# Role of estradiol in the feminization of lordosis behavior in female mice

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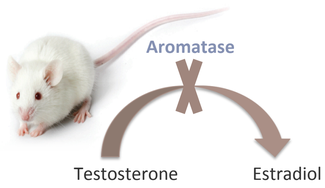
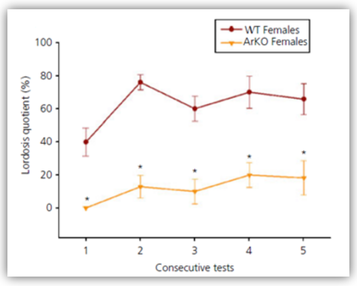
## INTRODUCTION

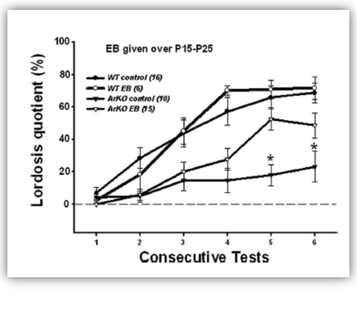



✓ArKO mouse : No estradiol synthesis due to targeted mutation *Cyp19* gene




✓Estradiol is required at some point during development for the expression of lordosis behavior in adulthood

*BAKKER, J., HONDA, S., HARADA, N. & BALTHAZART, J. 2002. The aromatase knock-out mouse provides new evidence that estradiol is required during development in the female for the expression of sociosexual behaviors in adulthood. J Neurosci, 22, 9104-12.*



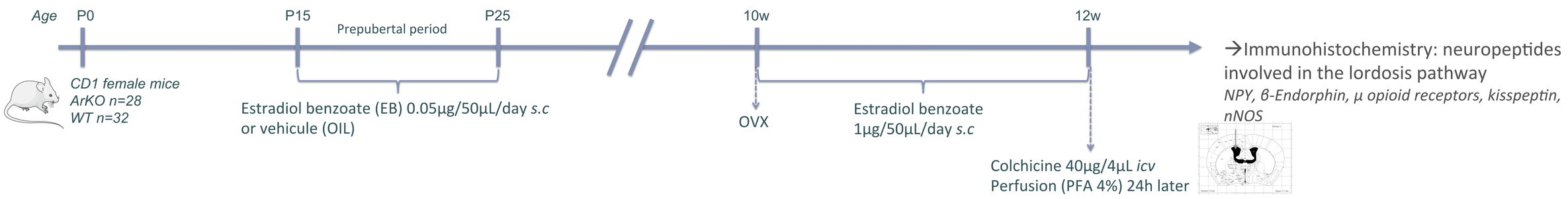

✓Estradiol feminizes lordosis behavior during a specific prepubertal period (P15-P25)

*BROCK, O., BAUM, M. J. & BAKKER, J. 2011. The development of female sexual behavior requires prepubertal estradiol. J Neurosci, 31, 5574-8.*

