New investigational treatment for bladder cancer

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A team of researchers, led by Columbia University Medical Center faculty, has identified a new investigational therapy for the treatment of bladder cancer. The discovery was made using a new research model, using mice, which replicates many aspects of human bladder cancer. The model also enabled the researchers to demonstrate that two major tumor suppressor genes, p53 and PTEN, are inactivated in invasive bladder cancer. The findings and this new model are described in a paper in the March 15, 2009 issue of *Genes & Development*.

The new model disrupts a signaling pathway, known as mTOR, which blocks tumor growth. Inhibiting mTOR with a drug called rapamycin was found to significantly slow the progression of bladder tumors in mice.

The research was led by Drs. Cory Abate-Shen and Carlos Cordon-Cardo, both professors in the Departments of Urology and Pathology & Cell Biology and associate directors in the Herbert Irving Comprehensive Cancer Center of Columbia University Medical Center and NewYork-Presbyterian Hospital.

"We believe that this new mouse model of human bladder cancer will be invaluable to the field of bladder cancer research. Already it has provided a relevant preclinical model for therapeutic investigations and a strong rationale for targeting the mTOR signaling pathway in patients with invasive bladder cancer," said Dr. Abate-Shen.

"Importantly, the new insights that this model has provided about the role of the inactivation of both p53 and PTEN in invasive bladder cancer may enable oncologists to more quickly identify patients with invasive disease, who may need aggressive treatment to slow the progression of their bladder cancer," said Dr. Cordon-Cardo, who is associate director for research infrastructure at the Herbert Irving Comprehensive Cancer Center and vice-chair of pathology at Columbia University Medical Center.

Bladder cancer is a serious health problem worldwide; it is the fifth most common malignancy and a major cause of cancer morbidity and mortality. Until now, there have been few mouse models that properly replicate the invasive capabilities of this disease, leaving researchers with few tools to help them develop new therapeutic approaches for combating it.

"This new mouse model is enormously important for the study of bladder cancer," said Daniel P. Petrylak, M.D., associate professor of medicine at Columbia University College of Physicians & Surgeons and Director of the Genitourinary Oncology Program at New York-Presbyterian Hospital/Columbia.

"Based on the initial findings about the efficacy of inhibiting the mTOR signaling pathway with rapamycin in the mouse model, I am excited to be collaborating with Dr. Abate-Shen to further investigate the implications of this research," said James McKiernan, M.D., the John and Irene Given Associate Professor and director of urologic oncology at the Herbert Irving Comprehensive Cancer Center, who was not involved in the study.

Role of p53 and PTEN in Bladder and Other Cancers

P53 and PTEN have been found to be mutated in a significant number

of advanced cancers, in bladder cancer representing approximately 41 percent of the invasive tumors and previously published research has demonstrated that their combined inactivation has profound consequences for tumor growth in many contexts, including lymphoma, prostate cancer and brain tumors. In 1997, Ramon Parsons, M.D., Ph.D., at Columbia University College of Physicians and Surgeons, led one of two teams that independently identified PTEN and discovered that knocking out PTEN sends a strong pro-growth signal on tumor cells.

Source: Columbia University Medical Center (news : web)