Discovery of new biomarker could provide personalized treatment options for bladder cancer

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A potential new target for treatment has been identified in an aggressive form of bladder cancer, Mount Sinai researchers report in a recent study. Bladder cancers are categorized into subtypes based on molecular features. These subtypes are associated with different prognoses and responses to conventional treatments such as chemotherapy. A type of bladder cancer called p53-like bladder cancer, named after an active gene signature its associated with, is typically associated with a particularly aggressive course though prognosis among individuals can be quite variable. The research team at Mount Sinai has identified two microRNA activity-based biomarkers that can provide insights regarding which patients with p53-like bladder cancer may have a better versus worse prognosis. MicroRNA is a type of genetic material that regulates gene expression.

The study, published in July 2018 in *Oncogene*, describes how researchers applied a computational method they had previously developed, called ActMiR, to bladder cancer genomic data in The Cancer Genomic Atlas (TCGA) to identify two novel biomarkers in p53-like bladder cancers that could accurately predict patient outcomes. The biomarker models were validated in multiple independent data sets.

"Our method for quantifying microRNA activity has been validated in multiple subtypes of breast cancer. I am glad to see that the method is validated in bladder cancer as well. MicroRNAs are promising

biomarkers and therapeutics. I hope our method can have a broader impact on selecting best MicroRNAs for biomarker and therapeutic development," said Eunjee Lee, Ph.D., a senior scientist in the Department of Genetics and Genomic Sciences at Mount Sinai and Director of Integrative Networks at Sema4.

"p53-like bladder cancers are generally resistant to standard chemotherapy treatment and prognoses for these patients are so varied," said Jun Zhu, Ph. D, Professor of Genetics and Genomic Sciences at Mount Sinai and Head of Data Science at Sema4, a Mount Sinai venture. "Our computational methods not only provided us with deeper insights into the cellular mechanisms underlying this elusive type of bladder cancer, but also reveal the potential of microRNAs as therapeutic targets in treating this type of bladder cancer."

However, there is still much more research and development to be done before we provide personalized treatment options for patients with this subtype of bladder cancer, said Dr. Zhu.

"Molecular subtypes of bladder cancer have provided tremendous insight into the biology of bladder cancer, but have had limited clinical impact to date," said Matthew Galsky, MD, Professor of Medicine at Mount Sinai. "One potential reason is the varying prognoses within subgroups and the lack of treatment options informed by molecular subtypes. Our study suggests that further dissecting the biology of these cancer subtypes is necessary to ultimately translate this information to better care of our patients."

"This elegant collaboration across multiple departments and disciplines to provide better patient outcomes is what precision medicine at Mount Sinai is all about," said Adam Margolin, Ph.D., Senior Associate Dean for Precision Medicine at Mount Sinai. "Expertise in genomics, data science, oncology and pathology working together from the lab to the

bedside is what makes these discoveries not only happen, but happen quickly, with the opportunity to deliver better outcomes to our patients immediately."

The research team says these collaborative methods applying advanced computational methods to genomic information will continue to provide insights allowing doctors to determine precisely which treatment methods are best for patients with specific types of cancers.

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