

LAY ABSTRACT

TITLE: Asymmetric development of the male mouse mammary gland and its response to a prenatal or postnatal estrogen challenge

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Abstract

The CD-1 mouse mammary gland is sexually dimorphic, with males lacking nipples. Recent studies have revealed that the underlying epithelium in the male mammary gland is sensitive to estrogenic environmental chemicals. In ongoing investigations, we observed asymmetric morphology in the left and right male mouse mammary glands. Here, we quantified these asymmetries in the embryonic, prepubertal, pubertal and adult male mammary gland. We found that the right gland was typically larger with more branching points compared to the left gland. We next evaluated the response of the left and right glands to 17 α -ethinyl estradiol (EE2) after perinatal or peripubertal exposures. We found that the right gland was more responsive to EE2 than the left at both periods of exposure. These results reveal novel aspects of male mammary gland biology and suggest that future studies should control for laterality in the evaluation of hazards associated with exposures to estrogenic chemicals.

Lay Abstract

Even though male mice lack nipples, in the mammary tissue that is below the skin, these males have small mammary ducts. Recent studies have revealed that the male mammary ducts are sensitive to estrogenic environmental chemicals. In this study, we observed that the left and right mammary glands are unequal (asymmetric) in size in the male mouse at several stages of development. We measured these asymmetries in the embryonic, prepubertal, pubertal and adult male mammary gland and found that the right gland was typically larger, with more branching points, compared to the left gland. We next evaluated the response of the left and right glands to 17 α -ethinyl estradiol (EE2), the estrogenic ingredient found in prescription birth control pills. We gave EE2 to pregnant female mice, which exposed the males during perinatal development, which is immediately before and just after their birth. We also administered EE2 directly to male mice at puberty. We found that the right gland was more responsive to EE2 than the left

at both periods of exposure; the right mammary ducts doubled in size when males were exposed to EE2, but no significant changes in duct size were observed on the left side. The mouse is a good model for predicting effects of estrogenic chemicals on the human mammary gland. Our results reveal novel features of the male mammary gland, which may provide insights into male breast cancer in humans.