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Sonic Hedgehog variations linked to recurrence, survival and response to therapy of bladder cancer

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Genetic variations in the Sonic Hedgehog pathway increase the likelihood of recurrence, reduce survival time and limit response to therapy for people with non-muscle invasive bladder cancer, scientists from The University of Texas M. D. Anderson Cancer Center reported today at the American Association for Cancer Research Frontiers in Cancer Prevention Research Conference.

"These variations are strongly associated with response to standard immunotherapy that patients receive after tumor resection," said senior author Xifeng Wu, M.D. Ph.D., professor in M. D. Anderson's Department of Epidemiology. "Discovering the genetic aspects of bladder cancer risk is another step toward personalized cancer therapy. We are combining genetic and epidemiological information to build a model that predicts bladder cancer risk and helps guide treatment in the clinic."

Patients who had zero or one of five GLI3 variations associated with response to the Bacillus Calmette-Guerin (BCG) immunotherapy to prevent recurrence had a mean recurrence-free survival time of 114.7 months compared with 9.9 months for those with two-to-five variations.

The Sonic Hedgehog cell signaling pathway plays an important role in embryonic development and stem cell maintenance.

"Abnormal activation of this pathway has been implicated in development of various cancers and progression to metastasis, so we hypothesized that genetic variations might affect bladder cancer patients' clinical outcomes," said Meng Chen, Ph.D., the study's first author.

The team evaluated 494 non-muscle invasive bladder cancer patients for 151 single nucleotide polymorphisms - variations of a single DNA building block in a gene - in nine genes in the pathway.

Patients with non-muscle invasive disease comprise 70-80 percent of all bladder cancer cases. They have a high recurrence rate, at 70 percent, but only 10-15 percent have their disease progress to the invasive stage.

The researchers found a variation in the GLI2 gene that was associated with a doubling of risk of recurrence. Patients with the variation had recurrence-free median survival time of 7.6 months compared to 16.7 months for those without the variation.

Five variations of the GLI3 gene produced the strong response to BCG immunotherapy.

There were no significant effects found in an analysis of 319 patients with invasive-muscle disease.

Source: University of Texas M. D. Anderson Cancer Center (news : web)

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