Review

What we have learned from urinary bladder cancer models

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ABSTRACT

Urinary bladder cancer (UBC) is a heterogeneous disease with highly variable clinical outcomes and responses to chemotherapy. Despite some advances in the molecular understanding of UBC, this knowledge still has not been translated to the clinic in terms of improvements in the prognosis and treatment of patients. Suitable urinary bladder tumor models representative of the human disease in terms of histology and behavior are needed to study factors involved in tumor initiation, progression and metastasis. Further, accurate model systems would facilitate identification of new therapeutic targets and predictive markers that could lead to optimization of existing therapies and development of new ones. Many established cancer cell lines derived from human urinary bladder tumors representing different grades and stages have been used as experimental models for UBC study. These cell lines reflect some of the genetic and morphologic alterations observed in human urothelial carcinoma and serve as simplified models to study the behavior of cancer cells *in vitro*. However, their translational potential is limited due to the artificial conditions, in which the cells are maintained, grown and tested. Animal models offer a more complex and realistic model for the establishment, development, and progression of tumors as well as to evaluate new therapeutic approaches. Over the years, the authors' group has worked with several UBC cell lines, established and characterized chemically induced UBC models, and patient-derived xenografts models. In this study, the authors will provide a summary of the UBC models developed by their group, analyze their translational potential and weaknesses, and define areas that remain to be explored.

Key words: Animal models; cell lines; tumor behavior; urothelial bladder cancer; xenografts

INTRODUCTION

Urinary bladder cancer (UBC) is a heterogeneous disease in terms of histopathology and clinical behavior. Around 70% of the patients are diagnosed with non-muscle-invasive bladder cancer (NMIBC) that often recur and, in about 10-30% of the cases progress to invasive disease despite local therapy. The remaining 30% are muscle-invasive bladder cancer (MIBC) at presentation and are associated with high risk of metastasis and progression even after radical surgery and systemic treatment.[1] The necessity of lifelong urveillance, repeated relapses, and chemoresistance makes UBC the malignancy with the highest lifetime treatment cost per patient.[2] Patient treatment and surveillance are typically based on tumor histopathological features, such as histologic type, differentiation degree and anatomical extent of the disease. However, it is still challenging to predict the risk of recurrence and progression for individual patients and to identify which patients will significantly benefit from adjuvant and/or neoadjuvant chemotherapy.

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