

Increased $\alpha 5\beta 1$ integrin could improve tumor cell-killing performance in geriatric patients

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A new report in the *Journal of Leukocyte Biology* describes an important step toward developing cancer treatments involving the body's immune system. Specifically, chimeric antigen receptor T cell (CAR-T) therapy involves collecting white blood cells from patients and re-engineering them into potent cancer-killing agents. This report showed that CAR-T cells from geriatric donors have specific defects that lead to decreased tumor cell-killing performance, when compared to younger donors. The study also uncovered the Geri-T method, which increases $\alpha 5\beta 1$ integrin expression to reverse age-related CAR-T dysfunction.

"Elderly patients represent the majority of the population with presently incurable solid tumors," said Steven C. Katz, M.D., FACS, associate professor of surgery, director of the Complex General Surgical Oncology Fellowship and director of the Office of Therapeutic Development at the Roger Williams Cancer Center in Providence, Rhode Island. "Based on this new study, we will be able to clinically test a novel method for generating highly efficient CAR-T cells irrespective of a patient's age. Older cancer patients may be screened for the presence of the crucial $\alpha 5\beta 1$ integrin, and the Geri-T method may be applied to produce highly effective CAR-T in the aging population."

To make this advance, Katz and colleagues isolated [white blood cells](#) from young and old healthy donors and measured levels of proteins involved in CAR-T production. Among the proteins examined, $\alpha 5\beta 1$ integrin was of particular interest, as it is a known mediator of retroviral transduction. Having found that $\alpha 5\beta 1$ integrin levels were lower among

elderly CAR-T cells, the researchers tested various cytokine or hormone treatments to determine if the levels could be restored. In addition to measuring protein levels, they tested how well the old and young CAR-T performed in tumor-killing experiments. The tests showed that though CAR-T cells from geriatric donors were functionally impaired, increased $\alpha 5\beta 1$ integrin expression reversed the dysfunctional effects, essentially rescuing the geriatric CAR-T cells.

"We are on the verge of FDA approval of genetically engineered personalized cellular drugs in the form of CAR T [cells](#), an event that will usher in a new era cellular therapies for diverse cancers and other diseases," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "These new studies about the importance of $\alpha 5\beta 1$ integrin for CAR T cell efficiency in elderly [patients](#) could have major implications for improving the efficacy of these promising treatments in challenging patient populations."

More information: Prajna Guha et al, Frontline Science: Functionally impaired geriatric CAR-T cells rescued by increased $\alpha 5\beta 1$ integrin expression, *Journal of Leukocyte Biology* (2017). [DOI: 10.1189/jlb.5HI0716-322RR](#)

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