HOXB13-mediated suppression of p21WAF1/CIP1 regulates JNK/c-Jun signaling in prostate cancer cell

C. Jung¹, Y. Kim¹, Y.S. Cho¹, T.W. Kang², M.S. Kim³
¹Anatomy, Chonnam National University Medical School, Gwangju, Republic of Korea
²Department of Urology, Chonnam National University Hospital, Gwangju, Republic of Korea
³Statistics, Chonnam National University, Gwangju, Republic of Korea

Aim/Background: Many prostate cancer (PCa) patients die with recurrent disease due to the emergence of hormone-independent cancer cells of which mechanism is not fully understood. Our previous studies demonstrated that most castration resistant prostate cancers (CRPC) overexpresses HOXB13 transcription factor to confer positive growth signals. Since HOXB13 also suppresses p21 expression, we studied the correlation of HOXB13 and p21 in PCa cells.

Methods: Immunohistochemistry was performed to correlate expression of HOXB13 and p21 in selected samples of PCa, including CRPC. Using HOXB13-altered cells, both western blot and reporter gene transcription assay was applied to elucidate the mechanism by which HOXB13 regulates p21. MTT in vitro proliferation assay was also applied to LNCaP PCa cells.

Results: While there were no statistically significant correlation between expression of HOXB13 and p21, HOXB13-deficient tumors have 3 times higher odds for p21-positive than HOXB13-positive tumors. Moreover, CRPC has more negative correlation than hormone-dependent PCa (HDPC). Further in vitro proliferation assay demonstrated that androgen did not affect growth suppressive function of p21 in androgen dependent PCa cells, suggesting that p21 seems to override androgen’s growth promoting function and suppression of p21 expression by HOXB13 is an important step for PCa cells to survive under no androgen influence. HOXB13 also inhibits AP-1 signals by the suppressed expression of JNK/c-Jun. While HOXB13 suppresses p21 expression by the regulation of JNK signals, alteration of p21 expression also affects c-Jun and AP-1 activity.

Conclusions: Overexpression of HOXB13 in CRPC is an important step to avoid growth-suppressive effect of p21 in a harsh condition such as in androgen-deprived environment.

Disclosure: All authors have declared no conflicts of interest.