A Mouse Model to Investigate the Reproductive Consequences of Testosterone Administration After Suppressing Puberty in Transgender Boys

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INTRODUCTION

- It is estimated that there are 150,000 transgender adolescents (aged 13-17 years) individuals in the United States, representing up to 2.7% of high school aged

- The cross-sex therapy in transmasculine adolescents begins with peripubertal gonadotropin-releasing hormone agonist (**GnRHa**) to **suppress** endogenous **puberty** followed by **testosterone** (T) treatment to induce pubertal progression consistent with the adolescent's **gender identity**

- Besides that, the **consequences** of **pausing** normal female **puberty** followed by a **T** treatment on **late fertility** is **unknown**.

Aim: To develop a translational mouse model investigate the reproductive consequences of T administration following pubertal suppression with GnRHa, mimicking hormone therapy in peripubertal transmasculine adolescents

METHODS

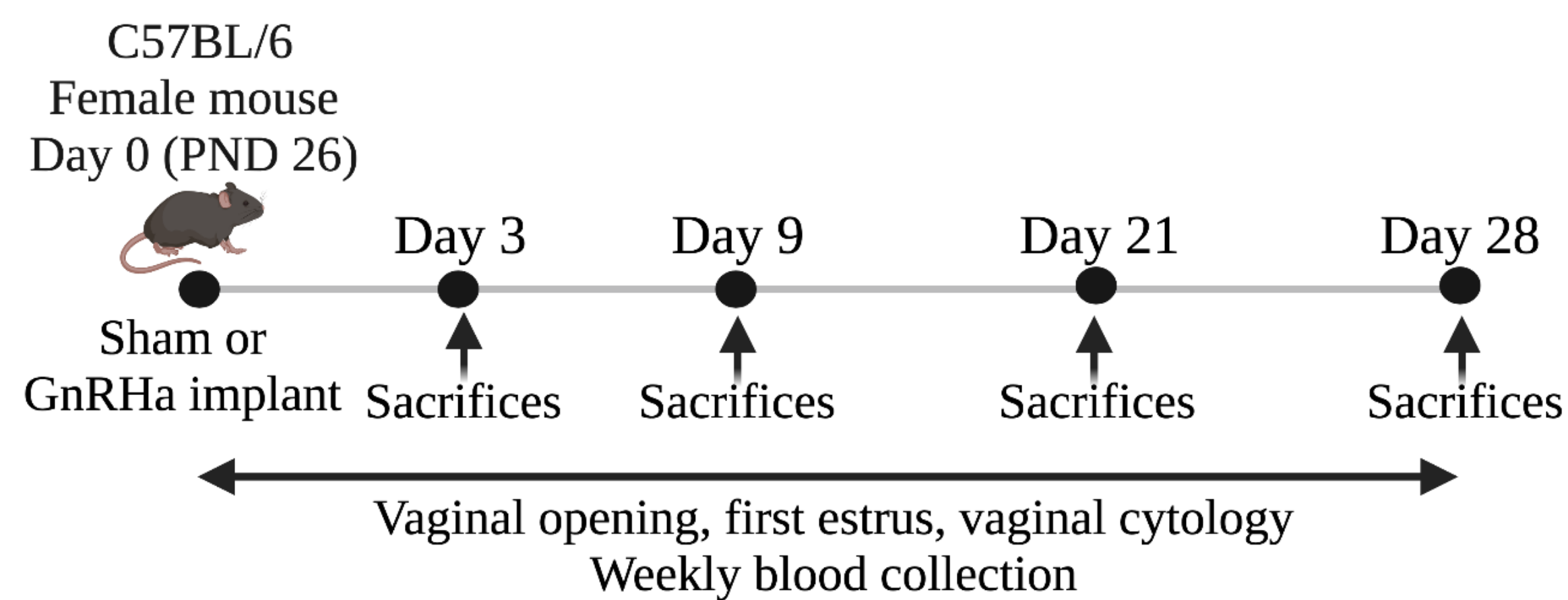### Experiment 1: Pubertal Suppression using a GnRH agonist

Figure 1. Experimental design

- Female mice (n=7 mice/group) were sc implanted with GnRHa (Goserelin acetate implant 3.6mg) or underwent sham surgery on PND 26

- Data collected: Body weight (BW), uterus mass, and paired ovaries weights. Lefty ovary was harvested for histology to assess corpora lutea (CL) counting. Terminal blood was collected to assess LH, FSH, and estradiol levels.

