

Inactivation of *Cops5* in smooth muscle cells causes abnormal reproductive hormone homeostasis and development in mice

Qian Huang^{1,2}, Yonghong Man², Wei Li², Qi Zhou^{1,2}, Shuo Yuan^{1,2}, Yi Tian Yap², Neha Nayak², Ling Zhang¹, Shizheng Song¹, Joseph Dunbar², Todd Leff³, Xu Yang⁴, Zhibing Zhang^{2,5}
 1. School of Public Health, Wuhan University of Science and Technology, Wuhan, Hubei, 430060, China; 2. Department of Physiology, Wayne State University, Detroit, MI, USA;
 3. Department of Pathology, Wayne State University, Detroit, MI, USA; 4. U Arthroplasty Research Laboratory, Hospital for Special Surgery, New York, NY, USA;
 5. Department of Obstetrics and Gynecology, Wayne State University, Detroit, MI, USA.

1. Introduction & Objective

- Spermatogenesis is a complex process that requires somatic cells to support germ cell development.
- COPS5 is a protein ubiquitously expressed *in vivo*. Global disruption of *Cops5* in mice resulted in embryonic lethality.
- Germ-cell specific disruption of *Cops5* caused severe defect spermatogenesis.
- The objective of this study is to investigate the role of COPS5 in the smooth muscle cells (SMC) in the testis.

2. Methods

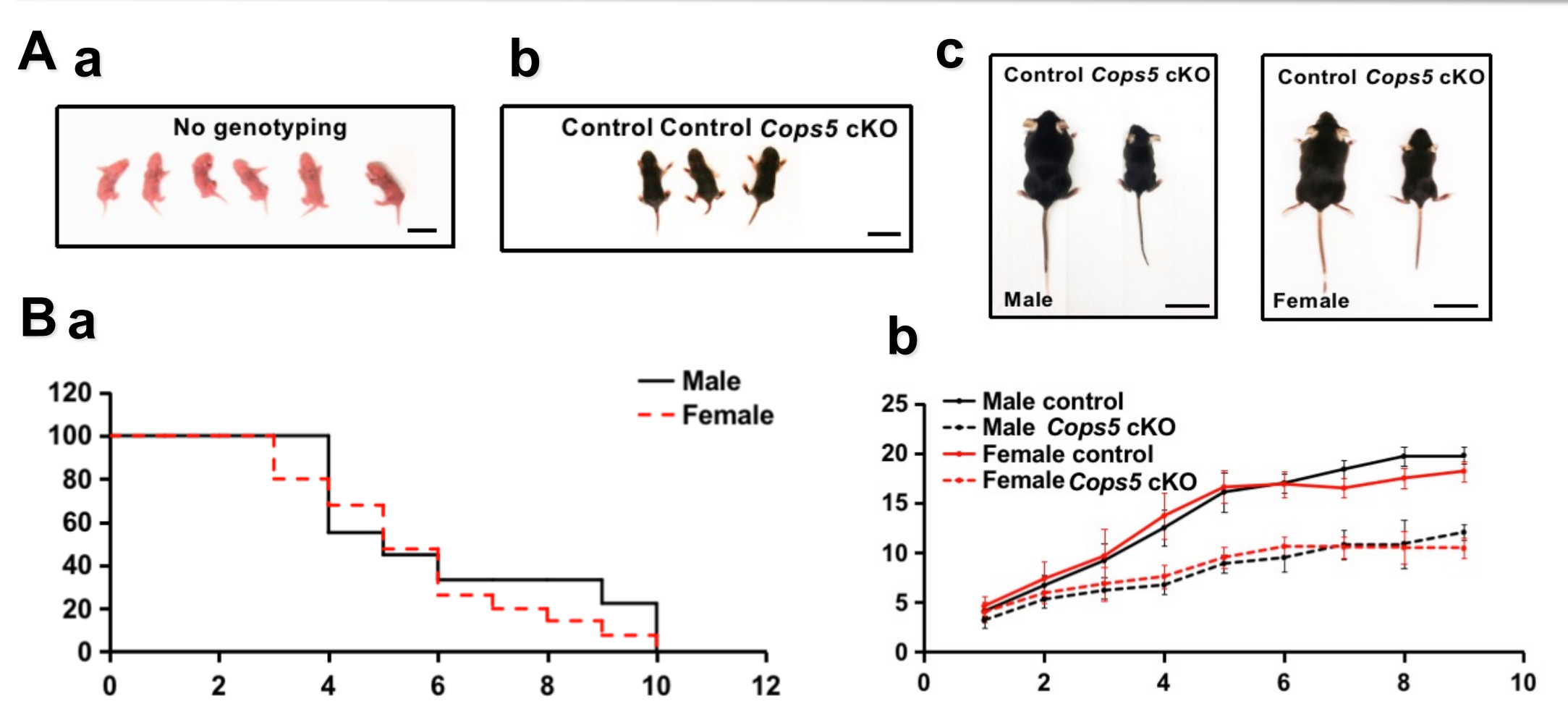
The *Myh11*-iCre (myosin heavy chain 11) mice used to study gene functions in SMC were crossed to the floxed *Cops5* mice.

