



Evaluation of AlkB homolog family molecules as molecular targets for cancer therapy

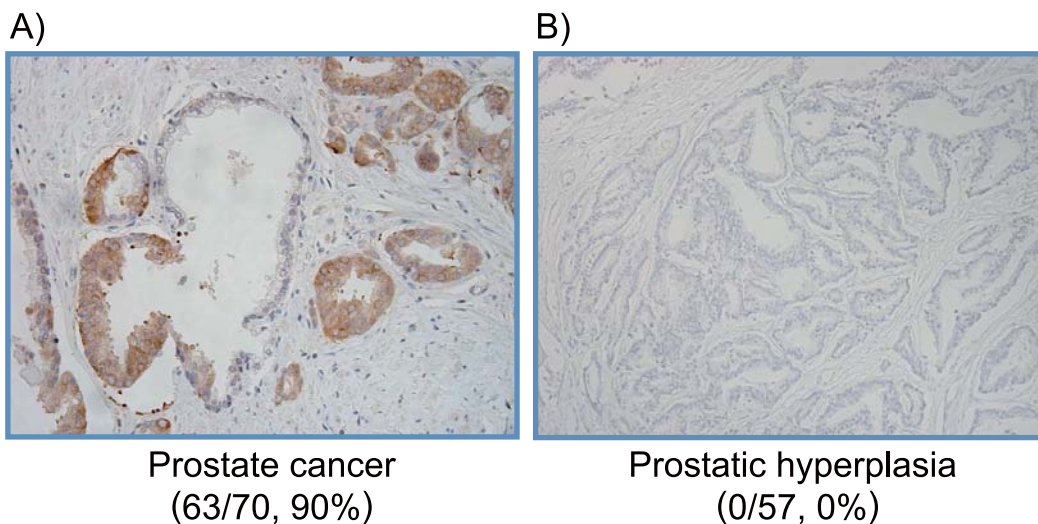
Outline

We identified a novel gene named prostate cancer antigen (PCA)-1 that is highly expressed in prostate carcinoma. Knockdown analysis by using PCA-1 siRNAs revealed induction of apoptosis of prostate cancer cells and attenuation of tumor formation in nude mouse xenografts; these findings indicate that PCA-1 may serve as a target molecule for prostate cancer therapy. PCA-1 possesses a domain that is similar to the 2-oxoglutarate- and Fe(II)-dependent oxygenase domain of the *E. coli* AlkB protein. At present, 7 human proteins with this domain are identified and called the AlkB homolog (ABH) family. Our aim is to clarify whether the ABH family molecules are possible candidates as target molecules for an effective cancer therapy.

Expected Outcome

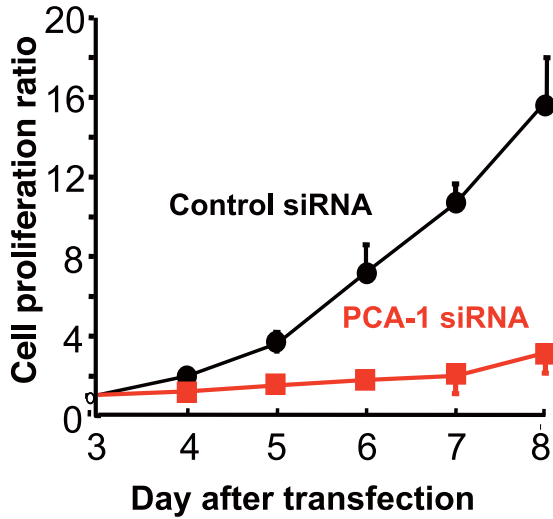
Immunohistochemical analysis of carcinoma specimens with the anti-ABH family molecule antibodies revealed that ABH4 and ABH8 were strongly expressed in breast cancer; ABH6, in colon cancer; and ABH5 and ABH8, in bladder cancer. Moreover, siRNAs against the ABH family molecules significantly suppressed the growth of cancer cells. We expect that the ABH family molecules may be novel molecular targets for cancer therapy.