Experiment 2: Transmasculine Adolescent Mouse Model: Pubertal Suppression followed by Gender-affirming hormone treatment
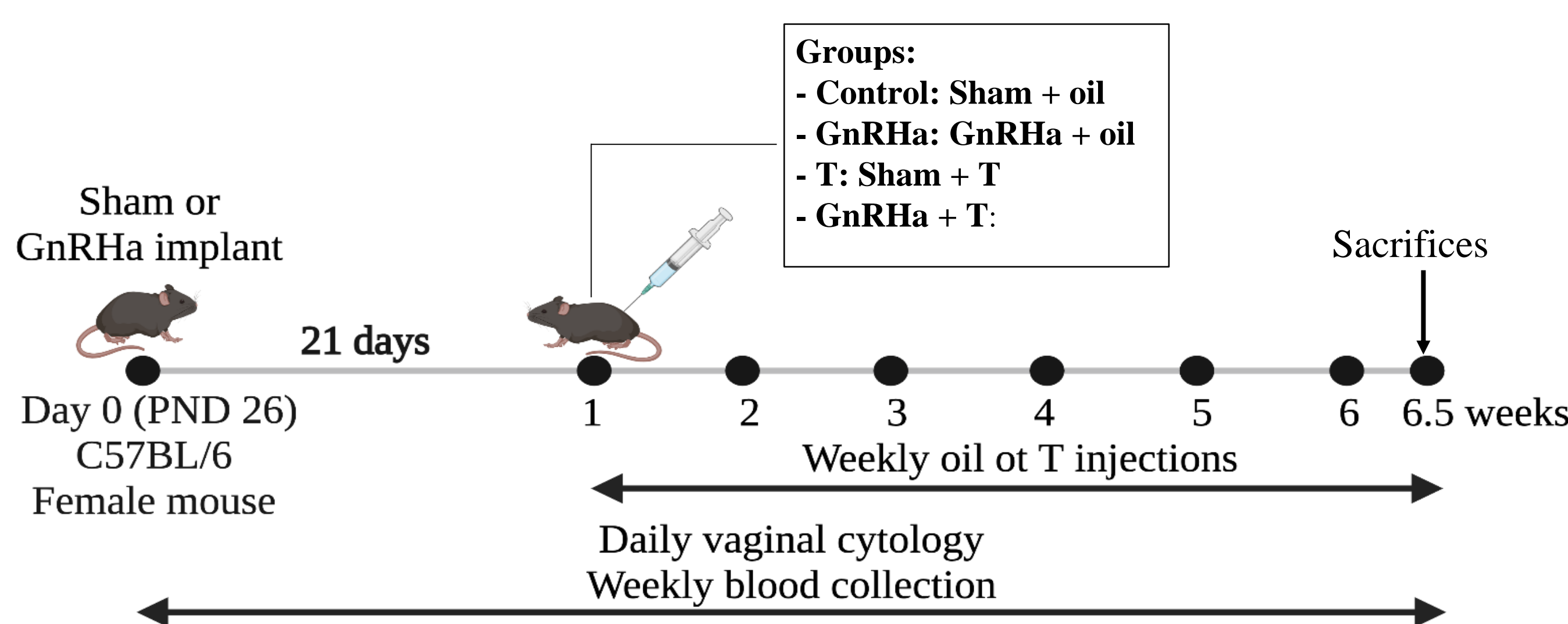

Figure 2. Experimental design

- Female mice (n=7 mice/group)) were sc implanted with GnRHa or underwent sham surgery on PND 26. 21 days after the implanting day, mice received weekly injections of T Enanthate (0.45mg/100µl/sc) Control mice received oil.

- Data collected: BW, uterus mass, and paired ovaries weights. Lefty ovary was harvested for histology to assess follicle counting. Terminal blood was collected to assess T levels

