

# Research discovers frequent mutations of chromatin remodeling genes in TCC of the bladder

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BGI, the world's largest genomics organization, Peking University Shenzhen Hospital and Shenzhen Second People's Hospital, announced today that the study on frequent mutations of chromatin remodeling genes in transitional cell carcinoma (TCC) of the bladder was published online in *Nature Genetics*. This study provides a valuable genetic basis for future studies on TCC, suggesting that aberration of chromatin regulation might be one of the features of bladder cancer.

Bladder cancer is the ninth most common type of cancer worldwide, which affects three times as many men as women. Almost all bladder cancers originate in the urothelium, so they are also known as one of the most common tumors of the genitourinary tract. Each year, about 360,000 new cases of bladder cancer are expected, and about 150,000 people will die of this disease in the world. In North America, South America, Europe, and Asia, TCC is the most common type of bladder cancer diagnosed, accounting for 90% of all bladder malignancies in those regions.

"Considering the high risks of TCC and the lack of comprehensive analysis, we and our partners initiated this project to identify other previously unidentified genes associated with the bladder cancer." said Professor Zhiming Cai, President of Shenzhen Second People's Hospital and the former President of Peking University Shenzhen Hospital. "I hope our unexpected discoveries in this study can provide more

important insights into potential diagnoses and the therapeutic applications." he added.

In this study, the exomes of nine patients with TCC were sequenced with BGI's exome sequencing platform. Then, all the somatically mutated genes were screened in a prevalence set of 88 additional patients with TCC at different tumor stages and grades. "After the detections and statistical analysis, we discovered 49 new significantly mutated genes associated with TCC, and these genes are previously unknown to be mutated in TCC." said Professor Yaoting Gui, the co-leading author of the study and Vice-Director of the Institute of Urology at Peking University Shenzhen Hospital, "Another interesting finding is that eight genes among them are associated with [chromatin remodeling](#), which could be related with frequent mutations in the majority of TCCs."

"We identified the genetic aberrations of the chromatin remodeling genes in 59% of the 97 individuals with TCC, and discovered one gene, UTX, could be altered substantially more frequently in tumors with low stages and grades." said Guangwu Guo, one of the co-leading authors of the study and PI of this project at BGI. "This study indicates UTX may pose a potential role in the classification and diagnosis of bladder cancer."

As we all know, aberrations of the chromatin remodeling genes may directly lead to the misregulation of multiple downstream effector genes, consequently promoting the tumor genesis process. "In our study, the newly discovered genetic mutations in the chromatin remodeling genes, except for UTX, are previous unknown in the primary tumors of TCC." said professor Cai. "Our results demonstrate that the disruption of the chromatin remodeling machinery may be one of the main mechanisms that lead to TCC."

Professor Jun Wang, Executive Director of BGI, said, "This study

provides further understanding of [bladder cancer](#) and other human cancers through the comprehensive analysis of genetic alterations in TCC. It also implicates the necessity to enhance the epigenomics research in the field of cancer studies in the future. "

Provided by Beijing Genomics Institute

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