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Novel gene target shows promise for bladder cancer detection and treatment

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Scientists from Virginia Commonwealth University Massey Cancer Center have provided evidence from preclinical experiments that a gene known as melanoma differentiation associated gene-9/syntenin (mda-9/syntenin) could be used as a therapeutic target to kill bladder cancer cells, help prevent metastasis and even be used to non-invasively diagnose the disease and monitor its progression.

The study, published in the journal *Clinical Cancer Research*, was a collaborative effort between Paul B. Fisher, M.Ph., Ph.D., who originally discovered the mda-9/syntenin gene, and Santanu Dasgupta, Ph.D., an expert in bladder cancer research. Through cell cultures and mouse models of human bladder cancer, the researchers demonstrated that mda-9/syntenin helps to regulate bladder cancer growth and metastasis. They also showed that an increase in the gene's expression correlates with disease progression, making it a promising target for detecting and monitoring the growth and metastasis of bladder cancer. In addition, suppressing mda-9/syntenin expression resulted in a substantial decrease in cancer growth and its ability to spread.

"Currently, there are no biomarkers that can accurately predict bladder cancer metastasis, or monitor its progression," says Fisher, Thelma Newmeyer Corman Endowed Chair in Cancer Research and co-leader of the Cancer Molecular Genetics program at VCU Massey, chairman of the Department of Human and Molecular Genetics at VCU School of Medicine and director of the VCU Institute of Molecular Medicine (VIMM). "Our findings could assist in the development of innovative

ways to detect, monitor and treat bladder cancer."

The team discovered that mda-9/syntenin regulates bladder cancer progression by impacting epidermal growth factor receptor (EGFR) signaling. EGFR is located on the surface of bladder cancer cells and plays a part in a variety of mechanisms that contribute to cell proliferation, the growth of new blood vessels, cell migration and resistance to apoptosis – a form of cell suicide. The researchers showed that mda-9/syntenin physically binds to EGFR and disrupts a variety of processes that help keep cancer in check.

Fisher has previously shown that mda-9/syntenin is overexpressed in a variety of cancers and is a key contributor to metastasis in melanoma. Fisher and Dasgupta plan to continue exploring the role of mda-9/syntenin in the development of bladder cancer. Future studies will utilize animal models to determine the mechanisms by which the gene helps to initiate the disease in order determine the point at which the gene's expression indicates a positive cancer diagnosis.

"Bladder cancer is often diagnosed through an invasive procedure that involves inserting a flexible camera through the urethra, which may cause some people to delay testing and, in turn, treatment," says Dasgupta, member of the Cancer Molecular Genetics program at VCU Massey, assistant professor in the VCU Department of Human and Molecular Genetics and VIMM member. "We hope that our studies will lead to new, less invasive ways to detect and treat bladder cancer and, ultimately, fewer deaths."

More information: *Clinical Cancer Research* Doi: 10.1158/1078-0432.CCR-13-0585

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