

# How to Thwart Cancer: Drug the Cells It Uses to Grow and Shapeshift

University of California San Francisco researchers identified how aging senescent fibroblasts promote cancer inside the body.

November 25, 2025 By University of California San Francisco and Melinda Krigel

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Senescent fibroblasts are aging cells in connective tissue that no longer divide and protect against tumor development. Yet, these same cells can promote cancer growth in a laboratory setting.

Until now, it was not clear whether the cells promote cancer inside the body. Now we know they do, and how.

Using advanced molecular tools (genetic reporters) and genetic mapping technology (spatial transcriptomics) in cancerous mouse and human lung tumors, researchers from University of California, San Francisco identified senescent fibroblasts within the tumor microenvironment and found that they cluster near a highly aggressive subset of tumor cells that can change identity to resist treatment.

The research team discovered that the aging senescent fibroblasts secrete protein molecules, such as APOE, that reprogram tumor metabolism, fueling the identity-changing behavior. Strikingly, when the researchers used senolytic therapies (drugs that clear senescent cells) to remove these fibroblasts, the identity changing cancer cells decreased dramatically, and aggressive tumors regressed in animal models.

Their [study](#) appeared Nov. 3 in Cell Stem Cell.

“Lung cancer is so difficult to treat because tumor mutations keep evolving to develop drug resistance,” said senior author [Tien Peng](#), MD, UCSF associate professor of pulmonary, critical care, allergy, and sleep medicine. “What’s exciting about this work is that we identified a druggable cell population within the stroma, or connective tissue, that supports the tumor.”

Using a drug-discovery approach to target senescent cells, the researchers were able to selectively clear senescent fibroblasts and, in doing so, reverse the metabolic and cellular changes that drive aggressive lung cancer.

Because senescent cells exhibit distinct drug sensitivities compared to cancer cells, targeting

them may provide new therapeutic avenues to counteract tumor drug resistance.

“This work not only confirms the seminal observations of cell biologist Judith Campisi two decades ago in living tissue but also uncovers a potential therapeutic opportunity: targeting senescent cells in the tumor niche to block cancer adaptation and growth, offering a new path toward translating basic aging biology into clinical oncology,” said Peng.

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