PROSTATE CANCER

Antagonizing the prolactin receptor prevents tumorigenesis in a transgenic mouse model of prostate cancer

Prolactin-induced tumor development from prostate epithelial cells can be halted by blocking the hormone's receptor, according to a study published in the *Proceedings of the National Academy of Sciences*.

Although it is a pituitary hormone, prolactin is also expressed in human prostate, and has been identified as a survival factor for prostate cancer cells. It acts via Stat5, a signaling molecule triggered by activation of the prolactin receptor in cultured prostate cells.

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A group led by Vincent Goffin at INSERM in Paris, France, used a transgenic approach to investigate the role of local prolactin in mouse prostate, which does not produce endogenous prolactin. Mice engineered to produce prostatic rat prolactin also expressed activated Stat5, suggesting that Stat5 is a hallmark of prostatic prolactin activity.

The team also observed high-grade prostatic *in situ* hyperplasia in the prostates of 6-month-old transgenic mice, which was maintained and amplified at 20 months, indicating a continuum in the process of tumorigenesis from benign hyperplasia to locally invasive malignancy. Local prolactin-induced proliferation was particularly increased in the basal cell compartment—correlating with recent studies which suggest that basal cells are the cells of origin for prostate cancer.

The group also investigated the effect of blocking prolactin signaling in the prostate, using a double-transgenic mouse model expressing local prolactin plus a prolactin receptor antagonist. In these mice, dorsal prostate weight was reduced compared to their single-transgenic littermates, and prostatic hypertrophy was inhibited to a wild-type level. In addition, activated Stat5 was dramatically reduced in the double transgenics. These data show for the first time that antagonism of the prolactin receptor is an effective mechanism to prevent prostatic tumorigenesis.

The development of androgen independence is currently a major stumbling block to the effective treatment of prostate cancer. Targeting alternate pathways, such as that mediated by prolactin, provides a promising new avenue of investigation.

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Original article Rouet, V. *et al*. Local prolactin is a target to prevent expansion of basal/stem cells in prostate tumors. *Proc. Natl Acad. Sci. USA* **34**, 15199–15204 (2010)