



The Effect of Chemotherapy Agents Doxorubicin and Cisplatin on the Developing Foetal Gonads *in vivo*

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BACKGROUND

Cancer during pregnancy is rare, affecting about 1 in 1,000 women [1]. Chemotherapy can be administered after the first trimester, but studies on its effects on foetal gonads are limited - concerning given the gonadotoxicity of many agents.

[1] Dalmartello M et al. Frequency of Pregnancy-Associated Cancer: A Systematic Review. Cancers (Basel). 2020

AIMS

The aim of this study was to assess the impact of *in vivo* doxorubicin (DOX) and cisplatin (CIS) treatment on:

- 1) germ cells using marker DDX4/MVH
- 2) DNA damage using marker γ H2AX
- 3) average diameter of the seminiferous cords in the testis
- 4) ovarian vasculature integrity in the ovary using aSMA and H&E stained ovaries

DESIGN

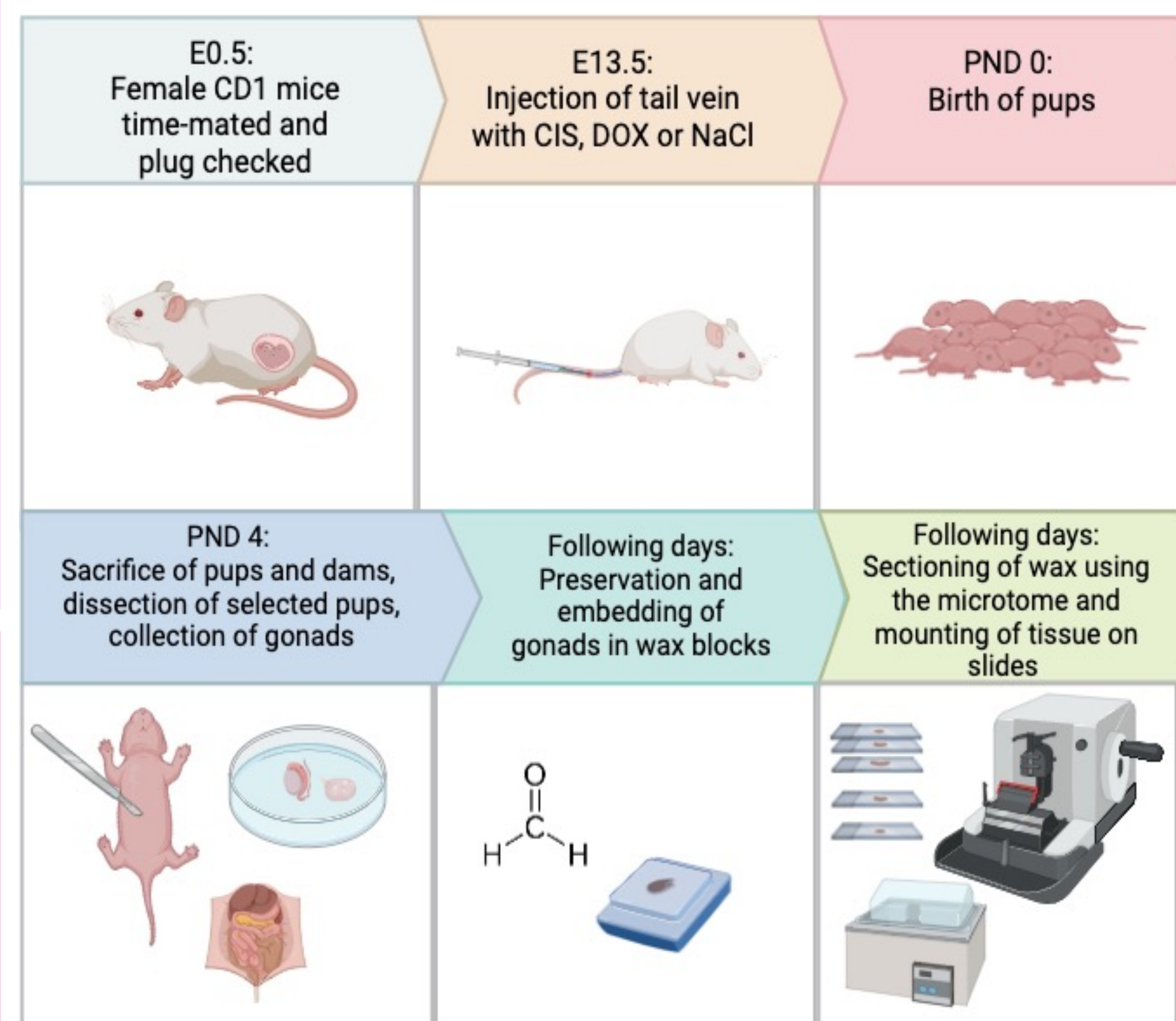


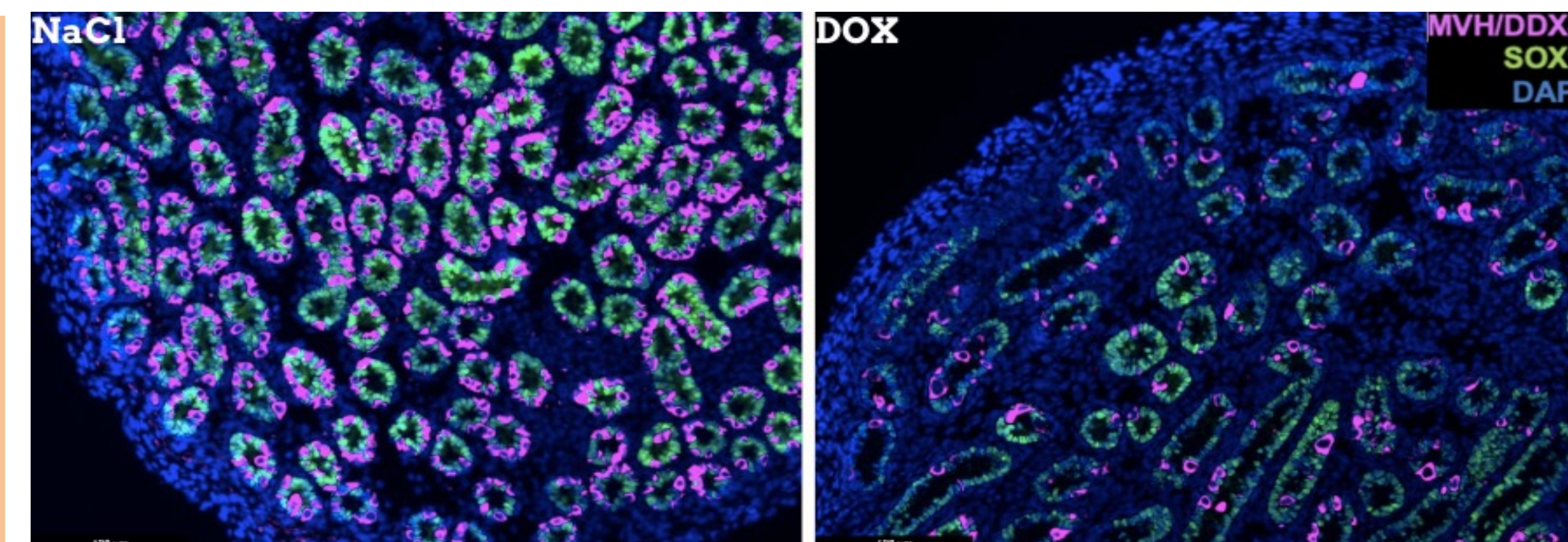
Figure 1: Experimental Design. Image was created using BioRender.

METHODS

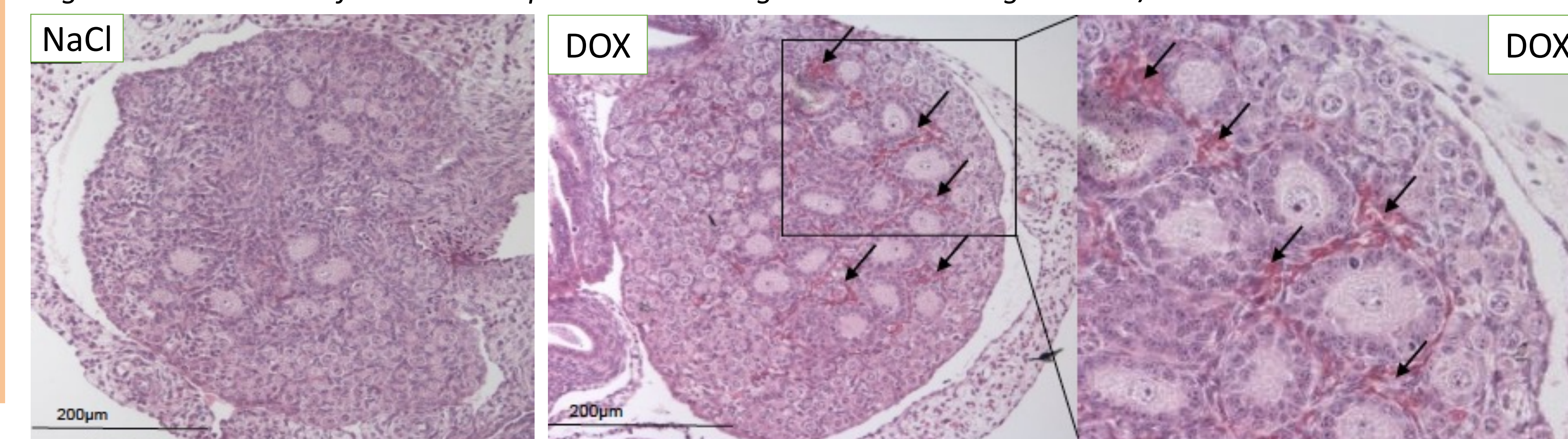
- ❖ Standard immunofluorescence lab protocol
- ❖ Standard H&E lab protocol
- ❖ Analyses were performed using ImageJ
- ❖ Graphs were generated with Prism 10

