

**EXPRESSION OF EPIGENETIC SILENCER EZH2 IN EARLY
INVASIVE PT1 UROTHELIAL BLADDER CANCER**

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Urothelial bladder cancer is the most common malignancy of the urinary tract. Early invasive bladder cancer (stage pT1) is a tumor that has invaded subepithelial connective tissue, without spread to bladder muscle, and represents a major challenge for diagnosis and therapy. EZH2 transcriptional repressor has a crucial role in oncogenesis of the bladder. The aim of this research was to investigate the expression profile of EZH2 in pT1 bladder cancer, to analyze the correlation with clinicopathological factors, and to assess the possible prognostic significance of EZH2 expression. In that purpose 279 tumor samples embedded in tissue microarrays were analyzed immunohistochemically to EZH2 expression. High EZH2 nuclear expression was observed in 44.5% of the tumors. High EZH2 expression was strongly associated with high histologic grade ($p < 0.001$). In addition, EZH2 significantly correlated to male gender, and the occurrence of carcinoma *in situ* in the adjacent urothelium ($p = 0.019$, and $p = 0.026$, respectively), while divergent differentiation and disease recurrence showed no significant association with EZH2 staining. High EZH2 expression strongly correlated with cancer specific death ($p = 0.010$). Kaplan-Meier survival analysis demonstrated that high EZH2 expression predicted worse survival of the patients ($p < 0.001$). Impact of EZH2 expression to recurrence free survival was not significant. High EZH2 expression in early invasive urothelial bladder cancer indicates aggressive behavior of the tumor and poor prognosis. EZH2 has promising roles in urothelial bladder cancer as a complementary diagnostic tool in selection of the patients that require closer clinical attention, and as a potential target for anticancer therapy.

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