## OBJECTIVE

***Determining neural targets of estradiol in the feminization of the lordosis pathway***

## METHODS




## RESULTS

### *I. Effects of prepubertal estradiol treatment on energy balance*

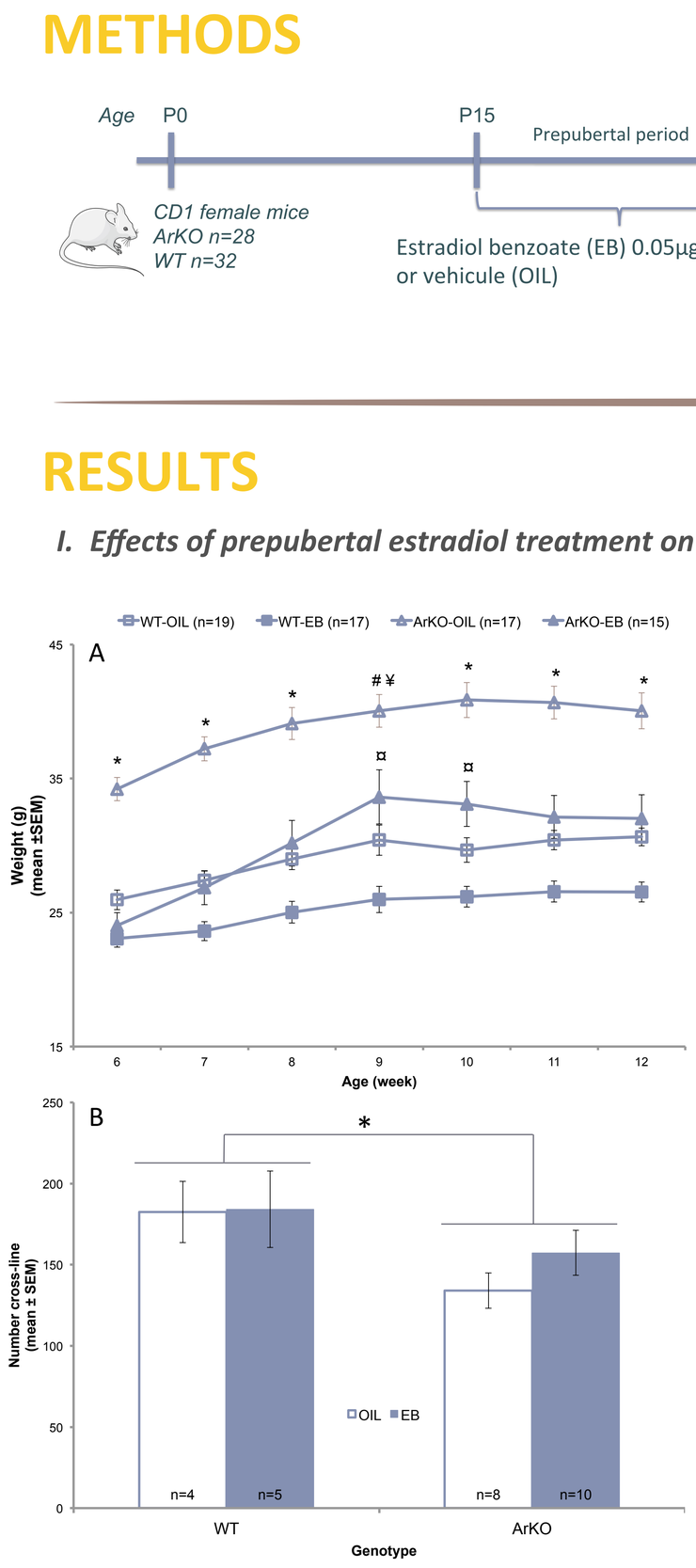
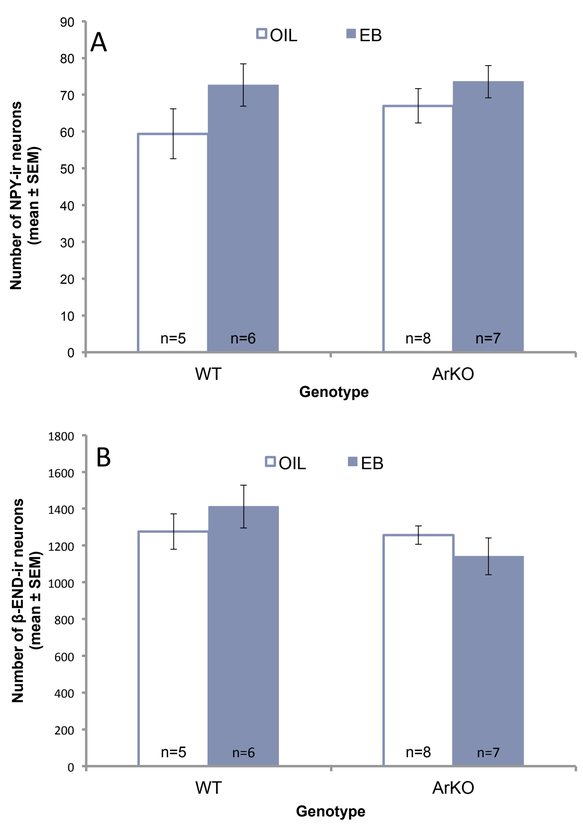