3. Keywords

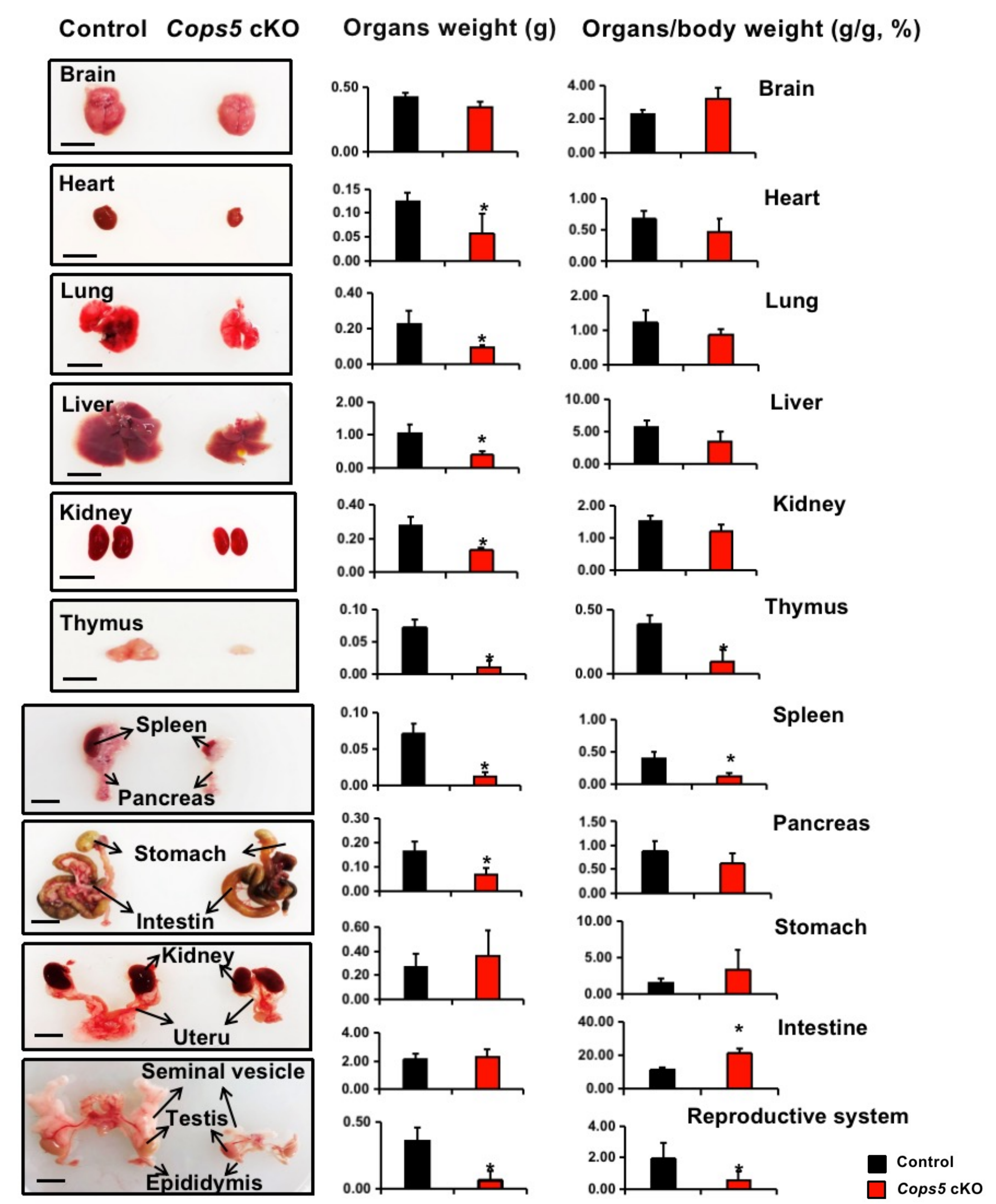
COPS5; Smooth muscle cells; Endocrine system

