学 位 論 文 の 要 旨

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主論文の題名

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

主論文の要旨

In prostate cancer (PCa), serum prostate-specific antigen (PSA) is a useful marker. We reported that prolonged gradual serum PSA decline after androgen deprivation therapy (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 used androgen-sensitive prostate epithelial cells (LNCaP, 22Rv1, and RWPE-1), prostate stromal cells (PrSC), and primary cultures of prostate fibroblasts (pcPrFs). In LNCaP and 22Rv1, PSA production was increased by co-culture with fibroblasts. Serum PSA declined rapidly after ADT becoming undetectable within 14 days in mice inoculated with LNCaP alone *in vivo*. In contrast, LNCaP were co-inoculated with fibroblasts, serum PSA levels were still high 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; however, those in mice inoculated with LNCaP plus fibroblasts decreased gradually. Co-inoculation of fibroblasts with LNCaP 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.