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In a surprise finding, gene mutation found linked to low-risk bladder cancer

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An international research team led by scientists from Georgetown Lombardi Comprehensive Cancer Center has discovered a genetic mutation linked to low-risk bladder cancer. Their findings are reported online today in *Nature Genetics*.

The investigators identified STAG2 as one of the most commonly mutated genes in bladder cancer, particularly in tumors that do not spread. The finding suggests that checking the status of the gene may help identify patients who might do unusually well following cancer treatment, says the study's senior investigator, cancer geneticist Todd Waldman, MD, PhD, a professor of oncology at Georgetown Lombardi.

"Most bladder cancers are superficial tumors that have not spread to other parts of the body, and can therefore be easily treated and cured. However, a small fraction of these superficial tumors will recur and metastasize even after treatment," he says.

Because clinicians have been unable to definitively identify those potentially lethal cancers, all bladder cancers patients—after surgery to remove tumors—must undergo frequent endoscopic examinations of their bladder to look for signs of recurrence, says Waldman. This procedure, called cystoscopy, can be uncomfortable and is expensive.

"Our data show that STAG2 is one of the earliest initiating gene mutations in 30-40 percent of superficial or 'papillary-type' bladder tumors, and that these tumors are unlikely to recur," says David

Solomon, MD, PhD, a lead author on the study. Solomon is a graduate of the Georgetown MD/PhD program and is currently a pathology resident at the University of California, San Francisco.

"We have developed a simple test for pathologists to easily assess the STAG2 status of these tumors, and are currently performing a larger study to determine if this test should enter routine clinical use for predicting the likelihood that a superficial bladder cancer will recur," Solomon says.

For the study, the researchers examined 2,214 human tumors from virtually all sites of the human body for STAG2 inactivation and found that STAG2 was most commonly inactivated in bladder cancer, the fifth most common human cancer. In follow up work, they found that 36 percent of low risk bladder cancers—those that never invaded the bladder muscle or progressed—had mutated STAG2. That suggests that testing the STAG2 status of the cancer could help guide clinical care, Waldman says. "A positive STAG2 mutation could mean that patient is at lower risk of recurrence."

The researchers also found that 16 percent of the bladder cancers that did spread, or metastasize, had mutated STAG2.

STAG2 mutations have been found in a number of cancers, and this finding in bladder cancer adds new information, he says.

More information: Frequent Truncating Mutations of STAG2 in Bladder Cancer, DOI: 10.1038/ng.2800

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