Exploring Experimental Hematology: June 2019 (Volume 74)

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Exploring Experimental Hematology: CD123 CAR T cells for the treatment of myelodysplastic syndrome

My reason for reading this paper:
This paper showed how CAR T cells technology can be used to treat myelodysplatic syndrome (MDS), a disorder caused by inefficient hematopoiesis. In this disease, hematopoietic progenitors do not develop properly and remain immature. Further complications can lead to the formation of acute myeloid leukemia and an increased likelihood of dying from this disease.

Strategy used in this paper:
The authors focused on the molecule CD203 to kill cancer stem cells involved in this disease. CD203 is a cell surface receptor whose expression increases on MDS stem cells. In contrast, this marker is only weakly expressed by normal blood stem cells. Choosing CD203 is advantageous because killing CD203-positive cells should not affect normal hematopoiesis. The authors showed that they could successfully make CD203-specific CAR T cells targeting MDS stem cells in a murine xenograft model (see Figure 4C-4F).

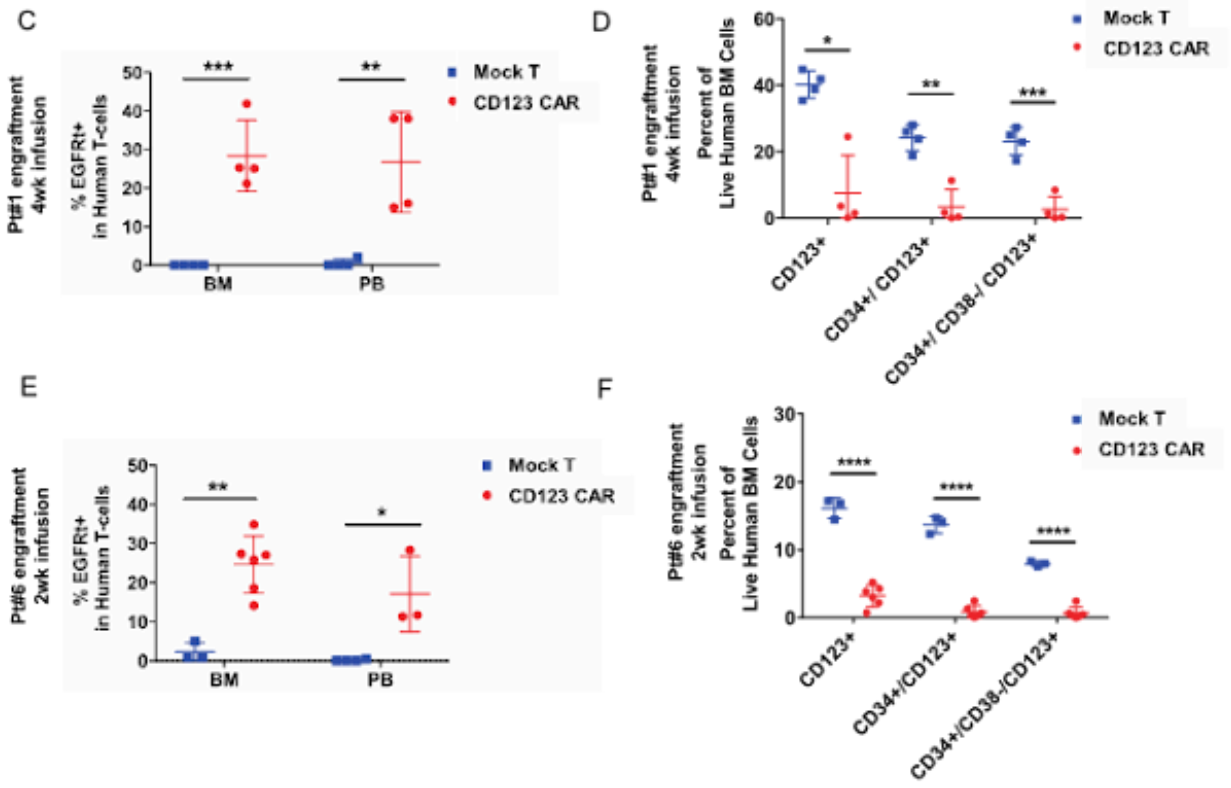

Figure 4C-4F: Panels C and E show the higher engraftment level of CD123 CAR T cells derived from two patients compared to unmodified T cells in the xenograft MDS model. Panels D and F show how the CD123 CAR T cells have been able to reduce dramatically the amount of CD123+ cells in the bone marrow.

Reasons you should read this paper:
MDS is a disease mostly affecting elderly people. Considering the general aging of the human population, MDS has the potential to affect many people in the future. Having multiple therapeutic options to treat MDS is therefore critical.

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In this issue of Simply Blood, Christophe Lancrin is exploring *Experimental Hematology* by highlighting and deconstructing one of his favorite manuscripts from the ISEH society journal: "CD123 CAR T cells for the treatment of myelodysplastic syndrome."
The power to utilize the adaptive immune system to kill cancer cells has long been recognized to have tremendous therapeutic potential but for many years this remained only an elusive dream. However, over the past few decades, tremendous progress has been made along this front. One notable (and Nobel worthy!) breakthrough was the understanding of immune checkpoints. This helped in the design of effective cancer immunotherapies by removing the “brakes” called PD1 and CTLA4 that restrict the immune response of T lymphocytes against cancer cells. Now, antibodies specific to these molecules have proven to be powerful weapons against cancers previously considered untreatable such as metastatic melanoma.

Chimeric antigen receptor T cells (CAR T cells) are the newest weapons in the immune arsenal against cancer. This therapy relies on genetically engineered T cells that express artificial receptors that target them specifically to cancer cells, which then triggers the killing of the tumor cells. This technology has been successfully used to treat acute lymphoblastic leukemia and diffuse large B cell lymphoma. In the article by Brett M. Stevens, Wei Zhang et al. (June 2019), the authors showed how they used CAR T cells technology to treat a different hematologic malignancy- myelodysplatic syndrome (https://www.exphem.org/article/S0301-472X(19)30319-4/fulltext?utm_campaign=STMJ_1562685267_SC&utm_medium=WEB&utm_source=WEB&dgcid=STMJ_1562685267_SC).