4. Results

***Cops5* cKO mice exhibited significant growth retardation and early death**



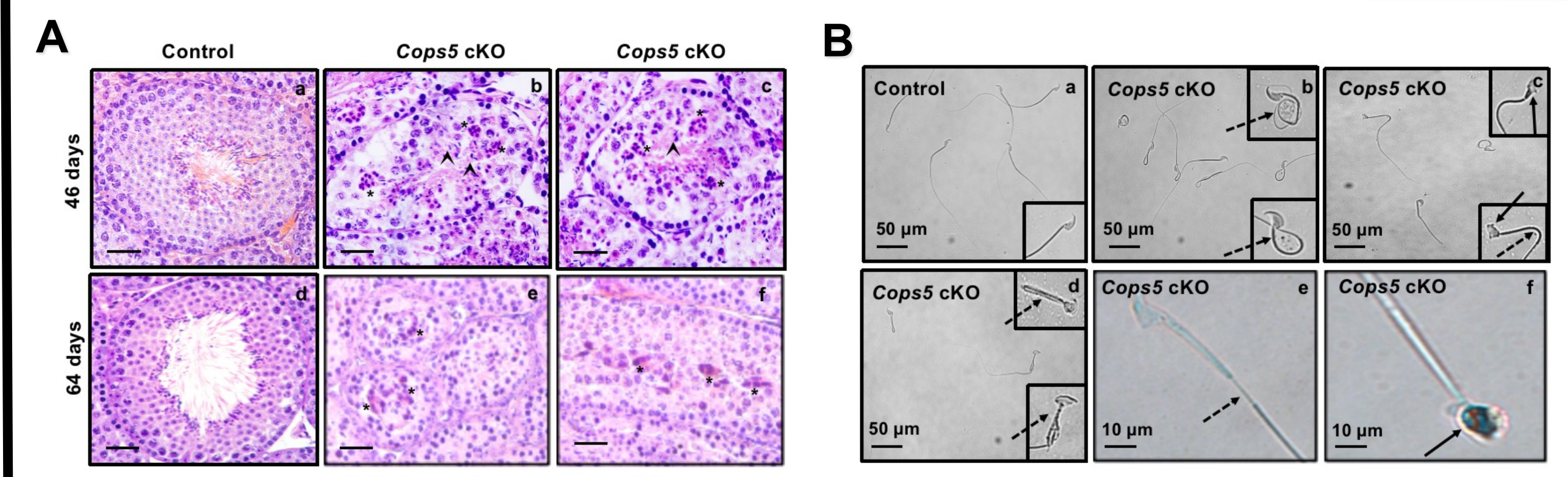
Development of selective organs, especially the reproductive organs was dramatically affected in the *Cops5* cKO mice



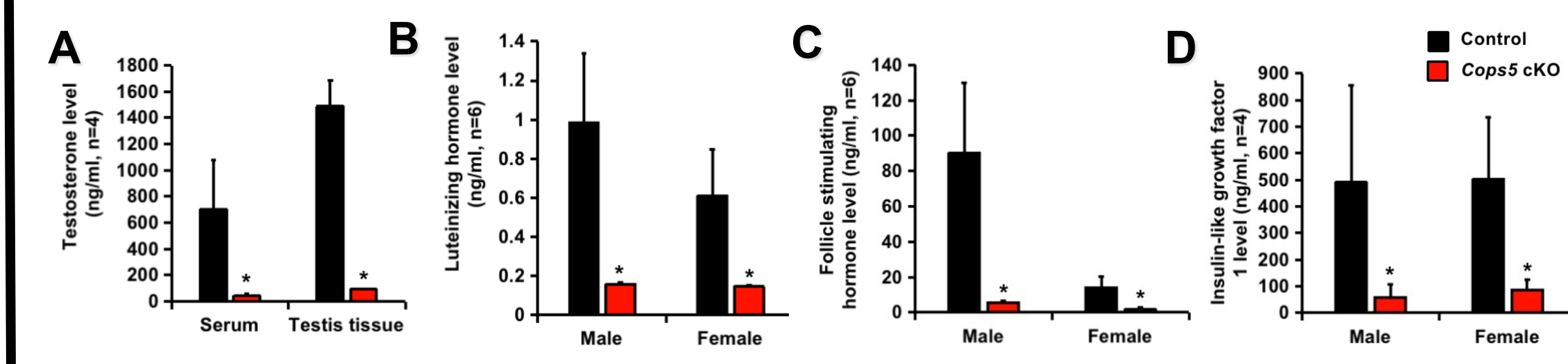
Fertility was reduced in *Cops5* cKO mice that survived to sexual maturity