RESULTS

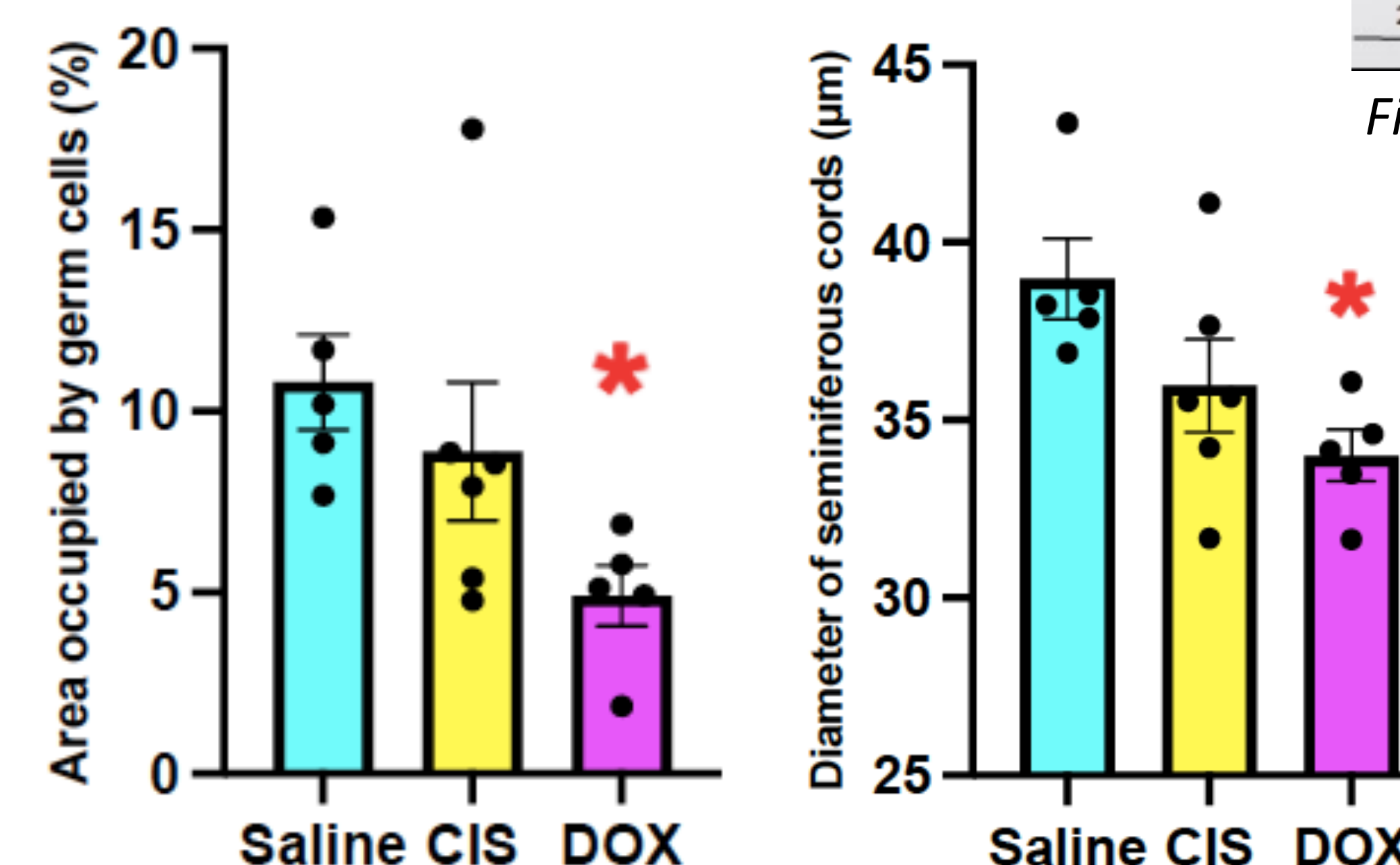
- ❖ **DOX-treated testes** had **significantly fewer germ cells** than controls ($p < 0.013$), corresponding with a **reduction in average seminiferous cord diameter** ($p < 0.011$).
- ❖ There was also a small, non-significant impact of CIS on testicular germ cell number.
- ❖ **No evidence of DNA damage** in the form of double-strand breaks was found in chemotherapy-treated foetal gonads of **either sex**.
- ❖ In the chemotherapy-exposed foetal ovaries, germ cells were unaffected, but a strong **trend of stromal vascular damage in the DOX-treated group** was noted in the H&E experiment.



Figures 2& 3: Immunofluorescence experiment showing the reduction in germ cells/diameter in DOX-treated testis



Figures 4&5: H&E experiment showing increase in abnormal vasculature in DOX-treated ovaries



CONCLUSIONS

- ❖ The study suggests that ***in vivo* DOX exposure is likely gonadotoxic** to the developing foetal mouse, primarily affecting the testis and potentially the ovary.
- ❖ CIS shows a milder, testis-specific effect.
- ❖ Further research with larger samples is needed to confirm if these findings have the same in the **human foetal gonads**.