Einblicke in die Forschungsarbeit

RESEARCH PROJECT

“New T cell therapy technology”

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New technology for T cell therapy

Clara Karches has graduated in the international doctoral program “Immunotargeting of cancer” (i-Target) at the LMU. She did her research in the Division of Clinical Pharmacology (Prof. Endres), University Hospital Munich. Her main focus was the improvement of T cell therapies for tumor treatment.

CAR T cell therapy

T cell therapy is based on the use of patients own T cells that are engineered ex vivo to recognize and eliminate tumor cells. In chimeric antigen receptor (CAR)- based T cell therapy, T cells are genetically modified to produce a special surface protein, the CAR. This synthetic receptor has two main functions: to target a specific protein on cancer cells and upon target recognition activate the T cells to destroy the tumor cells. So fare two CAR T cell therapies have been approved in Europe for the treatment of certain leukemias.

However, the activation of the immune system can also cause severe side effects. One of the most common is an overreaction of the immune system. These undesirable effects need to be controlled. This is the point where the strategy developed by Prof. Kobold and his team comes in.

Bispecific antibody to improve T cell therapy

The idea is to use a safety switch to make CAR T cell therapy safer and more controllable. For this purpose, T cells were equipped with a synthetic receptor that do not target tumor cells directly. Recognition of the tumor cells is mediated by an extra molecule, a bispecific antibody. This antibody simultaneously targets two different antigens. One antigen is a surface protein on the tumor cells and the second is the synthetic receptor on the surface of the T cells. Hence T cell activation occurs only via the antibody and in the presence of the tumor cells. If the antibody is not administered the T cells are not activated. The presence of the bispecific antibody is restricted by its half-life in the organism and can be regulated by certain substances. The aim of the technique is to better control the activation of the T cells in order to avoid unwanted and unpredictable severe side effects.

To prove the functionality of the technology, Ms Karches conducted experiments in different model systems. The results showed that T cells, which are targeted by the bispecific antibody, are able to destroy tumor cells selectively and controllably. Furthermore, the mechanism by which the activated T cells mediate the lysis of the tumor cells could be described.Certainly, further research is needed before this type of T cell therapy can be used directly for patients, but the basis for translation into clinical studies was laid with this work.

The research results described here have been published in the journal Clinical Cancer Research 2019, Clara Karches and Mohamed Reda Benmebarek et al. Bispecific antibodies enable synthetic agonistic receptor-transduced T cells for tumor immunotherapy.

More on the International Doctorate Program „i-Target“:

www.elitenetzwerk.bayern.de/doktorandenkollegs

More on the research project:

https://clincancerres.aacrjournals.org/content/25/19/5890.long