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）

Fibroblasts prolong serum prostate-specific antigen decline after androgen deprivation therapy in prostate cancer

【主論文審査結果の要旨】

著者らは論文において下記の内容を述べている。

In patients with prostate cancer (PCa), serum prostate-specific antigen (PSA) is a useful marker for evaluating the effects of androgen deprivation therapy (ADT). Intuitively, most urologists expect that a more rapid PSA decline in response to ADT would be positively associated with extended survival. Recently, we have reported that prolonged gradual serum PSA decline after ADT is strongly associated with favorable prognosis in PCa patients, however, the mechanism remains unknown. We investigated the role of fibroblasts in serum PSA decline after ADT. We performed in vitro experiments using androgen-sensitive, androgen receptor (AR)-positive prostate epithelial cell lines (LNCaP, 22Rv1, and RWPE-1 cells), commercially available prostate stromal cells (PrSC), and primary cultures of prostate fibroblasts (pcPrFs). In LNCaP and 22Rv1 cells, PSA production was increased by co-culture with fibroblasts under androgen-deprived conditions. In an in vivo model using LNCaP cells, serum PSA declined rapidly after ADT becoming undetectable within 14 days in mice inoculated with LNCaP cells alone. In contrast, when LNCaP cells were co-inoculated with fibroblasts, serum PSA levels were still high on 14 days post ADT and did not drop to undetectable levels until 21 days post ADT. Tumor volumes and Ki67 labeling indices were not altered between days 14 and 21 post ADT in mice inoculated with LNCaP cells; however, those in mice inoculated with

LNCaP cells plus fibroblasts decreased gradually. PSA protein was detected in all tumors on 21 days post ADT by immunohistochemical staining. Microvessel densities were higher on 14 days post ADT for tumors from mice inoculated with LNCaP cells plus fibroblasts as compared with LNCaP cells alone. In summary, co-inoculation of fibroblasts with LNCaP cells prolonged serum PSA decline after ADT and enhanced the efficacy of ADT. Prolonged serum PSA decline may indicate the presence of protective fibroblasts that preserve the AR dependence of PCa cells, improving treatment efficacy.

本論文は、前立腺線維芽細胞が、前立腺癌における内分泌療法後の血中 PSA (prostate specific antigen; PSA)動態および治療効果の増強に寄与し、前立腺線維芽細胞の性状解析により、前立腺癌の予後を予測できる可能性を示した論文であり、学術上極めて有益であり、学位論文として価値あるものと認めた。

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