RESULTS

Experiment 1

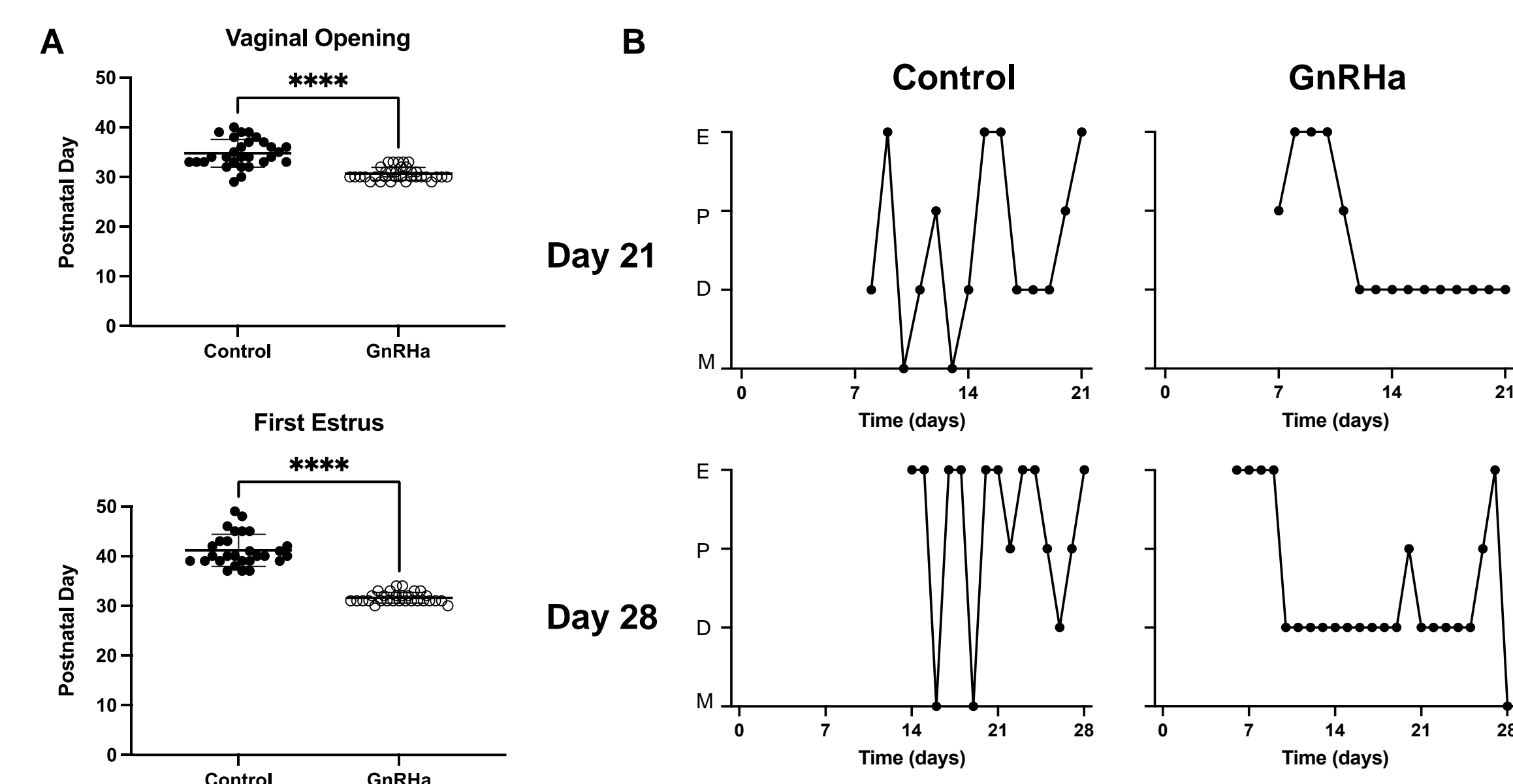**Figure 3. (A)** Day of the vaginal opening; B) Day of the first estrus, and C) Vaginal cytology traces. Data express as Mean ± SD, Student's t-test. ****p<0.001.
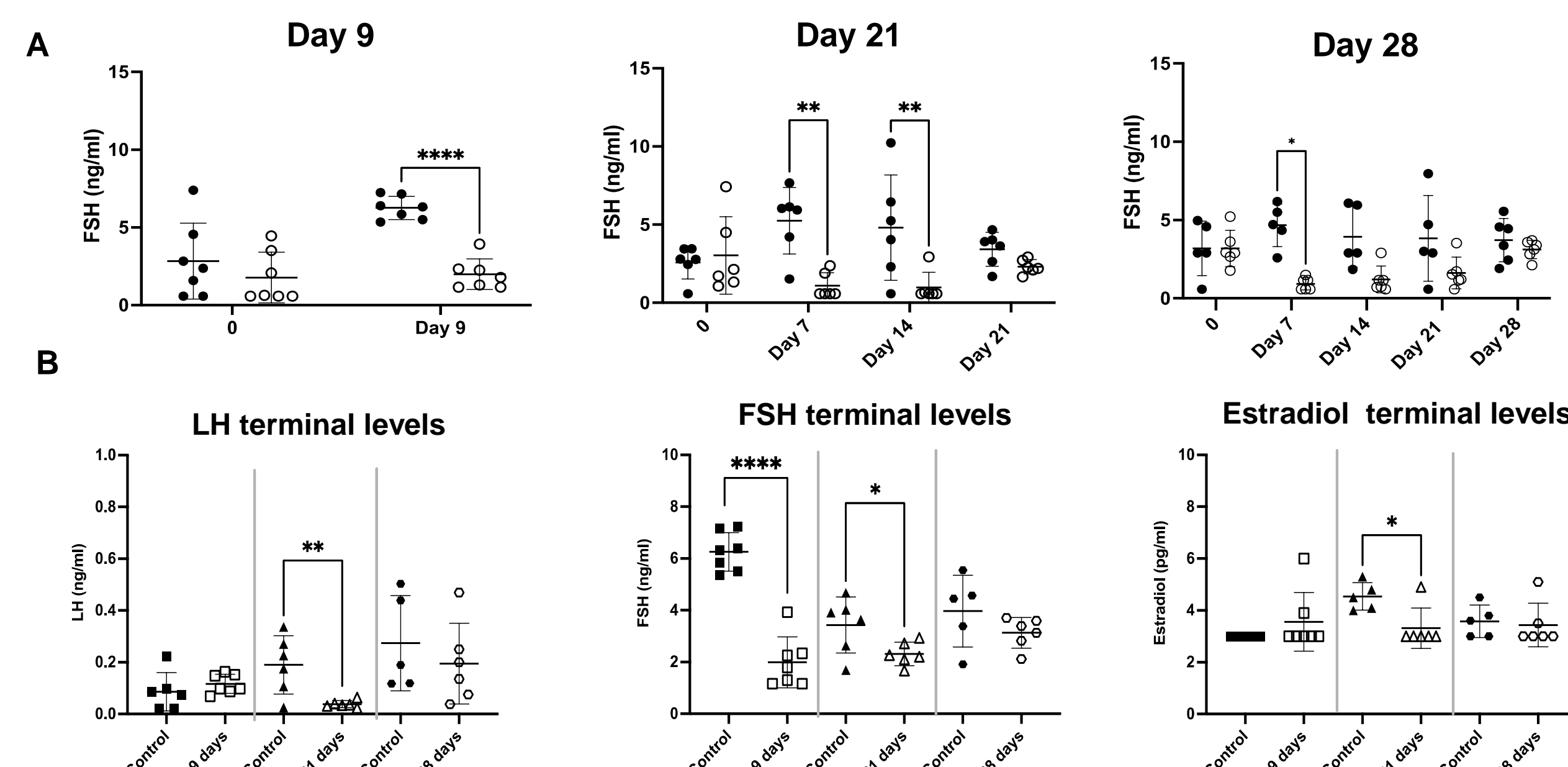

