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SBF-1, a synthetic steroidal glycoside, inhibits prostate cancer cell growth through the blockade of mTOR and SIX1 interaction

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Abstract

The AR (androgen receptor) is a primary therapeutic target in androgen-dependent prostate cancer. Challenges remain for AR-independent prostate cancer as they exhibit complex cellular signaling in their progression rather than relying on the AR. Currently, prostate cancer metabolic signaling became an achievable target in prostate cancer treatment. In the present study, synthetic steroidal glycoside SBF-1, a potent anti-tumor agent known to have a strong cytotoxic effect on different kinds of cancers. We investigated SBF-1 potentials in AR-independent prostate cancer treatment and its effect on prostate cancer metabolic signaling. SBF-1 inhibited the growth of AR independent prostate cancer cell lines DU145 and PC3. Also, SBF-1 downregulates AKT/mTOR pathway and inhibited the ENO1 (alpha-enolase 1) protein and gene levels. Besides, SBF-1 blocked the interaction between mTOR and SIX1, which, for the first time shown mTOR essential for the regulation of ENO1 through binding to SIX1 (sineoculis homeobox homolog 1), accordingly, nuclear mTOR is an essential coregulator for the transcription of the ENO1 gene. Blocking the interaction between mTOR and SIX resulted in robust cell growth inhibition also the downregulation of ENO1, a consensus target in prostate cancer treatment. Accordingly, the current study suggests that SBF-1 is a leading compound in treating androgen-independent prostate cancer. Also, targeting the interaction between mTOR and SIX1 considered a better strategy in Androgen independent prostate cancer treatment

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