High expression of PCA-1 in prostate carcinomas

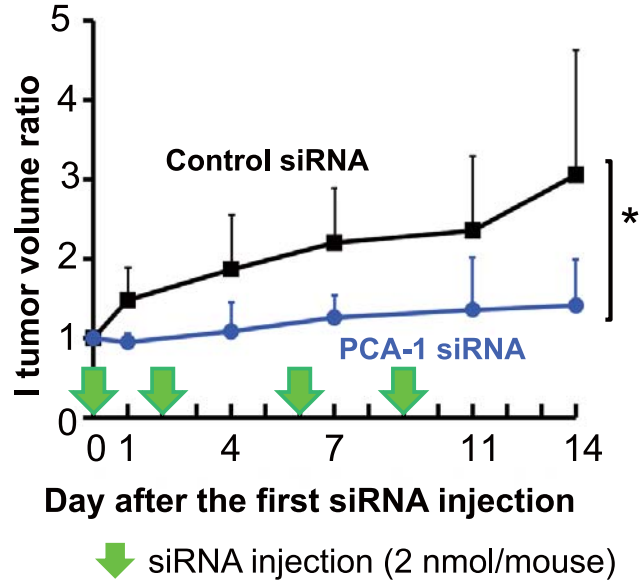


A, High expression of PCA-1 in an adenocarcinoma but not in the adjacent normal tissues of the prostate. B, Negative immunostaining of PCA-1 in benign prostatic hyperplasia. (PCA-1 positive/all cases, positivity %)

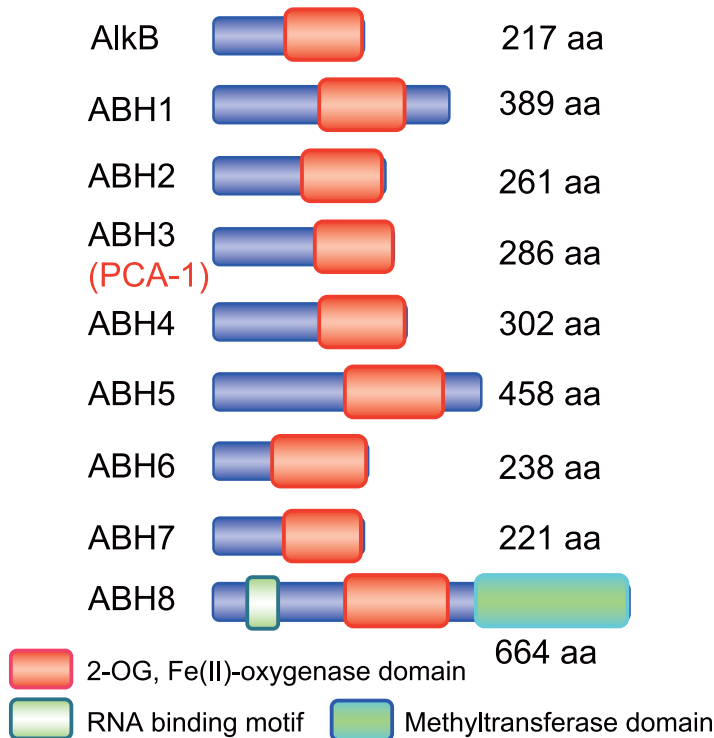
Inhibitory effect of PCA-1 siRNA on proliferation of DU145 cells



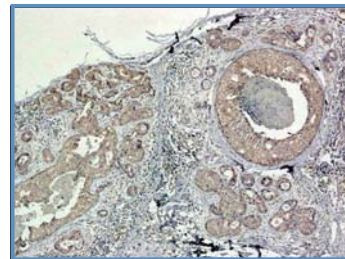
Anti-tumor effect of PCA-1 siRNA on DU145 prostate cancer xenograft in vivo



Schematic diagram of the human ABH molecules and expression of ABH family molecules in carcinomas



ABH4: Breast cancer



ABH8: Bladder cancer

