MedicalXpress

Researchers engineer 'micro-pharmacies' in CAR T cells to treat B cell lymphomas

September 29 2016

There has been much recent excitement about immunotherapy and the use of genetically engineered chimeric antigen receptor (CAR) T cells. Historically, CAR T cell immunotherapy has aimed to boost the immune system by giving immune cells the information they need to better recognize tumor cells as foreign and attack them. New work led by Hans-Guido Wendel, MD, of Memorial Sloan Kettering Cancer Center (MSK), and collaborator Karin Tarte of the University of Rennes, France, illustrates an untapped potential of CAR T cells to act as targeted delivery vehicles that can function as "micro-pharmacies" for precise therapeutic delivery.

Reported by an international team of researchers and set to publish online in *Cell* on September 29, this work both defines a critical lesion that leads to lymphoma development and identifies a potential new treatment modality.

The team identified, for the first time, a critical pathway that is disrupted in approximately 75 percent of human follicular lymphoma, a subset of B cell lymphoma: The HVEM receptor gene is mutated in some 50 percent of cases. These mutations disrupt the interaction with an inhibitory receptor called BTLA leading to lymphoma growth and a supportive microenvironment niche.

After discovering this, the researchers noticed that the key molecules in the pathway are accessible to therapeutic attack. They then proceeded to develop strategies to restore HVEM function by delivering the HVEM

protein directly to lymphomas through an engineered CD19-directed CAR T cell in vivo. This cell was specifically designed to continuously produce the soluble HVEM protein locally. Serving as a so-called micro-pharmacy, these CAR T cells deliver this anticancer protein directly to the tumor site by seeking out CD19-expressing B cells and remaining there to distribute the tumor-suppressing protein. Testing of these micro-pharmacies in animal models produced significant therapeutic responses that were more effective than control CAR T cells and CD19 CAR T cells.

The findings illustrate a new way to repair the tumor-suppressive HVEM-BTLA interaction and put the brakes back on lymphoma cells. In addition, this study further shows that CAR T cells can do more than directly attack cancer cells and that they can be used as micro-pharmacies for precise therapeutic delivery. This is expected to increase on-target therapeutic activity and also reduce exposure of normal tissues and thus unwanted side effects of cancer therapy. Additional studies are warranted to explore the use of engineered immune cells as a platform to deliver antitumor agents.

Provided by Memorial Sloan Kettering Cancer Center

Citation: Researchers engineer 'micro-pharmacies' in CAR T cells to treat B cell lymphomas (2016, September 29) retrieved 2 December 2023 from https://medicalxpress.com/news/2016-09-micro-pharmacies-car-cells-cell-lymphomas.html