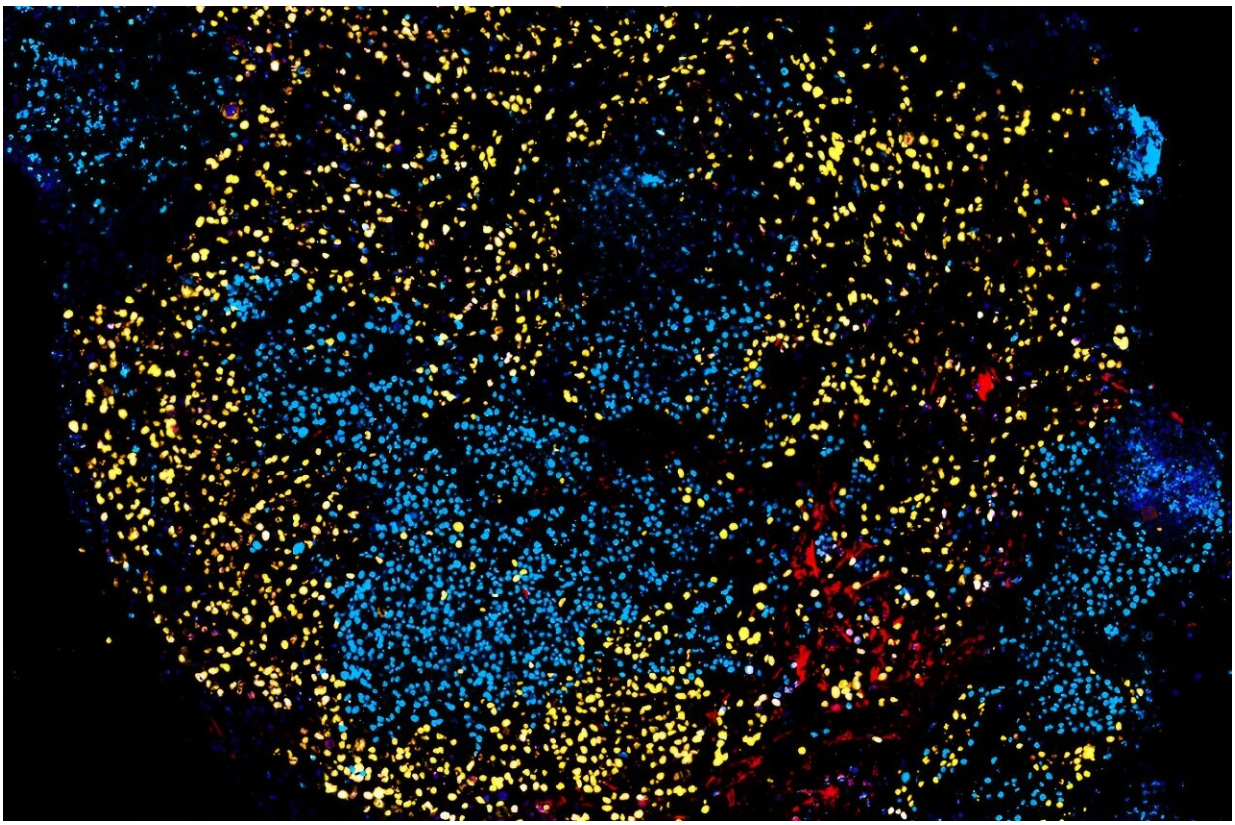
# Novel study reveals how aging immune system fuels cancer growth, potentially opening new avenues for prevention

September 5 2024



Credit: *Science* (2024). DOI: 10.1126/science.adn0327

A novel study by researchers at the Icahn School of Medicine at Mount Sinai addresses a critical yet under-explored question in cancer research:

Why is aging the biggest risk factor for cancer? The study reveals how an aging immune system spurs tumor growth, offering new insights into cancer prevention and treatment, especially for older adults.

