

Artificial Antigen-Presenting Cells for Expanding TILs and MILs in Cancer Immunotherapy



Current immunotherapies include tumor-infiltrating lymphocytes (TILs) and marrow-infiltrating lymphocytes (MILs) that are expanded outside the patient to generate cultures of tumor killing cells that are then reinjected into patients. However, expanding these cells can take weeks to months causing T-cell exhaustion, a state of functional unresponsiveness. A new method of rapidly expanding T cells that prevents exhaustion involves stimulating TILs or MILs with artificial antigen presenting cells (aAPCs) that contain a novel complement of transmembrane proteins to expand lymphocytes, and secrete antibodies to block T-cell exhaustion. This technology is a faster and simpler method of expanding TILs or MILs.

COMMERCIAL OPPORTUNITY

- The use of autologous TILs and MILs presents new opportunities to treat cancers beyond the scope of traditional therapies. TILs and MILs are presently expanded by incubating the TILs and MILs with allogeneic Peripheral Blood Mononuclear Cells (PBMCs). This method requires longer expansion times, larger amounts of human interleukin-2 (hIL-2), and the expensive process of securing PBMCs from multiple healthy donors.
- A new technology involves aAPCs made from K562 cells that express short chain variable antibody fragments (scFvs) enabling them to bind CD3 and CD28, thereby stimulating T cell proliferation. Our method takes two weeks, half the time typically necessary for the procedure. The aAPCs allow the expansion of T cell populations with reduced expense and increased yields of T cells when compared to standard methods. Additionally, the aAPCs can be engineered to secrete antibodies that block inhibitory PD-1/PD-L1 signaling to prevent T cell exhaustion.
- The market is attractive, as evidenced by dozens of clinical trials that are currently underway for TILs, and several more for MILs. Overall, the aAPC system is less costly because a renewable cell line replaces the need for allogeneic feeder cells from donors typically associated with TIL production, and requires less IL-2 for TIL expansion. Furthermore, the faster production means that patients with cancer could receive treatments earlier.

TECHNOLOGY

TILs and MILs are isolated by enzymatic digestion of tumor fragments and bone marrow, respectively. The TILs or MILs undergo an initial proliferation phase by co-culturing with irradiated aAPCs. Our aAPCs are retrovirally transduced K562 cells with hCD3scFv, hCD28scFv, and CD137L. After TIL proliferation, tumor killing TILs are identified by high expression of interferon- γ using flow cytometry, after which these TILs undergo a rapid expansion by further co-culture with aAPCs. The expansion of TILs proceeds faster after stimulation with aAPCs than standard methods, showing more robust T cell activation and reduced expression of T cell exhaustion markers after co-culturing for only two weeks.

PUBLICATION/PATENT

- Provisional patent filed for Dr. Marco Davila October 31, 2016.

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LICENSING OPPORTUNITY

