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New gene target for aggressive lung cancer discovered

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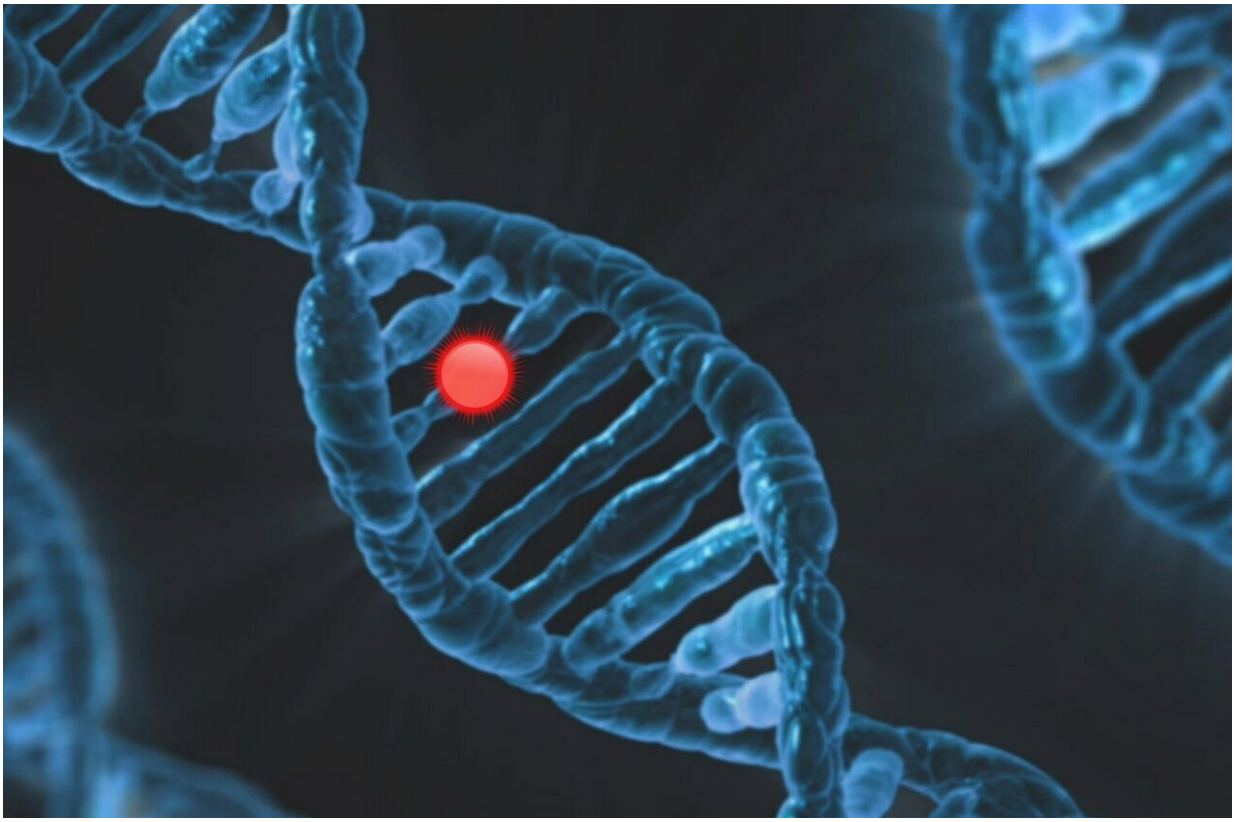

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Northwestern Medicine scientists have identified and described a new gene that is responsible for activating an aggressive subtype of small-cell lung cancer, the P subtype, for which there is no current effective

treatment.

"This type of cancer is resistant to a lot of drugs and not many studies focus on it," said lead study author Lu Wang, an assistant professor of biochemistry and molecular genetics at Northwestern University Feinberg School of Medicine. "By identifying this important gene, we now have a very good drug target to work with."

"It's devastating to patients and their families when we tell them there is no effective treatment for this type of cancer," Wang said.

Part of the problem is that small-cell lung cancer treatment has remained relatively unchanged, primarily relying on chemotherapy. Most patients will develop chemo-resistance, Wang said, impacting the overall efficacy of the limited available treatment options, and leading to cancer reoccurrence.

The gene the scientists discovered is essential for this tumor subtype to thrive, Wang said, based on genome-wide CRISPR screening. When Wang's team deleted this gene in small-cell lung cancer cells in vitro and in mice, the cancer cells could not survive. Scientists plan to develop a drug to disrupt the function of the gene to treat this subtype of lung cancer in patients.

They have named the gene POU2AF2 based on the novel functions reported in their new paper.

"Our ultimate goal is to implement a more personalized approach to small-cell lung cancer clinical treatment by targeting mechanisms that contribute to tumor growth based on factors that regulate molecular subtypes," said Wang, who also is a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

The study will be published Oct. 5 in *Science Advances*.

Lung cancer remains the leading cause of cancer mortality in the United States with an estimated 131,880 deaths predicted for 2022, according to the American Cancer Society. Each year, more people die of lung cancer than of colon, breast and prostate cancers combined.

Despite improved screenings and medical advances in lung cancer treatment overall, lung cancer is still mainly diagnosed at later stages when the tumor has spread to other parts of the body, making it hard to treat. This dilemma is especially the case for small-cell lung cancer, an aggressive form of lung cancer diagnosed at late stages for 70% of cases, Wang said.

The scientists' findings can potentially serve as a biomarker to identify this subtype of small-cell lung cancer at earlier stages.

More information: Aileen Szczepanski et al, POU2AF2/C11orf53 functions as a co-activator of POU2F3 by maintaining chromatin accessibility and enhancer activity, *Science Advances* (2022). DOI: 10.1126/sciadv.abq2403. www.science.org/doi/10.1126/sciadv.abq2403

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