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Accelerated Ovarian Failure AOF mouse model: a model of transitional menopause

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We use this protocol and it's working

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Abstract

Until recently, aging and ovariectomy (OVX) have been the primary rodent models available to examine effects of ovarian hormone loss. These models fail to adequately recapitulate the hormonal changes of the human menopause process. The intact aging model fails to achieve very low estrogen levels at post-menopause, and the OVX model lacks a peri-menopause phase. Conversely, the novel model of AOF successfully replicates the human peri- and post-menopause stages, including erratic estrous cycles and hormone fluctuations, followed by undetectable estrogen levels[1, 2]. In the AOF model, the ovotoxin 4-vinylcyclohexene diepoxide (VCD, Sigma-Aldrich) is injected (130 mg/kg in 0.5% dimethyl sulfoxide in sesame oil; 5 days/week for 3 weeks; i.p.) in mice which induces selective depletion of ovarian primary and primordial follicles[3]. Previous studies from the Milner lab and other groups confirmed that VCD administration does not negatively affect peripheral tissues nor crosses the blood-brain barrier [1, 2]. In addition to reducing confounds associated with surgical manipulations, the AOF model maintains the presence of ovarian tissue which importantly parallels to human menopause. Based on assessment of ovarian follicle depletion and responses of plasticity markers in brain areas known to be estrogen responsive, timepoints for pre-, peri- and post-AOF have been established [1-4].Timepoints in the AOF model include peri-AOF (>58 days) and post-AOF (>139 days) corresponding to human peri-and post-menopause respectively [1-5].

References

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Materials

Reagents:

DMSO
sesame oil
ovotoxin 4-vinylcyclohexene diepoxide (VDC) **Sigma Aldrich Catalog #**94956

Ovotoxin 4-vinylcyclohexene diepoxide (VDC) preparation

2h 30m

1 Determine the number of mice to treat with VCD to calculate how much VCD is needed each day.

2 Weigh all the mice and obtain an average weight at least once a week for the duration of the VCD treatment. This works only if mice have very similar weighs (+/- a few grams around the average). It is recommended to use the high end of variation for calculations to make sure the heaviest mice get enough VCD.

3 In the chemical hood, measure volume of VCD from new vial.

4 Calculate how much sesame oil to add to the VCD vial in order to prepare the working solution (130 mg/kg).

5 Add sesame oil using a pipet with wide opening trying to avoid bubbles which can affect your volume measurements.

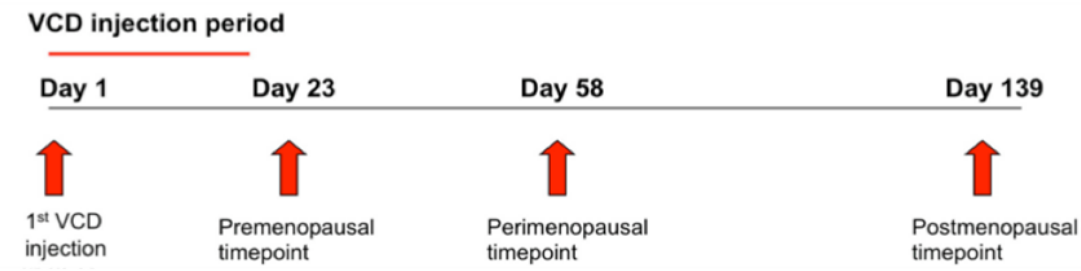
6 Stir solution for 02:00:00 . 2h

7 Parafilm well and store it in the fridge.

8 Every day before use, stir vial for 00:30:00 again. 30m

VDC injections

9



5 days / week for 3 weeks = i.p injection ; 130 mg/kg in 0.5% dimethyl sulfoxide in sesame oil