Genotype	Male fertility (2 week < age)	Vaginal plugs (n=4)	Average litter size (n=4)	Female fertility (2 week < age)	Vaginal plugs (n=5)	Average litter size (n=5)
Control	4/4	4/4	9.00 ± 1.60	5/5	5/5	7.80 ± 0.96
<i>Cops5</i> cKO	0/4	0/4	0*	0/5	5/5	0*

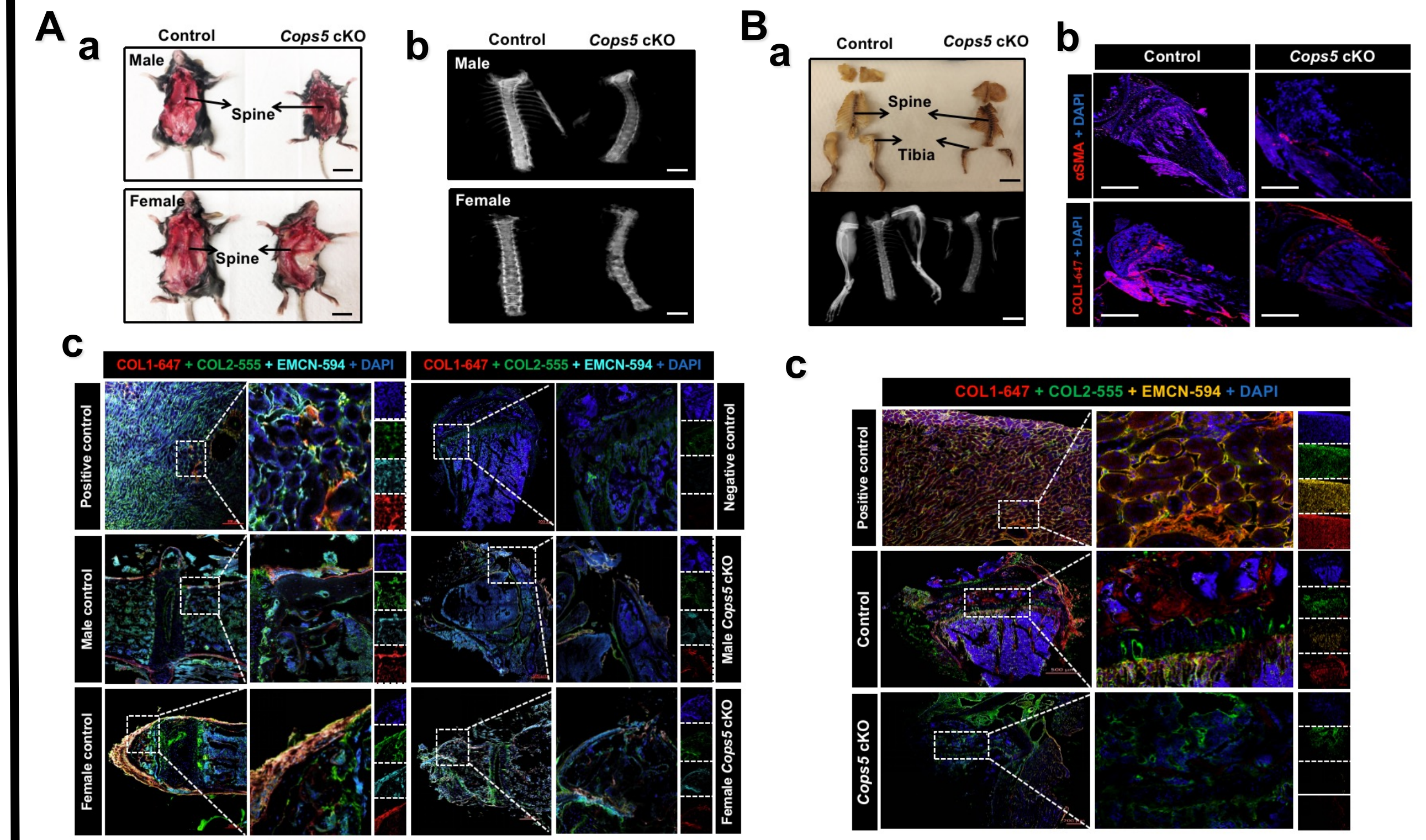
Spermatogenesis was abnormal in the *Cops5* cKO males that survived to sexual maturation



