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TCR/CD3-SPECIFIC CAR NK-92 CELLS FOR PURIFICATION OF TCR-MODIFIED T CELL PRODUCTS

Keywords: CAR, immunotherapy, T cell product, allogeneic, off-the-shelf CAR T cells, NK cells

INVENTION NOVELTY

The invention comprises a method to optimize the purity and cell yields during the manufacturing of allogeneic “off-the-shelf” CAR T cells with reduced risk for adverse immune reactions (Fig. 1).

VALUE PROPOSITION

The technology relates to a cell-mediated purification method for TCR-modified (CAR) T cell products for cellular therapy applications. Allogeneic CAR (chimeric antigen receptor) T cell therapies have gained substantial attention in the field of cancer and autoimmune treatment since they potentially address some of the limitations associated with autologous CAR T therapies, such as manufacturing complexity, cost, and scalability. However, administration of allogeneic cell products carries a significant risk when the donor T cells recognize the recipient's tissues as foreign, which can lead to life-threatening graft-versus-host disease (GvHD). The novel technology offers a strategy to minimize the potential for alloreactivity of allogeneic T cell products and improves their safety profile by elimination of TCR+ T cells from the cell cultures. The technology avoids cell loss associated with conventional purification methods (magnetic bead-based purification), but rather supports effective expansion of CAR-T cells without affecting their effector function to overall improve yield per manufacturing run.

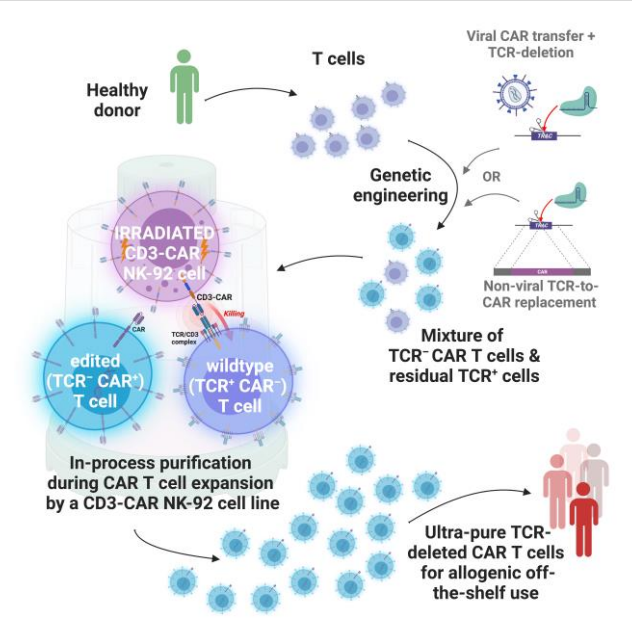

Fig. 1: Manufacturing of allogeneic “off-the-shelf” CAR T cells by means of TCR/CD3-specific CAR NK-92 cell lines for the removal of residual TCR+ T-cells from TCR-deleted CAR T-cell product (modified after Kath et al., 2023)

TECHNOLOGY DESCRIPTION

The novel technology employs a cytotoxically active CAR NK-92 cell line to purify allogeneic TCR/CD3-negative T cell products, resulting in ultra-pure CD3-depleted CAR T cell products.

An NK-92 cell line was identified expressing a TCR/CD3-specific CAR which enables effective depletion of TCR+ T cells in co-culture. Two consecutive co-culture cycles with these gamma-irradiated CAR NK-92 cells enabled highly efficient eradication of residual TCR/CD3+ T cells in TCR-knock-out or TCR-knock-in CAR T cells. The irradiated NK-92 cells do not need to be removed after co-culture as they are short-lived due to the irradiation. The method replaces the complex bead-mediated depletion procedure (MACS) with an uncomplicated co-culture that also prevents the loss of the valuable allogeneic T cells, thereby improving cost-per-dose.

DEVELOPMENT STATUS

In vitro proof of concept in semi-closed culture systems suitable for large-scale manufacturing of TCR-edited CAR T cells.

COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development.

PATENT SITUATION

A European priority application (EP22200627.2) was filed in 2022, followed by a PCT application (PCT/EP2023/078031) in 2023.

FURTHER READING

Kath J, et al.: CAR NK-92 cell-mediated depletion of residual TCR+ cells for ultrapure allogeneic TCR-deleted CAR T-cell products. Blood Adv. 2023 Aug 8;7(15):4124-4134, https://doi.org/10.1182/bloodadvances.2022009397.

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