Figure 4. (A) Weekly FSH levels at different timepoints; **(B)** Terminal hormones levels for LH, FSH, and Estradiol. Data express as Mean ± SD, Student's t-test. *p<0.05, **p<0.03, ****p<0.001.
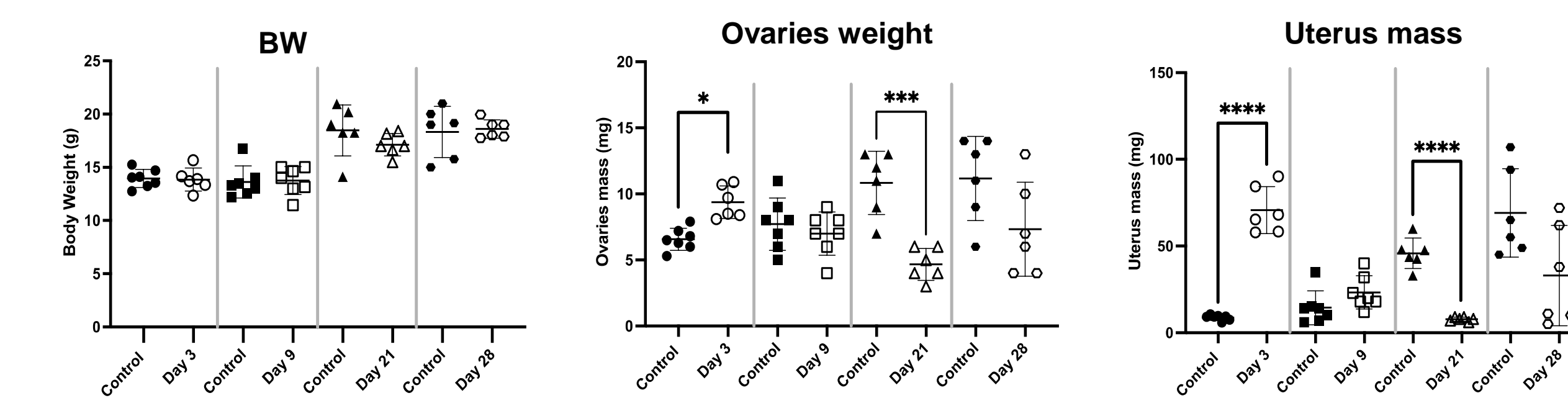

