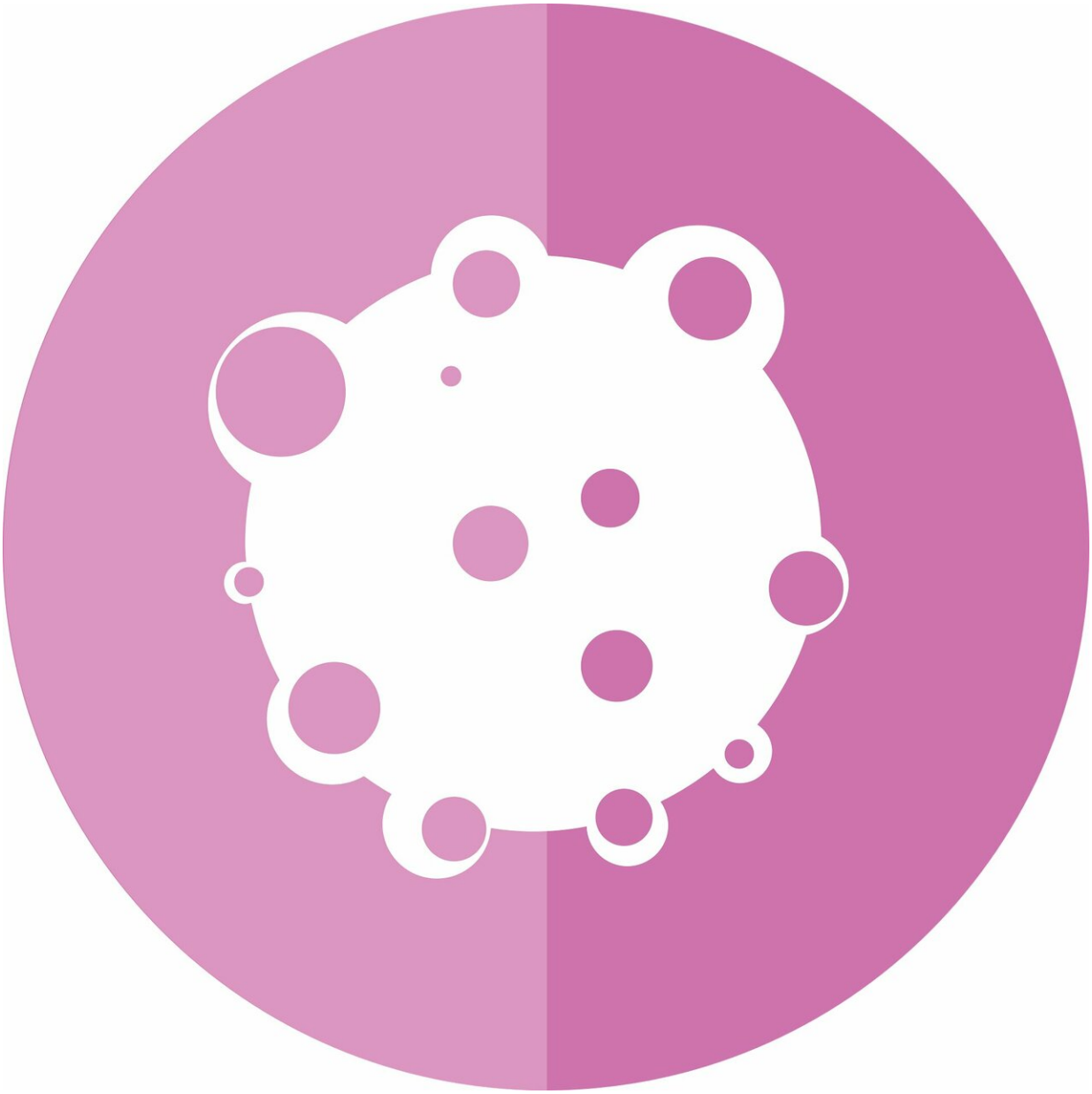
Heating up tumors could make CAR T therapy more effective, study finds

March 27 2019



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A preclinical study led by scientists at the UCLA Jonsson Comprehensive Cancer suggests that heating solid tumors during CAR T-cell therapy can enhance the treatment's success.

The researchers found that when a heating technique called photothermal ablation was combined with the infusion of CAR T cells, it suppressed melanoma tumor growth for up to 20 days in mice. Among the mice that were treated with the combination, 33 percent were still tumor free after the 20-day mark.

T cells that have been genetically engineered with chimeric antigen receptor, or CAR, have successfully been used to treat many patients with lymphoma and leukemia. But CAR T cell therapy has been less successful for treating solid tumors because the tumors have a protective microenvironment, which makes it harder for the CAR T cells to break into the tumor and keep the T cells activated.

The UCLA scientists decided to test whether combining CAR T therapy with photothermal therapy could overcome that obstacle. Photothermal therapy is a minimally invasive technique that uses heat from laser energy to kill cancer cells; it is already being used to treat a variety of cancers and other medical conditions. The researchers tested a mild hyperthermia about 40 degrees Celsius (about 104 degrees Fahrenheit) to see if it could help enhance the CAR T cells to better attack the tumor.

The UCLA-led team tested the technique in mice that were injected with human melanoma tumors. A photothermal agent was injected into the tumors and then irradiated with the laser to heat them. Then, CAR T

cells were injected intravenously. Raising the temperature of the laser to about 40 degrees Celsius helped expand blood vessels associated with the tumor, enhancing T cell growth.

By enhancing the power of CAR T cell therapy, the technique could eventually improve the prognosis for people with hard-to-treat solid tumors. The researchers will continue testing the strategy in animals to optimize the heating duration and temperature before determining whether it can be tested on humans.

Zhen Gu, a professor of bioengineering at the UCLA Samueli School of Engineering, member of the Jonsson Cancer Center and member of the California NanoSystems Institute at UCLA, is the study's co-senior author. The paper's other senior author is Dr. Gianpietro Dotti of the University of North Carolina, Chapel Hill. The first author is Qian Chen, a postdoctoral researcher in Gu's laboratory.

The research is published in the journal *Advanced Materials*.

More information: Photothermal Therapy Promotes Tumor Infiltration and Antitumor Activity of CAR T Cells, *Advanced Materials* (2019). DOI: 10.1002/adma.201900192 , onlinelibrary.wiley.com/doi/fu … .1002/adma.201900192

Provided by University of California, Los Angeles