

PREDICTIVE VALUE OF CLAUDIN-4 EXPRESSION IN NON-MUSCLE INVASIVE UROTHELIAL BLADDER CANCER

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Claudin-4 is an integral membrane protein of tight junctions, and its expression is frequently altered in epithelial cancers. Non-muscle-invasive urothelial bladder cancer (NMIBC) is a common neoplasm with an unpredictable clinical course that requires more precise stratification and risk assessment. The aim of this study was to investigate the association between Claudin-4 expression and clinicopathologic features of NMIBC, and to assess the predictive impact of Claudin-4 regarding to disease prognosis. The study comprised tumor tissue samples obtained from 441 patients with urothelial bladder cancer who had undergone transurethral resection. Samples were embedded in tissue microarrays and analyzed immunohistochemically for Claudin-4 expression. High expression was found in 41.6% of pTa and 47.8% of pT1 tumors. High Claudin-4 expression significantly correlated to high histologic grade ($p = 0.002$), and hematuria ($p = 0.038$). High Claudin-4 expression was more frequently observed in tumors with divergent differentiation, early invasive cancers associated with carcinoma in situ, and recurrent disease, however, these associations were not statistically significant. Kaplan—Meier survival analysis failed to indicate a significant difference in overall survival between the patients with high and low Claudin-4 expression. Conversely, recurrence-free survival was significantly associated with Claudin-4 expression ($p = 0.023$). In conclusion, overexpression of Claudin-4 is associated with high tumor grade and shorter recurrence-free survival. As an indicator of aggressive tumor behavior, Claudin-4 may serve as a potentially useful and accessible addition to the pathohistological panel for the prediction of clinical behavior of urothelial bladder cancer, as well as a promising therapeutic target.

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