Figure 5. Body measurements. Data express as Mean ± SD, Student's t-test. *p<0.05, ***p<0.01, ****p<0.001.
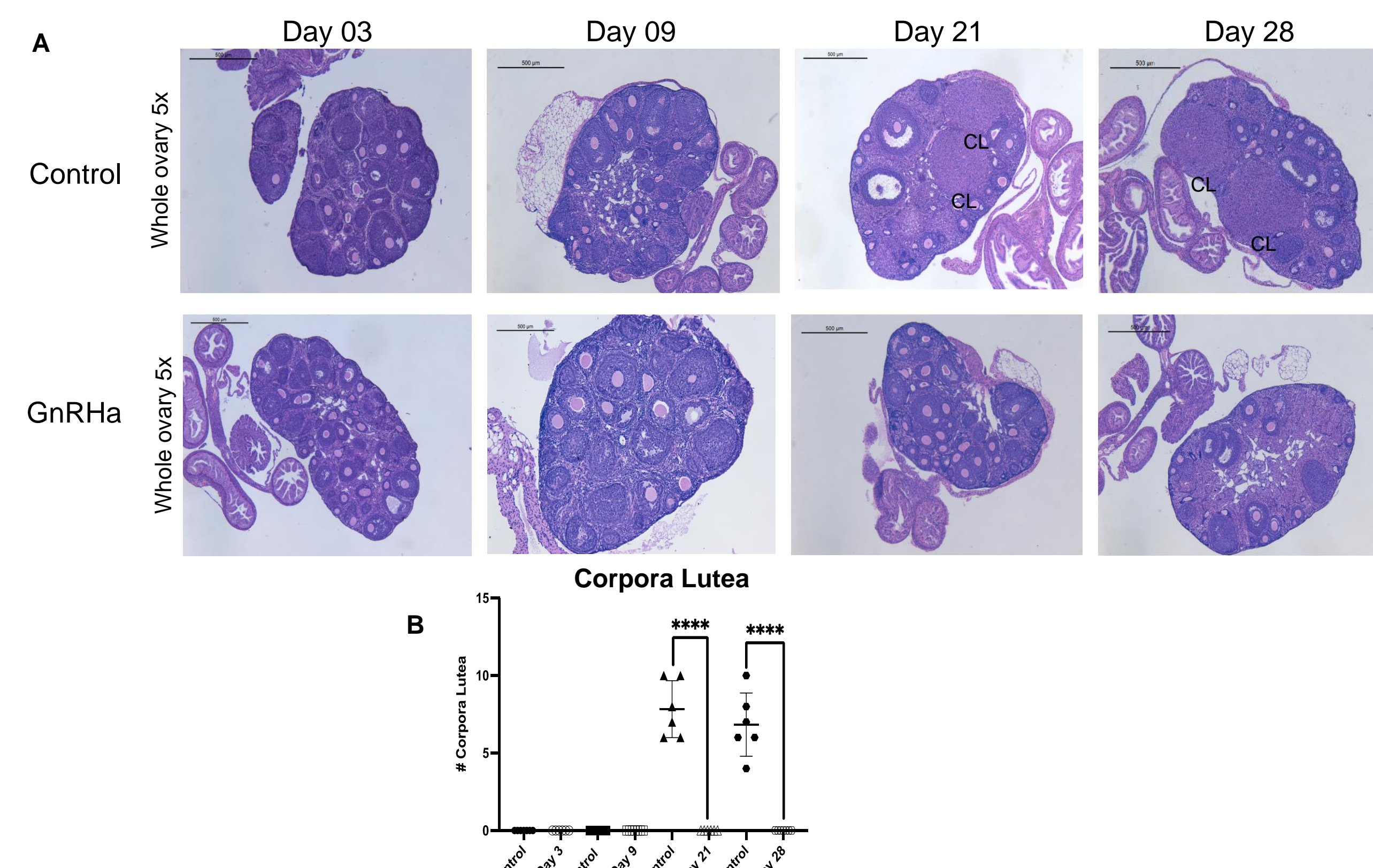

