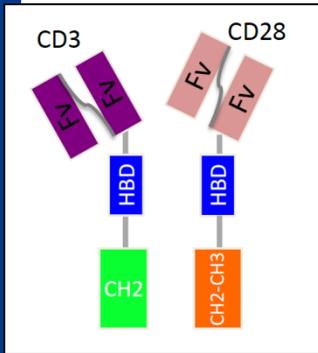# Bispecific Antibody for the Generation of CAR-T cells for Cancer Immunotherapy

Chimeric antigen receptor T cell (CAR-T) therapy re-engineers T cells from cancer patients to target tumor antigens. However, expanding these cell populations can take several weeks, and involves the use of reagents such as Dynabeads®, and efficient CAR-T construct transduction with retroviral vectors requires reagents like RetroNectin®. An engineered bispecific antibody can stimulate patient T cell expansion by the T cell binding CD3 and CD28, while the antibody's heparin-binding domain (HBD) can augment retroviral binding to the T cell. These engineered antibodies can bind both T cell antigens and the viral vector, providing a less costly and efficacious alternative to coated beads and RetroNectin. By cutting the manufacturing expense, this antibody contributes to reducing the cost of CAR-T therapy.

COMMERCIAL OPPORTUNITY

- Current technologies for T lymphocyte expansion involve Dynabeads® CD3/CD28 paramagnetic beads ($11,360), which have been known to reduce CAR-T yields due to tight binding after T-cell stimulation. Following expansion, efficient viral transduction of the T cells with the CAR-T construct has typically required using RetroNectin® Recombinant Human Fibronectin ($10,094).

- Engineered bispecific antibodies are a less costly, modifiable and efficacious alternative to coated beads and RetroNectin® for gene transfer.

- The marketplace is attractive for the development of improved CAR-T methodologies, as dozens of clinical trials are currently being carried out by a number of companies including Kite Pharma, Juno Therapeutics, Cellectis, Bellicum Pharmaceuticals, Ziopharm Oncology, and Bluebird Bio.

- The price for the engineered bispecific antibodies could be estimated from the savings generated by eliminating Dynabeads® and RetroNectin® for a total savings of $21,454.

TECHNOLOGY

This synthetic antibody is designed to engage T cell antigens such as CD3 or CD28, and it also contains a heparin binding domain. The antibody may contain at least one single chain antibody (ScFv), at least one Fab fragment, at least one Fv fragment, etc. For example, the antibody can be VLI-VHI--HBD-FC, wherein VLI and VHI present a light and heavy chain variable domain respectively, HBD is a heparin binding domain, and Fc is an immunoglobulin Fc domain. Through binding immune cell antigens, it activates the immune cells, while the HBD binds the viral vector, therefore bringing the immune cells into close proximity with viral particles for effective gene transfer. This antibody is a efficacious alternative to the expensive paramagnetic beads and retronectin used for T cell activation and transduction.

PUBLICATION/PATENT

- Provisional patent filed for Dr. Marco Davila on February 22, 2017.

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