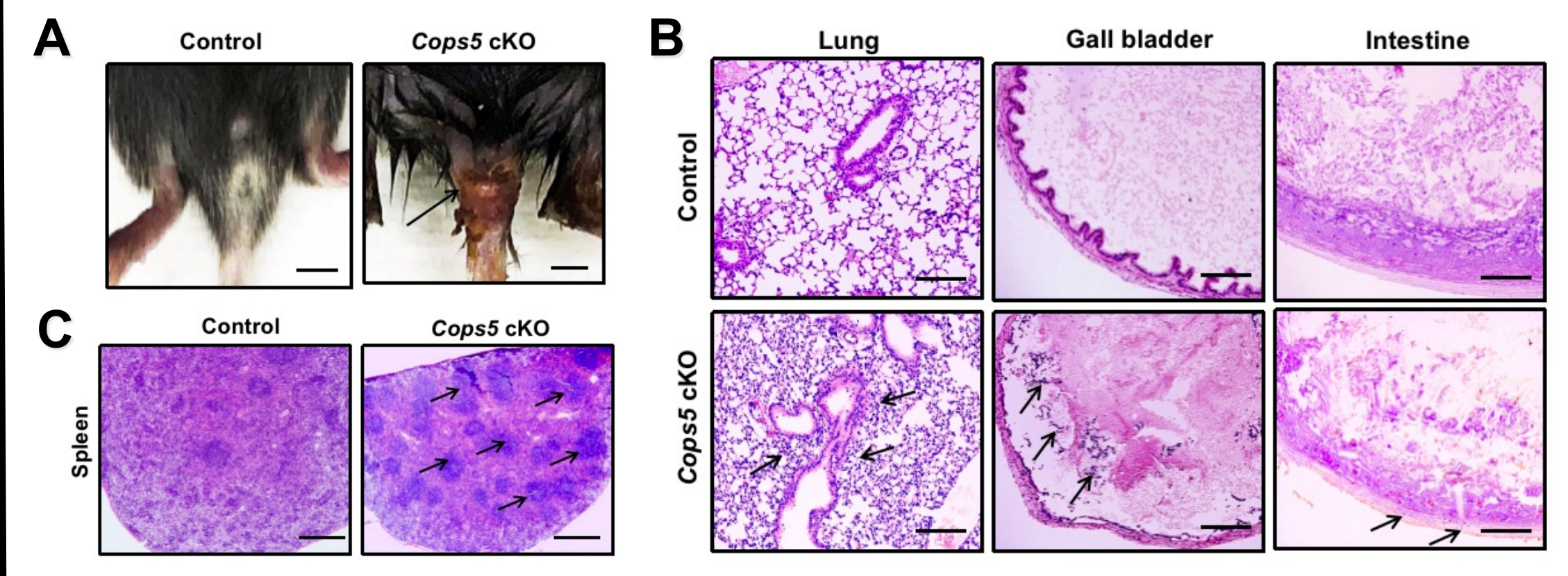
Sex hormone levels were dramatically reduced in the *Cops5* cKO mice