Figure 6. (A) Representative comparison of hematoxylin and eosin stained ovaries **(B)** Corpora lutea counting. Data express as Mean ± SD, Student's t-test. ****p<0.001.
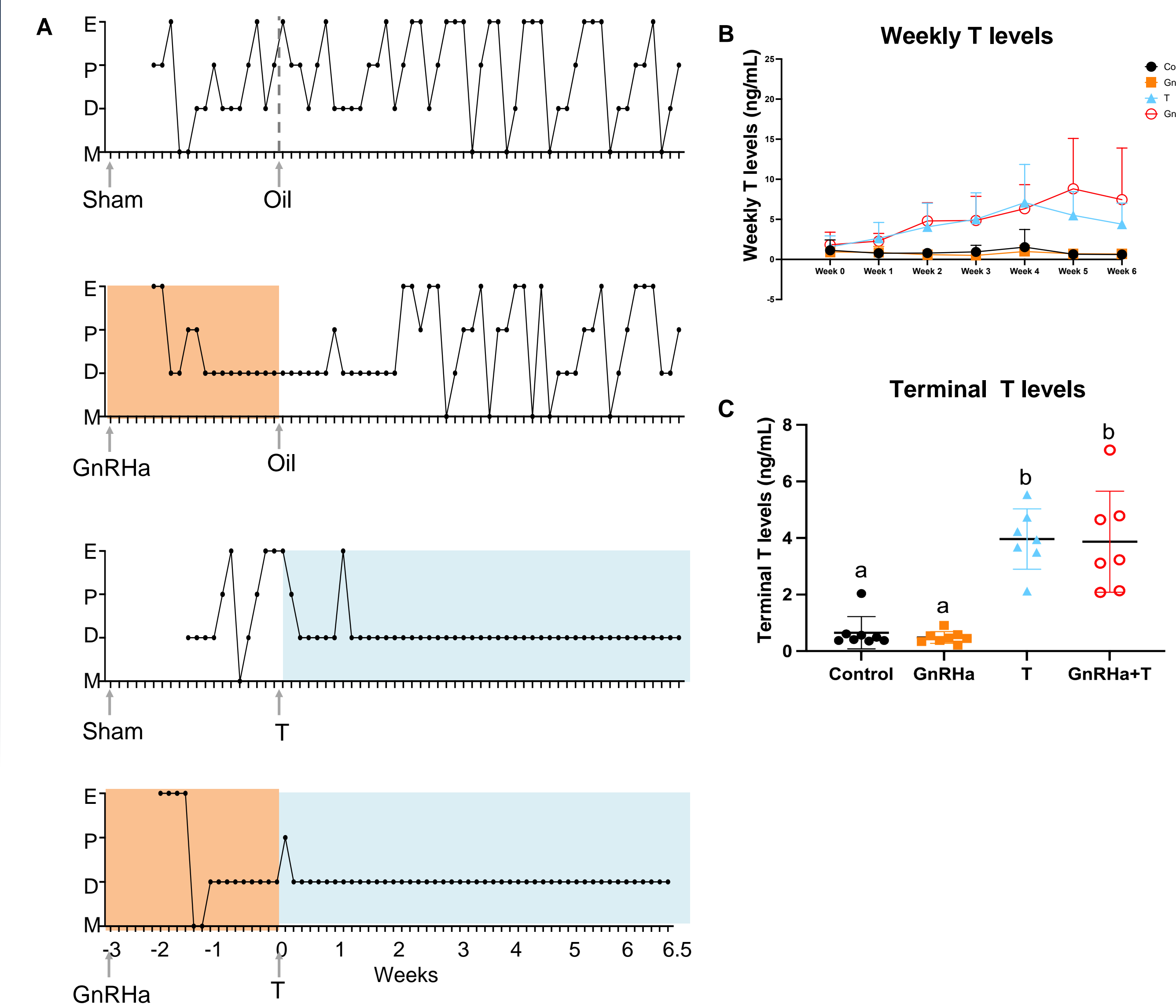
Experiment 2

