

学位論文審査結果の要旨

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(学位論文審査結果の要旨)

Activation of FGF2-FGFR signaling in the castrated mouse prostate stimulates the proliferation of basal epithelial cells.

(主論文審査結果の要旨)

著者らは論文において以下の内容を述べている。

The prostate gland is unique in that it undergoes rapid regression following castration but regenerates completely once androgens are replaced. Residual ductal components play an important role in the regeneration of a fully functional prostate. In this study, to examine how androgen status affects prostate structure and components, we conducted histopathological studies of the involuted and regenerated mouse dorsolateral prostate (DLP). In the castrated mouse DLP, the number of luminal epithelial cells decreased in a time-dependent manner. On Day 14 postandrogen replacement, the number of luminal epithelial cells was completely restored to the baseline level. In contrast, the number of basal epithelial cells gradually increased in the castrated mouse prostate. The Ki67-labeling index of prostate basal epithelial cells was significantly increased after castration. The number of basal epithelial cells decreased to baseline after androgen replacement. After castration, mRNA expression levels of specific growth factors, such as Fgf2, Fgf7, Hgf, Tgfa, and Tgfb, were relatively abundant in whole mouse DLPs. In organ culture experiments, basal epithelial proliferation was recapitulated in the absence of dihydrotestosterone (DHT). The proliferation of basal epithelial cells in the absence of DHT was suppressed by treatment with an FGF receptor inhibitor (PD173074). Moreover, FGF2 treatment directly stimulated the proliferation of basal epithelial cells. Taken together, these data indicated that the FGF2-FGF receptor signal cascade in the

prostate gland may be one of the pathways stimulating the proliferation of basal epithelial cells in the absence of androgens.

前立腺腺上皮細胞の前駆細胞を供給する細胞群、すなわち前立腺において幹細胞が存在するのは基底上皮細胞群と言われている。基底上皮細胞からは悪性度の高い前立腺癌が生じる可能性があり、その異常増殖を刺激するシグナル経路の解析は意義深いものである。そして本論文は、基底上皮細胞が去勢下（低アンドロゲン状態）のマウス前立腺において増殖刺激を受けていることを解明した論文として学術上極めて有益であり、学位論文として価値のあるものと認めた。

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