Genetic alterations linked with bladder cancer risk, recurrence, progression, and patient survival

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A new analysis has found that genetic alterations in a particular cellular pathway are linked with bladder cancer risk, recurrence, disease progression, and patient survival. Published early online in *Cancer*, a peer- reviewed journal of the American Cancer Society, the findings could help improve bladder cancer screening and treatment.

Alterations in the regulators of G-protein signaling (RGS) pathway, which is important for various cellular processes, have been implicated in several cancers. Eugene Lee, MD, of the MD Anderson Cancer Center in Houston, and his colleagues sought to determine the role of RGS alterations in bladder cancer risk, recurrence, disease progression, and patient survival. Dr. Lee is currently a fellow of Dr. Ashish M. Kamat. The researchers worked together with Dr. Xifeng Wu's Epidemiology Lab. They studied 803 patients with non-muscle invasive or muscle invasive bladder cancer and 803 healthy individuals.

After evaluating 95 single nucleotide alterations or variants in 17 RGS genes, the investigators identified several that were linked with overall risk of bladder cancer. The strongest association was seen with the rs10759 variant on the RGS4 gene: it was linked with a 0.77-fold reduced risk of overall bladder cancer. The researchers also found that with an increasing number of unfavorable variants, the risk of bladder cancer increased. "Screening for bladder cancer has proven to be difficult on a population level, and our work may be a first step in

identifying molecular markers for potential genetic-based screening tests. This will help recognize specific groups at increased risk beyond the existing known risk factors such as smoking and chemical exposure," said Dr. Lee.

Dr. Lee and his team also revealed that in patients with non-muscle invasive bladder cancer, 11 variants were linked with recurrence and 13 variants were linked with progression. Ten were associated with earlier death in patients with muscle invasive bladder cancer; rs2344673 was the most significant, with an average survival of 13.3 months in patients with the variant compared with 81.9 months in patients without it.

In the current era of personalized medicine, an individual's genetic information can provide valuable information on screening, treatment, and surveillance. "Our study provides an initial step in how we can use a patient's genetic makeup to identify those at risk for bladder cancer. Furthermore, we can identify patients who already have a diagnosis of bladder cancer that are at increased risk of worsening of disease or dying from their cancer," said Dr. Lee. "The goal is to find as many genetic alterations that confer risk and create a panel of markers that would aid in diagnosis, treatment, and follow- up."

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