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Significance of $p57^{Kip2}$ down-regulation in oncogenesis of bladder carcinoma: an immunohistochemical study

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ABSTRACT

Aims and background. Cyclin-dependent kinase inhibitors have important roles in the oncogenesis of various tumors including urothelial cancer. The aim of this study was to establish the importance of $p57^{Kip2}$, a unique cyclin-dependent kinase inhibitor, in the oncogenesis of bladder carcinoma. This article also focused on another cyclin-dependent kinase inhibitor, $p27^{Kip1}$, and telomerase enzyme and examined the relationship between these proteins.

Material and methods. Thirty-one patients with urothelial carcinomas of the bladder and 7 cases with normal urinary bladder mucosa were included in the study. Immunohistochemical study was performed by monoclonal antibodies of $p27^{Kip1}$, $p57^{Kip2}$, and the telomerase subunit (hTERT). All immunohistochemical preparations were evaluated by an immunohistochemical histological score.

Results. $p57^{Kip2}$ and $p27^{Kip1}$ expression were seen in all of the cases of normal mucosa. In carcinoma cases, 8 of 31 (25.8%) showed $p57^{Kip2}$ nuclear positivity and 20 of 31 (64.5%) expressed nuclear $p27^{Kip1}$. HSCOREs of carcinoma cases showed lower scores of nuclear $p57^{Kip2}$ and $p27^{Kip1}$ than normal mucosa, but only HSCOREs of nuclear $p57^{Kip2}$ ($P = 0.001$) showed statistical significance. Despite unknown significance, cytoplasmic $p57^{Kip2}$ and $p27^{Kip1}$ were also evaluated. Immunohistochemical analysis showed that carcinomas expressed higher HSCOREs of hTERT than normal mucosa, and there was a significant difference ($P = 0.026$) between muscle invasive carcinomas and normal mucosa.

Conclusions. The data showed that $p57^{Kip2}$ down-regulation along with $p27^{Kip1}$ is a well-established feature of urothelial carcinoma. Probably, this down-regulation of cyclin-dependent kinase inhibitors supports the proliferation phase of oncogenesis. In the study, we also showed that hTERT expression was up-regulated in higher stages of urothelial carcinoma.

Key words: *bladder, hTERT, $p27^{Kip1}$, $p57^{Kip2}$, urothelial carcinoma.*

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