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Rare cancer of immune cells linked to gene mutations in bone marrow and smoking

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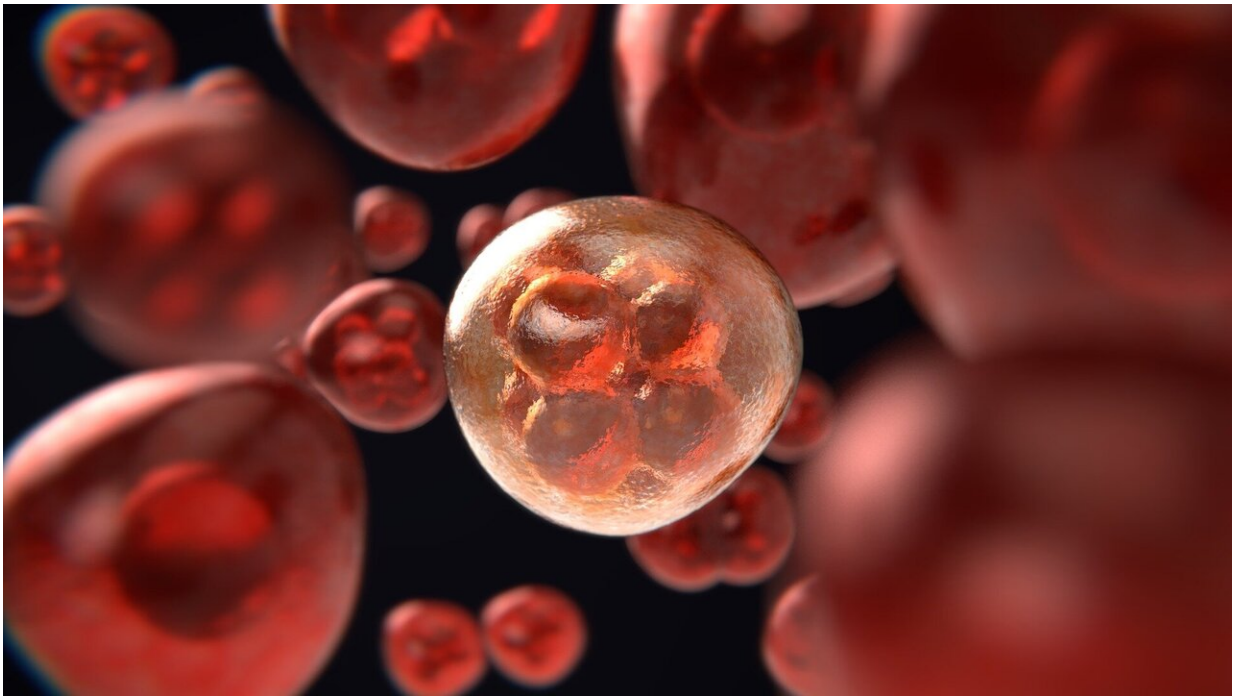

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Mutations in blood cells likely caused by smoking and aging-related changes may lead to a rare type of blood cancer that affects immune cells, shows a study published today in *eLife*.

The findings may lead to new ways to diagnose, treat or prevent rare blood cancers and to identify patients who could go on to develop a

second type of blood cancer.

Peripheral T cell lymphoma (PTCL) and angioimmunoblastic T cell lymphoma (AITL) are two uncommon types of cancers that affect immune T cells. "AITL can be very aggressive, with only about one-third of patients surviving at least five years after their diagnosis," explains first author Shuhua Cheng, Senior Research Associate at the Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, New York, US. "To develop more effective therapies against AITL and PTCL, we need to learn more about what causes them."

Cheng and the team used next-generation genome sequencing to analyze 537 genes in 27 patients with AITL or PTCL for genetic changes that might lead to these T-cell tumors and to secondary cancers in some patients. They found that in about 70% of the patients, there were mutations in precursor cells, most likely stem cells, in the bone marrow that can lead to the production of growing numbers of blood cells with these mutations, as well as early development of the T-cell tumors. These mutations in the precursor cells have been thought to be related to aging.

In addition, the team found that the mutations associated with the progression of these tumors might be linked to smoking or exposure to second-hand smoke. This suggests that the cessation of smoking or avoiding exposure to second-hand smoke may have beneficial effects in preventing the development of these T-cell tumors. They also found that patients with a higher mutation burden of one of the genes associated with the early development of these tumors were at higher risk of developing additional types of tumors.

"Our results provide new information on how exposure to smoking may cooperate with early mutations in blood precursor cells to lead to the development of certain T-cell cancers," says senior author Wayne Tam, Professor of Pathology and Laboratory Medicine at Weill Cornell

Medicine. "The findings suggest a potential new way to identify patients with AITL or PTCL who are most at risk of developing secondary tumors, and may also help scientists and clinicians improve how these cancers are prevented, diagnosed and treated."

More information: Shuhua Cheng et al, Mutation analysis links angioimmunoblastic T-cell lymphoma to clonal hematopoiesis and smoking, *eLife* (2021). DOI: 10.7554/eLife.66395

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