**FIGURE 1 | A| Effect of prepubertal treatment with estradiol on body weight.** Body weights of ArKO and WT female adult mice treated with oil or EB over the prepubertal period (P15 to P25) were monitored weekly during a 6-week period. Repeated measures ANOVA followed by Tukey *post-hoc* test revealed statistical differences (or a trend): ArKO-OIL vs. all other groups at 6 to 8 and 10 to 12 weeks of age ( * $p$<0.01 for all), ArKO-OIL vs. WT-OIL and WT-EB (# $p$=0.0002 for both) and ArKO-OIL vs. ArKO-EB (¥ $p$=0.065) at 9 weeks of age, ArKO-EB vs. WT-Oil and WT-EB (¤ $p$<0.02 for all). **B | Effect of prepubertal treatment with estradiol on spontaneous activity in the open field.** Number of line crossed measured during 10 minutes in a open-field arena in female adult ArKO and WT mice treated with oil or EB over the prepubertal period (P15 to P25). Two-way ANOVA revealed a statistically significant difference between genotype (* $p$=0.036).

✓Prepubertal estradiol treatment reversed the excessive weight gain of ArKO female mice
✓ArKO female mice exhibit a lower spontaneous activity

***→ Estradiol might have an organizational effect on energy balance, but not through a modification of basal locomotor activity***

### *II. Effects of prepubertal estradiol treatment on the expression of neuropeptides involved in the lordosis pathway*



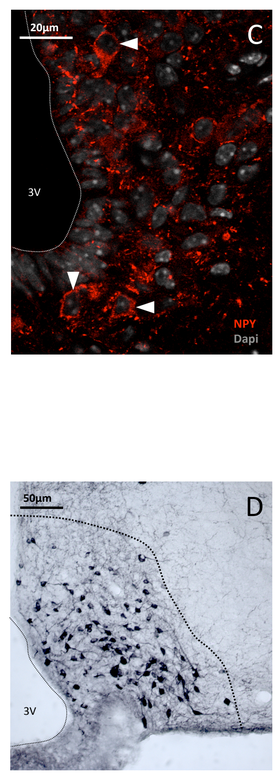




**FIGURE 2 | Effect of prepubertal treatment with estradiol on the expression of arcuate nucleus (ARC) neuropeptides involved in lordosis behavior. A** | Number of NPY-ir neurons were analyzed in one brain section comprising the ARC of ArKO and WT female mice treated with oil or EB over the prepubertal period (P15 to P25). **B** | Total number of β-END-ir neurons were analyzed along the rostro-caudal extension of the ARC of ArKO and WT female mice treated with oil or EB over the prepubertal period (P15 to P25). **C** | Illustration of NPY-ir neurons (white arrow) in the ARC observed through confocal microscopy (x60 magnification) **D** | Illustration of β-END-ir neuron in the ARC observed through light microscopy (x20 magnification).

✓Prepubertal treatment with estradiol did not affect the expression of NPY and β-END in the arcuate nucleus of adult ArKO female mice

***→ Organizational action of estradiol on lordosis behavior might not occur through modulation of NPY and β-END basal expression in the ARC***

## PERSPECTIVES

✓Continue IHC analysis on neuropeptides involved in lordosis behavior expression *(nNOS, Kisspeptin, µ-opioid receptor)*
✓IHC analysis on prepubertal (P15 and P30) brains from ArKO female mice treated or not with estradiol over the P15-P25 period
✓Check if overweight reversal in estradiol treated ArKO female mice is due to hypophagia
✓Perform DiI axonal tracing on developing brains in order to assess if the projection between ARC and AVPV is correctly established in ArKO female mice

## ACKNOWLEGMENTS

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