Ca^{2+}-activated K^+ channel $K_{Ca}2.2$ inhibiter as a possible therapy for advanced prostate cancer

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Androgen deprivation (castration) therapy andwith anti-androgens have become standardremain the clinical mainstay of treatments for metastatic and aggressive prostate cancer (PCa). Yet, these therapies are limited by the inevitable onset ofmost PCa patients will progress to castration-resistant PCa (CRPC) for several reasons such as the overexpression of androgen receptors (AR). Thus, it is necessary to develop Novel therapies are desired for the advanced PCa. Ca^{2+}-activated K^+ channels (K_{Ca}) are key molecules inregulate cancer cell behaviors including proliferation progression. We revealed the predominant expression of $K_{Ca}2.2$ in human androgen-sensitive prostate cancer cell line, LNCaP cells, using a real-time PCR, western blotting, and whole-cell patch clamp recording. The treatment with UCL1684, a $K_{Ca}2.x$ channel blocker inhibited the store-operated Ca^{2+} entry in LNCaP cells, resulting in suppressive effect on proliferation of LNCaP cells. The pharmacological or siRNA-mediated inhibition of AR for 48 hr decreased the expression level levels of $K_{Ca}2.2$ transcripts in LNCaP cells, whereas the UCL1684-induced inhibition of $K_{Ca}2.2$ activity did not affect the expression levels of AR transcripts, suggesting that $K_{Ca}2.2$ is a downstream effector of AR signaling in LNCaP cells. The short-term androgen deprivation for 48 hr decreased the $K_{Ca}2.2$ protein expression, whereas the long-term one for 96 hr increased it. Together, $K_{Ca}2.2$ might be a possible therapeutic candidate in castration-resistant PCa.