Refining CAR-T therapy could halt ‘violent, life-threatening’ immune reactions

CAR-T cells that have been so successful against some leukemias and lymphomas often cause a violent and even life-threatening immune reaction.

The problem, the researchers reported on [January 17], is that CAR-Ts attack and kill cancer cells in the messiest way biologists have ever seen.

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That violent cell death, called pyroptosis, is the first step down the biological road that ends in the immune storm, he and his colleagues showed in human cancer cells growing in lab dishes as well as injected into mice and treated with CAR-Ts.

In addition to identifying the molecular steps that start with this violent cell death and end with the immune overreaction, or cytokine release syndrome (CRS), [immunologist Bo] Huang and his colleagues discovered a possible way to prevent it.

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Tweaking the receptor on CAR-T cells that recognize cancer cells seemed promising, but made the CAR-Ts less effective against cancer cells. A more effective approach, at least in mice, was to block the molecules that make tumor cells die via pyroptosis rather than less violently. That should “not affect [cancer-]killing efficacy,” Huang said, “but can prevent cytokine release syndrome.”

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