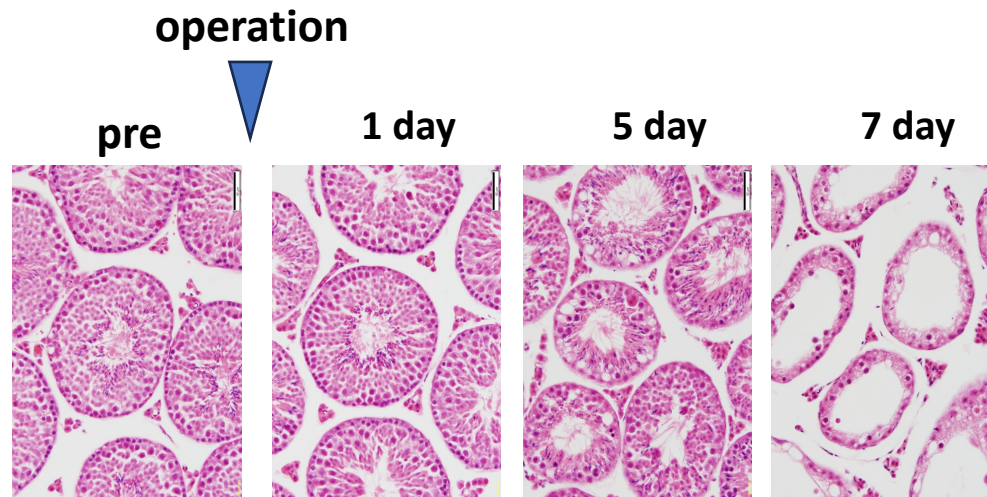


**Vitamin A deficiency =
RA signal suppression**

Retinoic acid and spermatogenesis

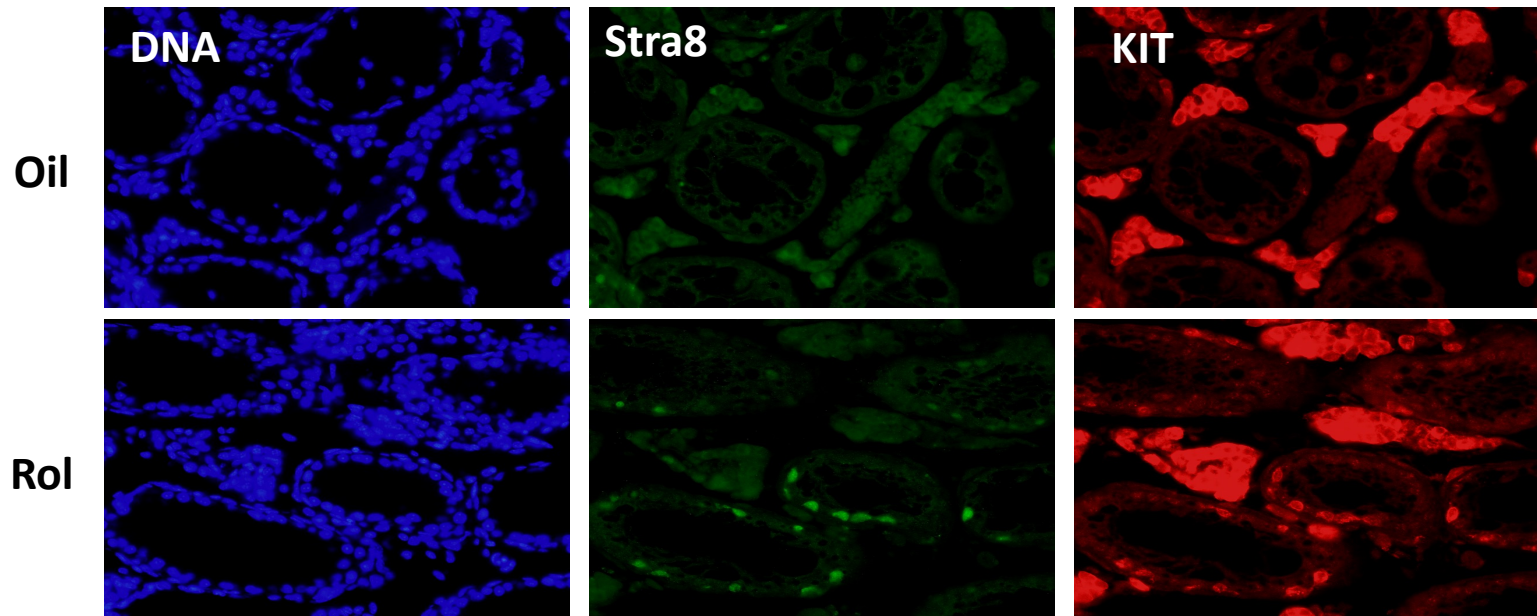


Post-operation changes in RA content



RA activation in cryptorchid mice

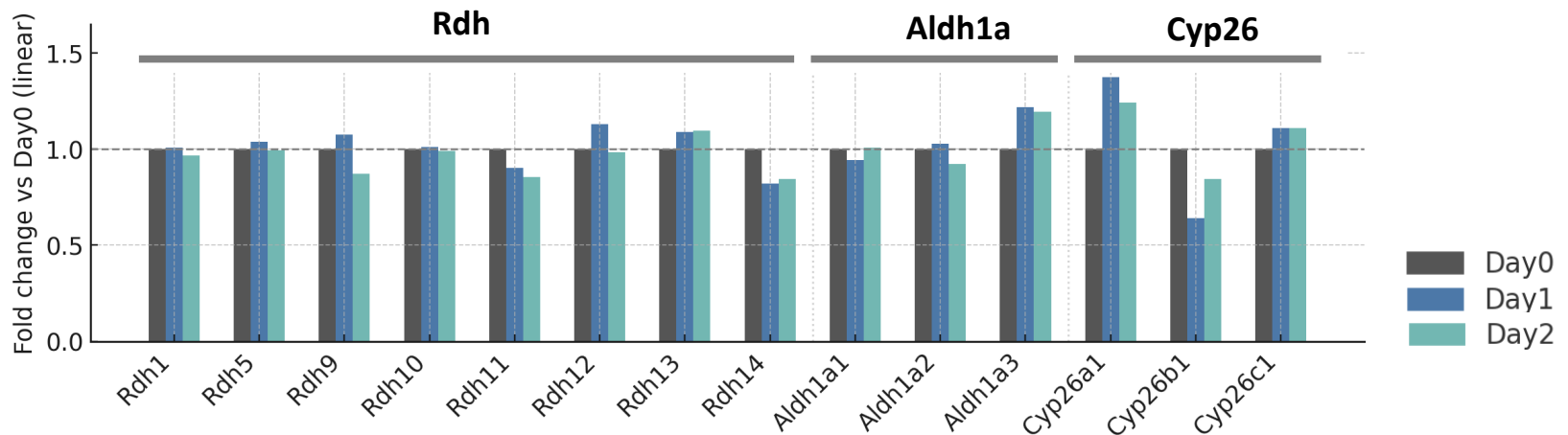
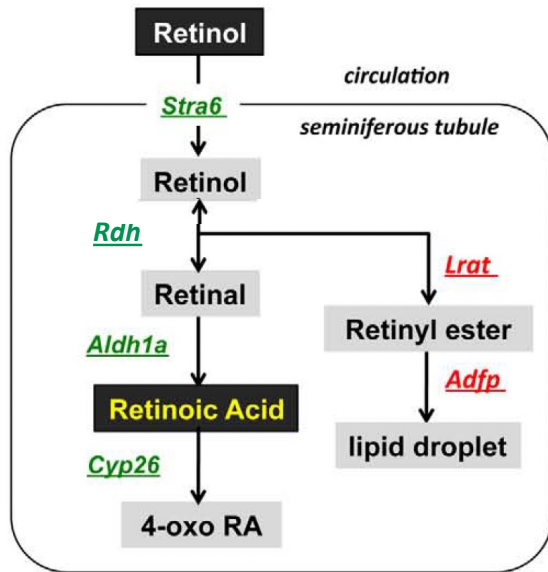
Cryptorchid (8 wo) → Vitamin A injection



Stem cell commitment (Kit⁻ to Kit⁺) can be induced by RA in cryptorchid testis

Commitment defect is not due to high temperature, but RA signal suppression

Enzyme RNA expression after operation



Take home message

- Multiple steps of spermatogenesis can be affected by “body temperature”
- Meiosis is affected by high temperature, through DSB repair impairment and asynapsis
- Damaged spermatocytes are eliminated by meiotic checkpoint
- Retinoic acid level is decreased in cryptorchid testis
- RA signal activation restores stem cell commitment in cryptorchid testis

