

Oncogenic splice variant of KLF6 as a prognostic marker in cancersMuhammad Shahzeb Khan,¹ Faizan Imran Bawany,² Muhammad Naeem³

Madam, Kruppel-like factor 6 (KLF6) is a zinc finger transcription factor that induces apoptosis in cancer cells leading to suppression of tumour growth. This tumour suppressor protein works by inhibiting cyclin-dependent kinases and is found to be mutated in various cancers including prostate and ovarian cancers. Recent evidence claims that this factor can induce apoptosis in prostatic cancer cells via up-regulation of activating transcription factor 3 (ATF3).¹ ATF3 is a pro-apoptotic protein and a key mediator for apoptosis under stressful conditions. However, it has also been shown that an oncogenic splice variant (KLF6-SV1) of KLF6 tumour suppressor gene targets BH3-only protein Noxa for degradation and blocks apoptosis effectively.² Moreover, in previous studies it has been proven that over-expression of KLF6-SV1 can increase the progression and metastasis of common cancers like those of prostate and ovary.^{2,3}

Recently, another important discovery was made showing that KLF6-SV1 is also a promising prognostic marker for breast cancer. The research team led by Dr. Narla concluded that KLF6-SV1 is linked to the metastasis and recurrence of breast cancer in females. In the study, it was found that patients who expressed high levels of this variant gene were 50 per cent more likely to die.⁴ Hence, it is thought that KLF6-SV1 levels are very good indicators

of the metastatic behaviour of tumours.

Breast cancers and prostate cancers are common cancers among the population. Identification of this marker as a predictor of metastasis presents an opportunity for medical professionals to work on levels of KLF6-SV1 as a therapeutic target. It has been shown that small interfering RNA against KLF6-SV1 stops tumour progression in the ovary.[2] With the discovery of this new breast cancer marker, it will be possible to develop new and more effective therapeutic drugs based on KLF6-SV1 that can potentially reduce mortalities due to breast cancer. Furthermore, additional studies should be conducted to research prognostic markers such as KLF6-SV1 in other forms of cancer. Knowledge and drugs oriented towards these markers can potentially lead to a higher survival rate in cancer patients as metastasis is a major cause of mortality in cancer.

References

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