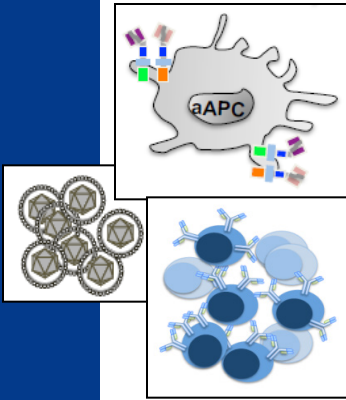


Artificial Antigen-Presenting Cells with a Heparin-Binding Domain for Producing CAR-Ts



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 artificial antigen presenting cell (aAPC) can stimulate patient T cell expansion by the T cell binding CD3 and CD28 expressed on the aAPC, while the aAPC's heparin-binding domain (HBD) can augment retroviral binding to the T cell. These aAPCs can induce equivalent proliferation as Dynabeads[®], and the HBD can replace RetroNectin[®] with comparable viral transduction efficiency. aAPCs should shorten the timeframe for therapeutic intervention and diminish the projected cost.

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).
- aAPCs with a HBD can be synthesized without great expense, stimulate greater yields of lymphocytes than Dynabeads[®] in as little as six days, and can replace RetroNectin[®]. There is no need to kill aAPCs prior to injection, as they are initially irradiated to prevent cell division, and later killed by the activated patient T cells.
- 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 aAPCs could be estimated from the savings generated by eliminating Dynabeads[®] (\$11,360), RetroNectin[®] (\$10,094), and the recombination-competent retrovirus screening which is not required for viral incubations under four days (\$15,000) for a total savings of \$36,454.

TECHNOLOGY

aAPCs are generated by retroviral transduction of NIH-3T3 cells with CD3-scFV-HBD(GFP), and with CD28-scFv-HBD(cherry), confirmed by flow cytometry, then irradiated with 40 Gy. T cells are enriched from patient blood by Ficol gradient centrifugation or negative antibody selection, then activated by incubation with aAPCs. aAPCs were incubated with T cells for four days, two days after which T cell proliferation is equivalent among cells stimulated with aAPCs compared to CD3/CD28 Dynabeads[®]. The induction of overall lymphocytes and the transduction efficiency is also similar between aAPCs and CD3/CD28 Dynabeads[®].

PUBLICATION/PATENT

- A provisional patent application was filed for Dr. Davila on September 19, 2016.

CONTACT Haskell Adler PhD MBA
Senior Licensing Manager
Haskell.Adler@Moffitt.org
(813) 745-6596

LICENSING OPPORTUNITY

