

Expression of the *APC* Tumor Suppressor Gene is Regulated during Mammary Gland Development and Differentiation

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Background and Purpose: With almost 270,000 new cases of breast cancer and over 40,000 deaths, breast cancer is one of the greatest health concerns facing women. The *APC* tumor suppressor gene has been shown to be inactivated in as many as 40% of sporadic breast cancers, and mice carrying a germline mutation in *Apc* are predisposed to mammary tumors. Our laboratory has shown previously that *APC* expression is induced during pregnancy and lactation in the mouse mammary gland, and *Apc*-deficiency results in defective lobulo-alveolar development. The current project tests the hypothesis that *APC* expression is regulated by lactogenic hormones both *in vitro* and *in vivo*. **Methods:** In the *in vitro* study, we exposed EpH4 mouse mammary epithelial cells to 10 nM 17 β -estradiol, 10 nM 17 β -estradiol with 100 nM progesterone, 50 ng prolactin in saline or vehicle (sesame seed oil with saline) for 4, 24 or 48 h. Total RNA was harvested from the cells. *APC* and *GAPDH* (as a normalization control) were amplified using Reverse-transcriptase (RT) real-time PCR to quantify gene expression. For the *in vivo* studies, ovariectomized C57BL/6 (strain) mice (n=7/group) were treated with daily injections of 1cc for 20 days. Mammary tissue was harvested and RNA was isolated. *APC* and *GAPDH* gene expression were evaluated by real-time RT-PCR. **Results:** EpH4 cells exposed to lactogenic hormone for 4 h demonstrated an increase in *APC* expression, particularly in the 17 β -estradiol and progesterone treated cells, compared to those treated with vehicle. At 24 and 48 h there were no obvious differences in *APC* expression between the treatment groups. Additionally, we observed that mammary tissues from mice treated with estradiol and progesterone had increased *APC* mRNA expression compared to those mice treated with vehicle or estrogen alone. **Conclusions:** These data suggest that expression of the *APC* tumor suppressor gene is regulated by lactogenic hormones in the mammary gland, and support a model in which *APC* is an important regulator of mammary gland function during pregnancy and lactation.