Contributors

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NBRP Qual

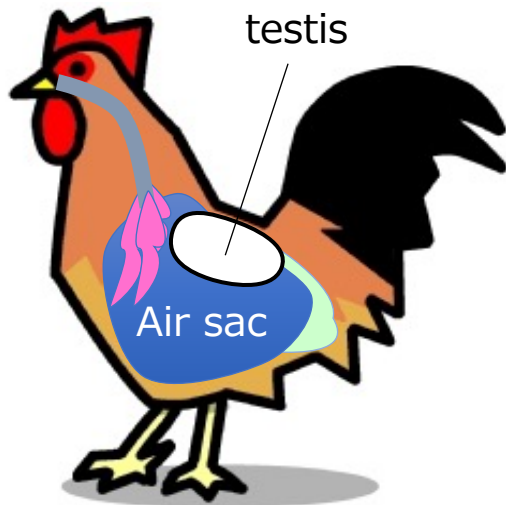
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Birds have testes in the abdomen



body core : 42 °C

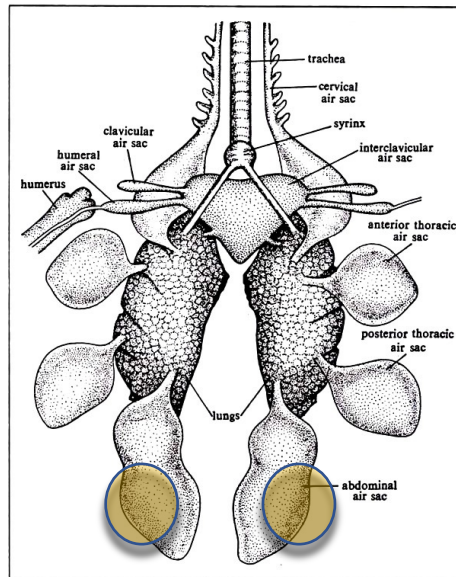
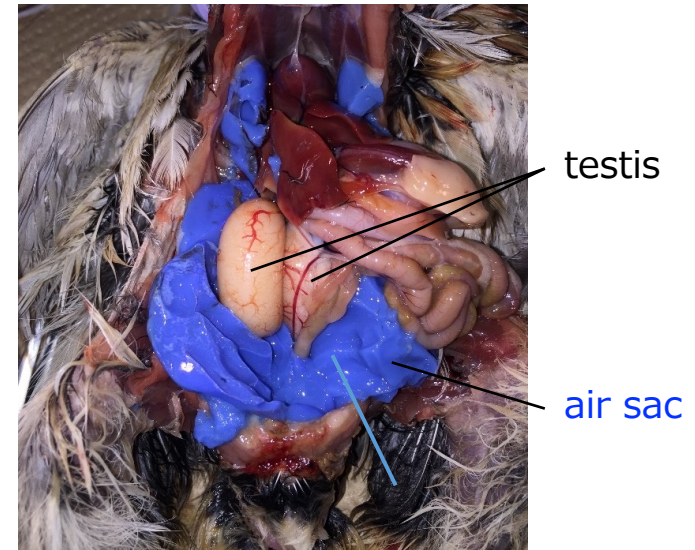
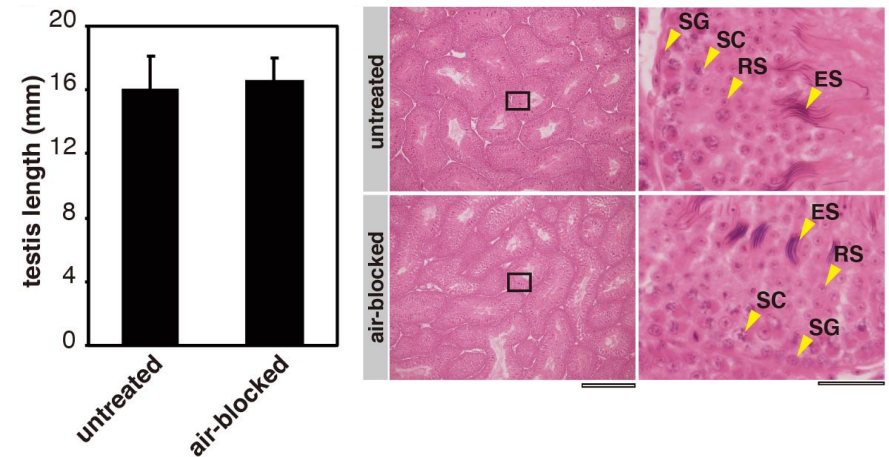
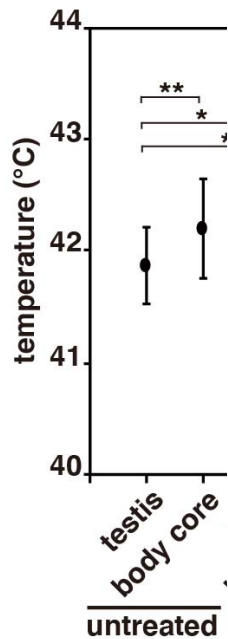


Fig. 9.18 : Air-sacs of Columba. Note that the diagram is schematic.



Are birds' testes cooled, and how much?
Are birds' spermatogenesis damaged by heat?

