Rare but important gene target found in many tumor types, suggesting new therapy possible

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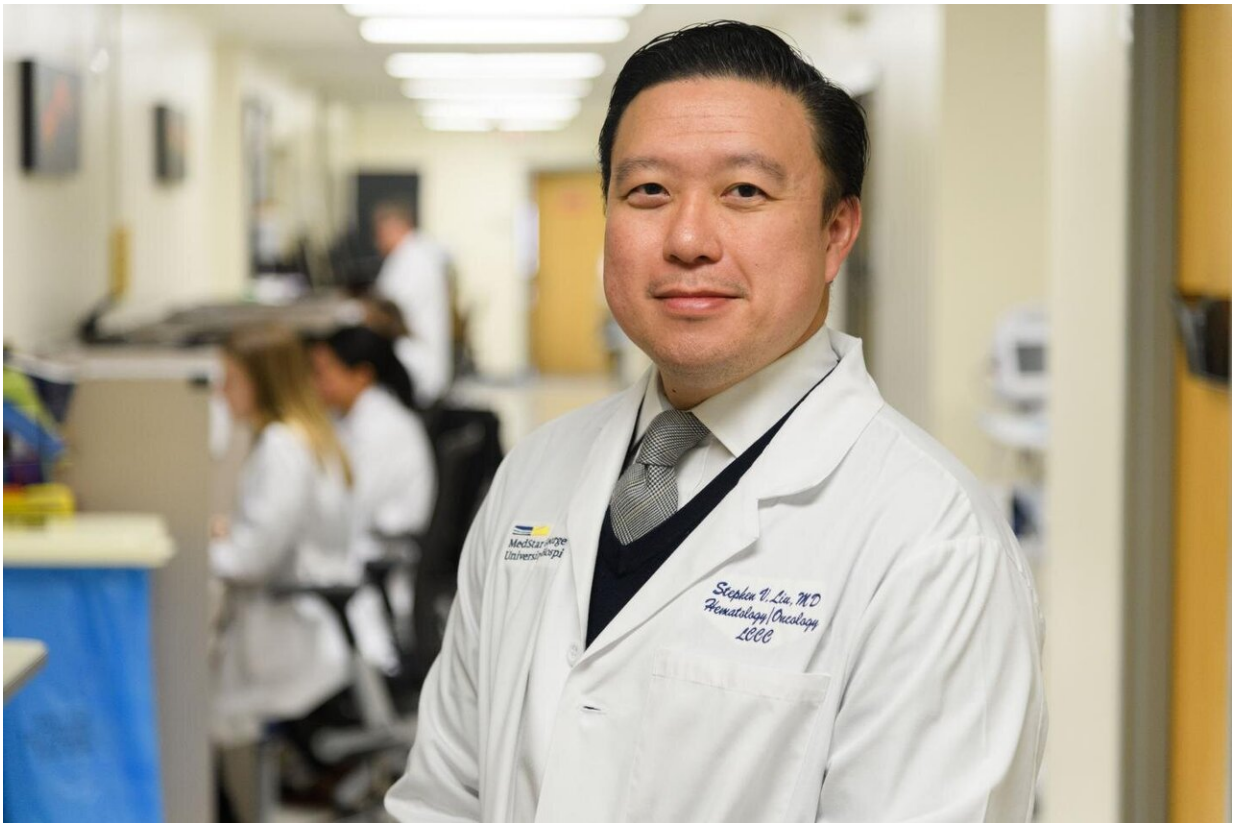

Stephen V. Liu, MD, an associate professor of medicine at Georgetown Lombardi Comprehensive Cancer Center. Credit: Georgetown University

A consortium of researchers led by Georgetown Lombardi

Comprehensive Cancer Center investigators have completed the largest analysis of a new gene fusion they believe is responsible for development of a wide spectrum of cancer types. They say their studies show that errant gene fusions in neuregulin-1 or NRG1, which are present in about 0.2 percent of cancers, can be targeted with existing agents, although a novel therapy could effectively shut these cancers down.

The discovery, reported in *Clinical Cancer Research*, represents an emerging field of research in which investigators focus on targetable genes responsible for the development of cancers instead of focusing on the organ or body site in which the cancer appears. This approach is known as "tumor agnostic."

Late last year, the FDA approved the first targeted cancer drug that is based on tumor genetics seen across many cancer types. The drug targets another gene fusion (NTRK) believed responsible for 1 percent of solid tumor cancers.

"What all cancer researchers want is to find the right treatment for the right patient, regardless of where the tumor is. The future is to profile tumors in order to find unique vulnerabilities that can be treated with effective molecular therapy, and this research represents another step toward that goal," says the study's senior researcher, Stephen V. Liu, MD, an associate professor of medicine at Georgetown Lombardi.

The NRG1 fusion occurs when the NRG1 gene, essential for normal development of the heart and nervous system, fuses together with another gene, such as CD74, a transmembrane protein often found on cancer cells. In this collaborative effort, the Caris Life Sciences' molecular database was researched to describe the incidence and characterization of NRG1 fusions in solid tumors. This study defined the incidence of NRG1 fusions in almost 22,000 tumor specimens—the

largest such study to date. The greatest incidence of NRG1 fusion was in non-small lung cancer, but the gene fusion, best found through RNA sequencing, was also found in kidney, gallbladder, bladder, ovarian, pancreatic, breast and colorectal cancers, as well as in sarcoma and neuroendocrine cancers.

"Patients with these NRG1-linked cancers may derive less benefit from immunotherapy or usual treatments for site specific cancers than they would receive from therapy that targets what is actually driving their cancer," says Liu.

The researchers also found NRG1 fusion "partners"—proteins that bind with NRG1 proteins to make a pro-oncogenic pathway —are variable within and across tumor types.

"Precision oncology can change treatment of cancer. It is elegant and rational —treatment of NRG1 cancers will be the next big advance in targeted therapy, and patients should be tested for these types of alterations," he says.

Provided by Georgetown University Medical Center