Gene family turns cancer cells into aggressive stem cells that keep growing

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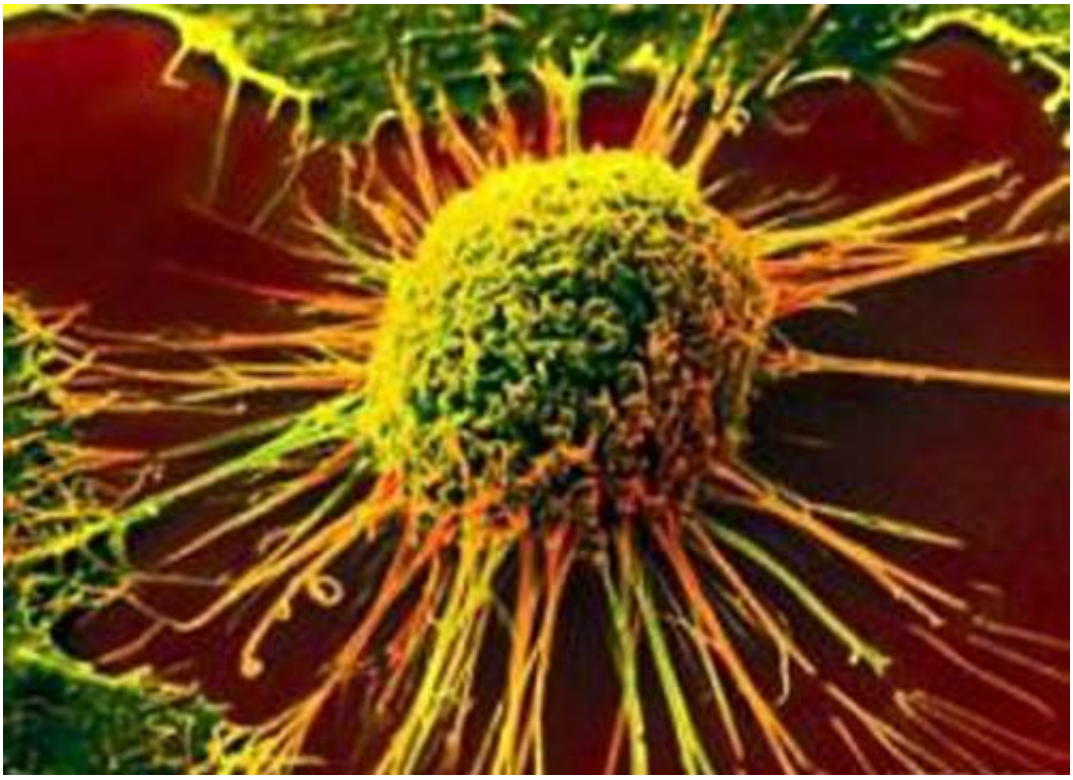

An examination of 130 gene expression studies in 10 solid cancers has found that when any of four related genes is overexpressed, patients have much worse outcomes, including reduced survival.

Researchers from Georgetown Lombardi Comprehensive Cancer Center

say their study, published Feb. 3 in *Oncotarget*, shows that this Ly6 family of genes allows cancer cells to act like cancer stem cells—which keep dividing and growing without pause.

"These are remarkable findings. We believe this family of genes produces cancer that easily metastasizes, is drug resistant and very difficult to destroy," says the study's senior investigator, Geeta Upadhyay, PhD, research assistant professor of oncology at Georgetown Lombardi.

Upadhyay and her collaborators are currently working on novel agents that can inhibit Ly6 gene expression.

Upadhyay's research was initially based on Sca1, a mouse gene investigators use to check for the presence of cancer stem cells in animals. In 2011, she found that Sca1 was more than just a biomarker—it played a key role in creating and maintaining the stem-like quality in cancer cells.

She then looked to see if Sca1 works the same way in humans, and found a family of Ly6 genes that mapped to the same chromosomal location in humans where Sca1 resides in the mouse genome. The Ly6 family of genes was structurally similar to Sca1 as well.

This study was designed to determine if any of the genes in the Ly6 family are important in human cancer.

The researchers used 130 published, publicly available studies that included information on patients' genes and their cancer outcomes. Some studies were from the Georgetown Database of Cancer; others were available at the National Institutes of Health.

They discovered that four different members of the family—Ly6D,

Ly6E, Ly6H, or Ly6K—are not active in normal tissue but are expressed in bladder, brain and central nervous system, colorectal, cervical, ovarian, lung, head and neck, pancreatic and prostate cancers. Investigators also found that high expression of these genes are linked to poor outcomes and reduced survival in ovarian, colorectal, gastric, lung, bladder and brain and central nervous system cancers.

"Correlation between Ly6 gene expression and poor patient survival in multiple cancer types indicate that this family of genes will be important in clinical practice—not only as a marker of poor prognosis, but as targets for new drugs," Upadhyay says.

This study of big data supports the "cancer moonshot" proposal to speed up research announced by President Obama at this year's State of the Union address, Upaddhyay says. "The cancer field makes rapid progress when researchers share data and this study, which examines the work of scores of research teams, illustrates what can be done."

"We applied bioinformatic tools to explore the clinical significance of increased LY6 in survival outcome in multiple cancer types. Systems biology tools are critical for steering basic research to solve critical clinical challenges and identify novel signaling nodes such as this one," says co-author Subha Madhavan, PhD, director of the Innovation Center for Biomedical Informatics at Georgetown.

Provided by Georgetown University Medical Center