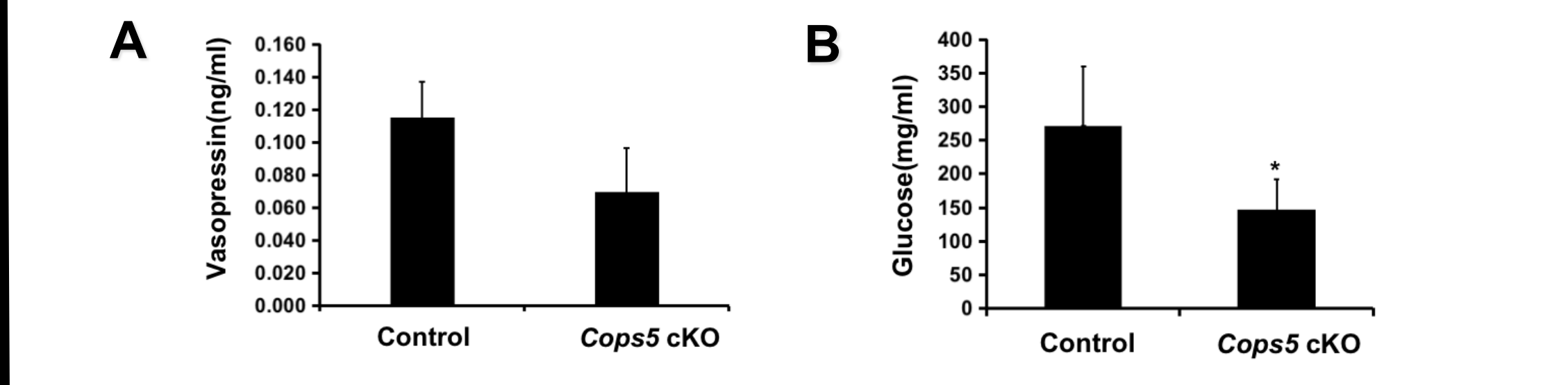
Cops5 cKO mice exhibited impaired skeletal development



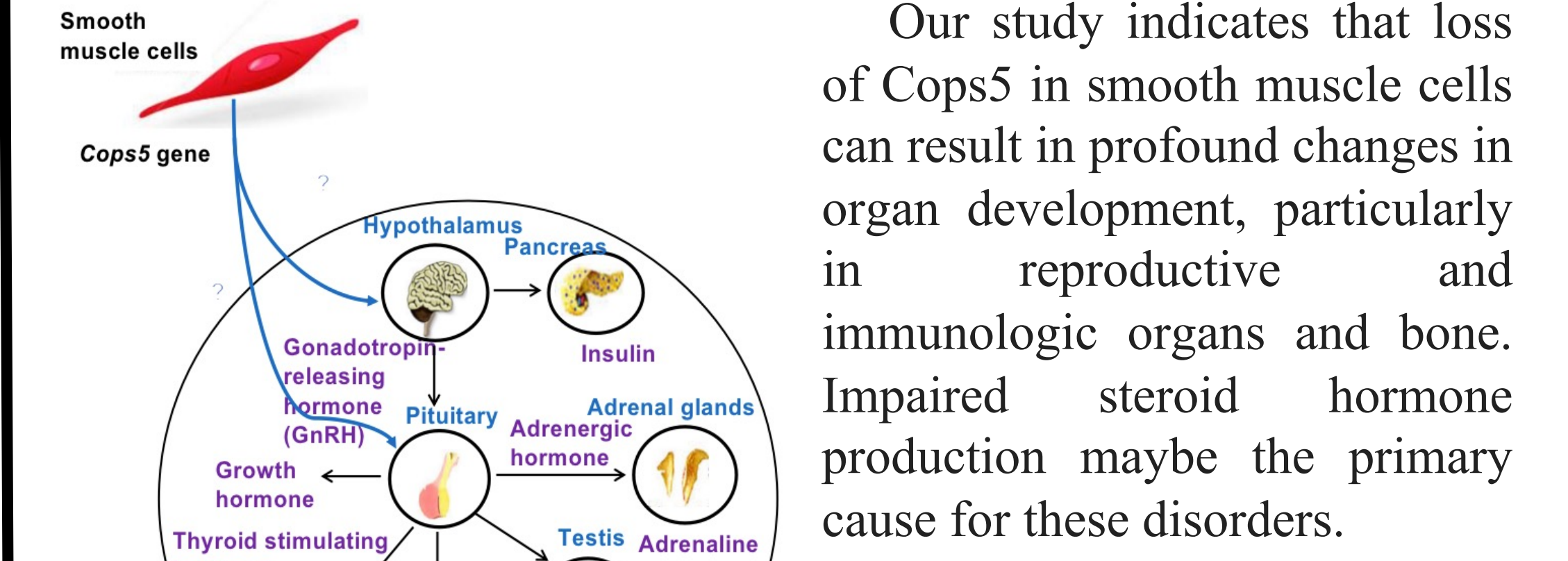
Infection risk was increased in the *Cops5* cKO mice



Level of serum glucose but not vasopressin was reduced in the *Cops5* cKO mice



5. Summary



6. Conference

The 46th Annual Meeting of American Society of Andrology, April 21-26, 2021, La Jolla, CA, USA.