DKMS Stiftung Leben Spenden

Project Summary

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Leveraging dasatinib as an ON/OFF switch for SLAMF7 CAR T cells to prevent fratricide and exhaustion and augment anti-myeloma potency

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CAR T cell therapy is one of the most promising immunotherapeutic approaches for the treatment of hematologic malignancies. Our goal in this project is to significantly improve the efficiency of CAR T cell production and to increase the potency and persistence of the administered CAR T cells.

In CAR T cell therapy, the patient's T cells are equipped with an artificial receptor - CAR - that enables them to recognize specific surface markers on cancer cells and subsequently eliminate them. The most prominent example are CD19 CAR T cell products, which are used to treat B cell leukemia and lymphoma. In our research group, we are testing several different CAR T cells, including those that recognize the surface marker SLAMF7, which is found on multiple myeloma cells.

Although CAR T cell therapy shows great promise, it faces hurdles in manufacturing such as insufficient expansion rates or suboptimal fitness of CAR T cells. For some CAR T cells, such as SLAMF7- or CD38-targeting CAR T cells, this problem is exacerbated by the fact that the CAR T cells also recognize and partially eliminate each other. Here, the production of sufficient therapeutic quantities becomes particularly critical. A second problem is that CAR T cells can become exhausted after administration to the patient. They are so busy destroying cancer cells that they themselves perish in the process.

We have shown in preliminary work for this project that the kinase inhibitor dasatinib (a drug commonly used for treating certain forms of leukemia) is able to control the function of CAR T cells as an ON/OFF switch, giving them a break from killing and other cell functions. We want to use this "pause button" to address above-mentioned problems. First, we will test whether the addition of dasatinib during manufacturing effects the quantity and quality of SLAMF7 (and other) CAR T cells. Second, we will test in preclinical models if administration of dasatinib enhances anti-myeloma efficacy of CAR T cells. This project aims to make CAR T cell therapy more effective, safer and more accessible to the patients.