

Autophagy Suppresses Bladder Tumor Formation in a Mouse Orthotopic Bladder Tumor Formation Model

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Abstract : Annual incidence of bladder cancer increases in the world and occurs frequently in the male. Most common type is transitional cell carcinoma (TCC) which is treated by transurethral resection followed by intravesical administration of agents. In clinical treatment of bladder cancer, chemotherapeutic drugs-induced apoptosis is always used in patients. However, cancers usually develop resistance to chemotherapeutic drugs and often lead to aggressive tumors with worse clinical outcomes. Approximate 70% TCC recurs and 30% recurrent tumors progress to high-grade invasive tumors, indicating that new therapeutic agents are urgently needed to improve the successful rate of overall treatment. Nonapoptotic program cell death may assist to overcome worse clinical outcomes. Autophagy which is one of the nonapoptotic pathways provides another option for bladder cancer patients. Autophagy is reported as a potent anticancer therapy in some cancers. First of all, we established a mouse orthotopic bladder tumor formation model in order to create a similar tumor microenvironment. IVIS system and micro-ultrasound were utilized to noninvasively monitor tumor formation. In addition, we carried out intravesical treatment in our animal model to be consistent with human clinical treatment. In our study, we carried out intravesical instillation of the autophagy inducer in mouse orthotopic bladder tumor to observe tumor formation by noninvasive IVIS system and micro-ultrasound. Our results showed that bladder tumor formation is suppressed by the autophagy inducer, and there are no significant side effects in the physiology of mice. Furthermore, the autophagy inducer upregulated autophagy in bladder tissues of the treated mice was confirmed by Western blot, immunohistochemistry, and immunofluorescence. In conclusion, we reveal that a novel autophagy inducer with low side effects suppresses bladder tumor formation in our mouse orthotopic bladder tumor model, and it provides another therapeutic approach in bladder cancer patients.

Keywords : bladder cancer, transitional cell carcinoma, orthotopic bladder tumor formation model, autophagy

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