Figure 7. (A) Vaginal cytology traces. **(B)** Weekly testosterone levels. **(C)** Terminal testosterone levels. Data express as Mean ± SD, ANOVA followed by Tukey test., p<0.05.
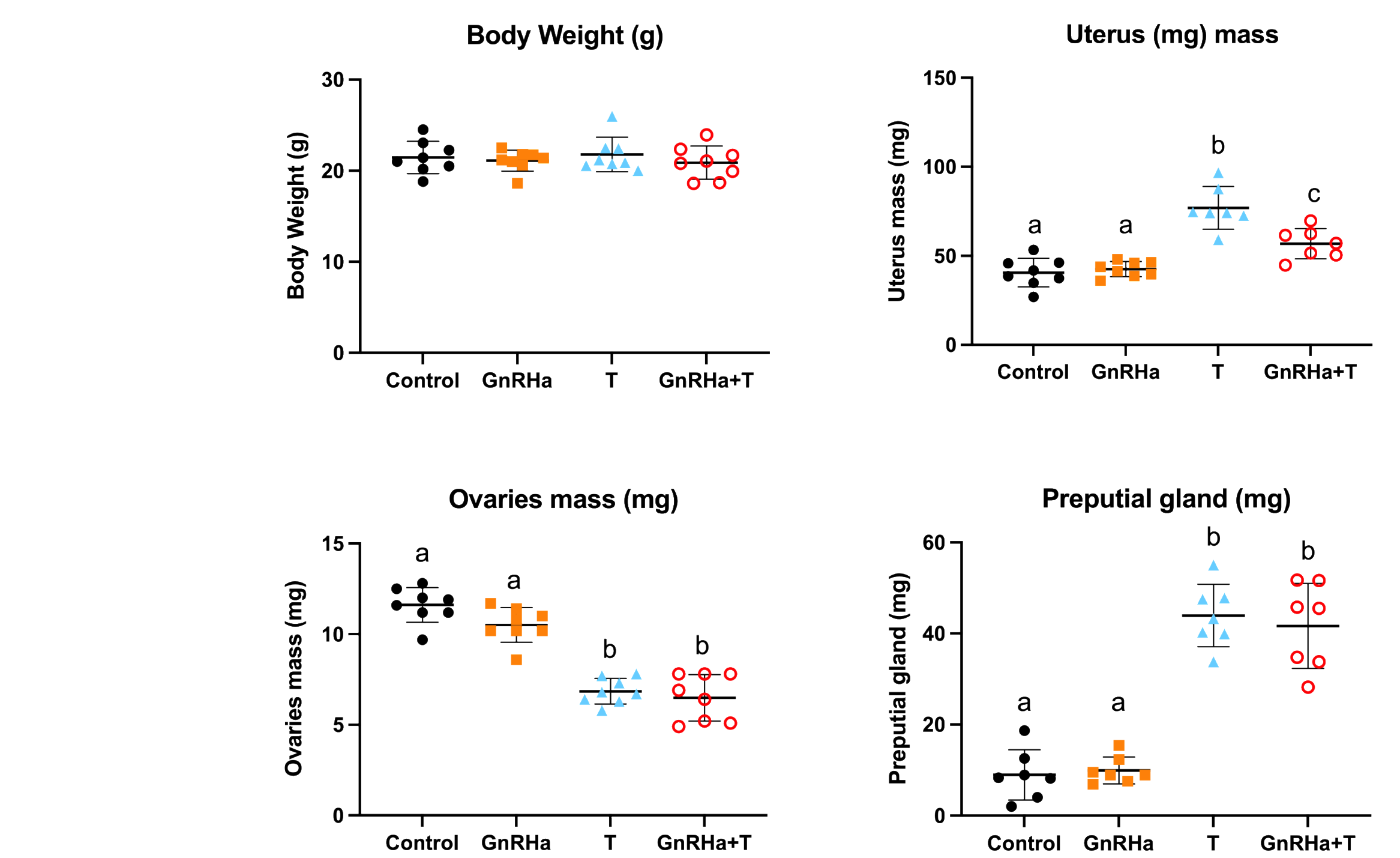