Details on the findings are reported in the September 5 Online First Release of *Science*. In preclinical models, the research team found that anakinra, a drug typically used for inflammatory conditions such as rheumatoid arthritis, can be repurposed to block harmful signals between early lung cancer lesions and the bone marrow. This is critical, say the investigators, because as the immune system ages, it creates harmful inflammation that can drive cancer development.

"As the immune system ages, it triggers harmful inflammation that can drive cancer growth—by promoting the accumulation of pro-tumor macrophages, a type of immune cell that suppresses the immune effector cells that normally kill tumor cells. This weakens the body's ability to fight cancer," says lead author Matthew D. Park, Ph.D., a sixth-year Icahn Mount Sinai MD/Ph.D. student in the lab of Miriam Merad, MD, Ph.D., senior corresponding author of the study.

"We found that by blocking specific inflammatory pathways, especially those involving molecules called interleukin-1 (IL-1) and IL-1β, this damaging process could be reversed in mouse models, offering a potential new approach to preventing cancer development in humans," says Dr. Merad, Dean for Translational Research and Therapeutic Innovation, Director of the Marc and Jennifer Lipschultz Precision Immunology Institute, and Chair of Immunology and Immunotherapy at Icahn Mount Sinai.

Cancer is a disease that becomes increasingly common as we age, with the risk rising sharply after the age of 60. Many theories have been proposed, including the cumulative effects of environmentally-induced damage and genetic mutations, but there has been little concrete data

explaining why aging drives cancer, say the researchers.

As part of the study, the research team used mouse models to investigate how aging affects cancer progression. They injected tumor cells into mice and observed that lung, pancreatic, and colonic cancer grew more rapidly in older mice compared to younger ones. Using bone marrow transplants from either young or old mice, the investigators simulated the effects of the immune system's aging. The team found that an aged immune system accelerates cancer growth, even in young mice. More strikingly, they found that rejuvenating the immune system significantly reduced cancer growth in older mice.

Using high-dimensional analysis of murine and human cancer tissues, the team identified specific cells and immune-related factors that accelerate cancer growth in the elderly. They then successfully blocked these factors, specifically IL-1α/β, demonstrating that inhibiting these molecules can reduce cancer growth in aged mice.

"Our study shows that an aged immune system promotes cancer progression, independent of the age of the cancer cells or the surrounding tissue. We've long suspected that inflammation can suppress anti-tumor immunity, particularly in older individuals and cancer patients. However, this is the first robust evidence proving that chronic inflammation from an aging immune system predisposes to cancer," says Dr. Merad. "This research not only brings our lab into the field of immune aging, but also lays the groundwork for future studies, exploring its links to cancer and other aging-related conditions like cardiovascular disease and infections."

"This study reveals that targeting the aging immune system could significantly reduce cancer risk in older adults. It suggests that enhancing the immune response through immunotherapy might be more effective than directly targeting tumors. The discovery that anakinra, which blocks

the activity of IL-1□/β and is a drug already used for inflammatory conditions, can mitigate the harmful effects of immune aging on cancer opens the door to repurposing existing medications for cancer prevention ," says co-senior author Thomas Marron, MD, Ph.D., Director of the Early Phase Trial Unit at Mount Sinai's Tisch Cancer Institute. "We're now focused on translating these findings into clinical practice. Based on these results, we have now designed early-phase clinical trials to use anakinra in high-risk patients."

The ongoing trials are investigating whether targeting the immune system can prevent cancer progression, while the researchers continue to explore additional therapeutic targets. Their ultimate goal is to develop preventive measures that reduce harmful inflammation in older adults, thus significantly reducing the incidence of cancer.

**More information:** Matthew D. Park et al, Hematopoietic aging promotes cancer by fueling IL-1□-driven emergency myelopoiesis, *Science* (2024). DOI: 10.1126/science.adn0327.
www.science.org/doi/10.1126/science.adn0327

Provided by The Mount Sinai Hospital