

Abstract

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Different forms of prolactin have opposing effects on the expression of cell cycle regulatory proteins in differentiated mammary epithelial cells.

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BACKGROUND: Prolactin (PRL) is a hormone that contributes to both the growth and differentiation of mammary epithelial cells, activities likely to impact breast cancer in opposite ways. Whether PRL causes growth or differentiation has been solely attributed to the coexisting steroidal environment, with PRL stimulating mammary gland growth during pregnancy, and then milk production after the postpartum drop in estrogen and progesterone. However, previous work from our laboratory has shown that the form of PRL may also be an important factor. During pregnancy, unmodified PRL (U-PRL) promotes mammary growth, while an increase in phosphorylated PRL, or administration of a molecular mimic of phosphorylated PRL (S179D PRL), inhibits growth. Unknown, however, is whether these forms of PRL have opposite effects on growth in the absence of steroids and whether effects are directly on mammary epithelial cells.

RESULTS: To mimic the glandular epithelium in vitro, we used contact-inhibited, differentiated cells and showed that even with these minimally growing cells that treatment with U-PRL caused increased expression of cyclin D1 and cyclin-dependent kinase 4, increased activity of both cdk4 and cdk2, while having no effect on the inhibitory protein, p21. S179D PRL, by contrast, had no effect on cyclin D1 and cdk4 expression, but increased p21 expression and expression of the vitamin D receptor (VDR).

CONCLUSION: We conclude that increased U-PRL or decreased phosphorylated PRL can directly affect cell cycle control proteins in relatively differentiated mammary epithelial cells, thereby implicating the balance between these two forms of PRL in the early promotion of breast cancer.

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