Air sacs cool the quail testes by 0.3°C



But, spermatogenesis progress at 42°C

Hypothesis

Ancestral amniotes



Spermatogenesis undergoing at low temperature

Mammalian



Avian



Gain of endothermy

Testis-cooling machinery

scrotum, gubernaculum, counter-current
陰囊 精巢導帶 对向流

Unknown mechanisms
of adaptation

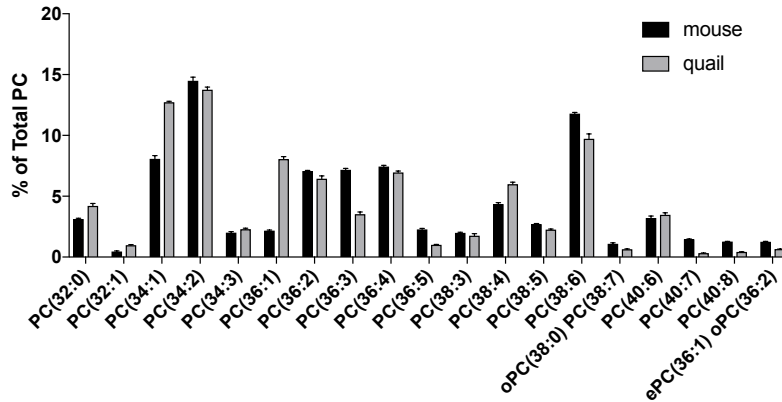
Meiotic checkpoint

Only sperm developed under
low temperatures fertilize

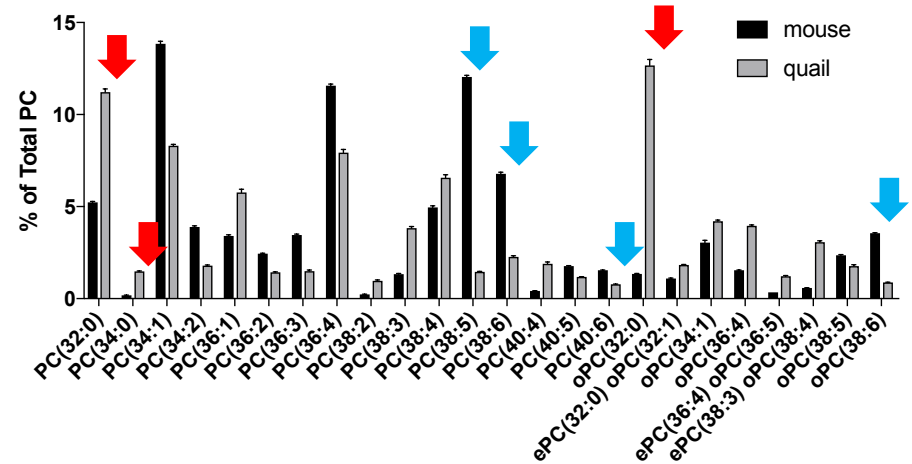
Spermatogenesis undergoing
at high temperature

Fatty acid contents in phospholipids

liver



testis



mouse
32°C

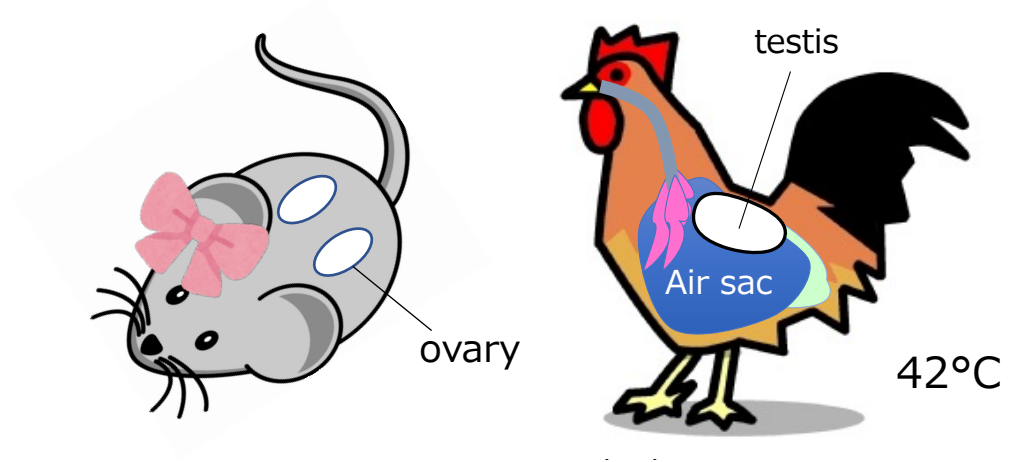


quail
42°C

Linear (saturated) fatty acids

Highly unsaturated fatty acids

Future questions



- What is the molecular mechanism of heat sensitivity?
 - Why can female meiosis progress in high temperature?
 - Why can avian spermatogenesis progress in high temperature?