Figure 8. Body measurements. Data express as Mean ± SD, ANOVA followed by Tukey test., p<0.05.
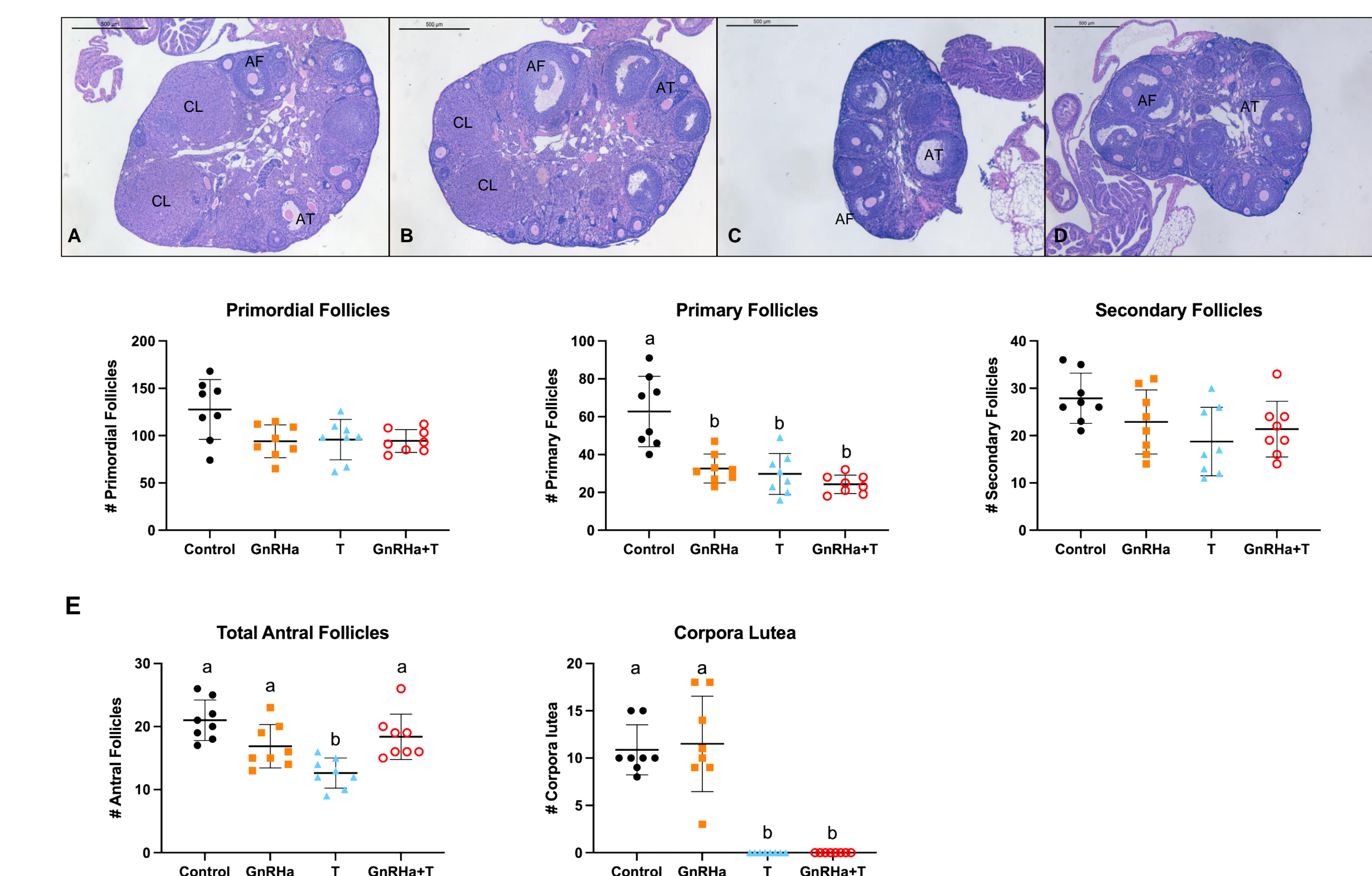

Figure 9. (A-D) Representative comparison of hematoxylin and eosin stained ovaries **(E)** Follicle counting. . Data express as Mean ± SD, ANOVA followed by Tukey test., p<0.05.

CONCLUSIONS

These preliminary findings suggest that this is an appropriate mouse model for investigating the impact of gender-affirming hormone therapy in peripubertal transmasculine adolescents.