

Immunotherapy for elderly cancer patients finds new promise in drug combination

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Cancer is much more likely in the elderly than the young, and their bodies often are less prepared to fight the disease and the often-toxic side effects of treatment.

But a new study from the [Cancer Therapy](#) & Research Center at The University of Texas Health Science Center at San Antonio shows that some types of immunotherapy previously thought to work only in younger patients can be used to help the elderly, with less toxic effects than many common therapies, if combined in ways that account for age-related changes in the immune system.

"We've shown that immunotherapy for [cancer](#) not only works in aged mice, but actually can work better in aged hosts than in young counterparts by capitalizing on the immune changes that happen with age," said Tyler Curiel, M.D., MPH, a professor in the School of Medicine at the Health Science Center and principal investigator of the study, published April 15 in *Cancer Research*.

As you age, most parts of your body begin to wear out. They keep doing what they're made to do, Dr. Curiel said, but over time, they don't do it as well. The general perception is that the immune system also simply declines with age. "That's really too simplistic," he said. "That's really not the full picture of what's happening."

The body's immune system does weaken with age, but it also changes, and that changes the rules for fighting disease within the body. Dr.

Curiel's group started by examining an immune therapy that they previously had shown to work in younger hosts, including cancer patients. It's designed to eliminate regulatory T cells (called Tregs), which are cells that turn off immune responses, allowing cancer to progress. Tregs increase in cancer. In young hosts, the drug turns off Treg activity, allowing the immune system to function better. In older hosts, even though the drug turns off the Tregs, it has no clinical benefit.

Dr. Curiel asked the question why, and in this paper his team explains the answer. In older mice, when the drug turned off the Tregs, the researchers found that another type of immune suppressor cell (a myeloid-derived suppressor cell or MDSC) exploded in number to take the Tregs' place, hampering clinical efficacy. That did not happen in young mice.

The team added a second drug that targets the MDSC, and found that with those tools to help immunity, the older hosts can combat cancer just as well as the younger hosts. Adding the second drug afforded no clinical benefit to young hosts, as their MDSC numbers had not increased.

"We've shown that an aged [immune system](#) can combat cancer just as well as a young one if you remove the impediments to successful immunity, which are different than those in younger hosts," Dr. Curiel said. "We've shown that if you test all your immune therapy just in young mice and young people, you'll never learn how it works in older patients — the ones most at risk for cancer. You might conclude that drugs don't work in aged hosts, when they do. But they have to be combined with some help."

After discovering this in melanoma, the researchers then looked at whether the same action held true in colon cancer, a major cancer killer in the elderly.

"The details were different in colon cancer. The bad immune cells that increased in the aged mice and how they were knocked down by the drugs were different than in melanoma," Dr. Curiel said. "But the result was the same — we identified a drug combination that was highly effective in the aged mice."

That means that not only must this strategy be developed with regard to the age of the patient, he said, it also must be specific to the cancer.

"It's a bit complicated, but it's possible to put into practice, and because these approaches could be so much more specific and so much better tolerated than conventional chemotherapy, it is well worth pursuing. We are grateful to the Voelcker Foundation and the Holly Beach Public Library Association for funding this work." he said.

The next step is to test these concepts in an [immune therapy](#) clinical trial for elderly patients, which the research team plans to do, Dr. Curiel said.

Provided by University of Texas Health Science Center at San Antonio

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