[CMAT1-R-TissueChips_KIS]

Assessing CAR-T Cell Quality with Engineered Tissue Chips

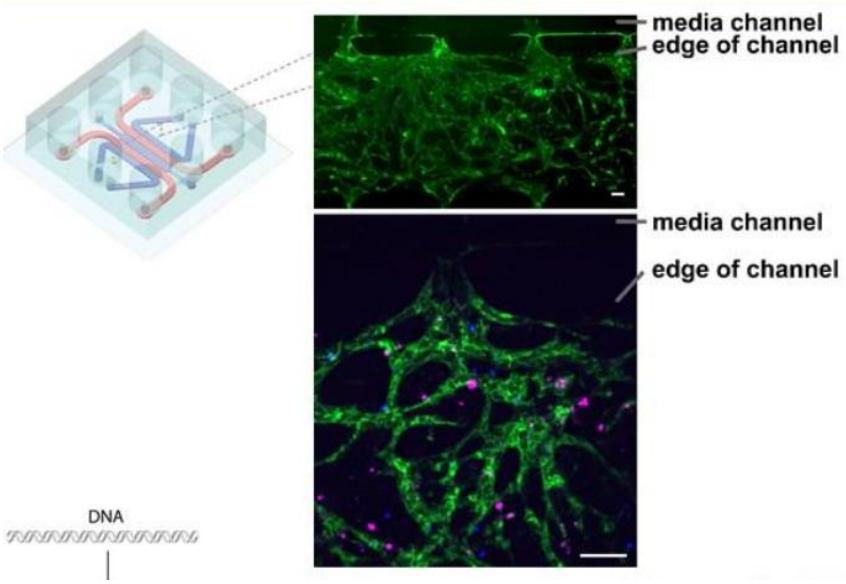
Outcome/accomplishment: The National Science Foundation (NSF)'s Engineering Research Center (ERC) for Cell Manufacturing Technologies (CMaT) has further evolved its designs for new tissue chips that rapidly assess chimeric antigen receptors (CAR) T-cell potency against multiple myeloma (MM) and glioblastoma cancers. CMaT researchers have demonstrated that a label-free glioblastoma cell co-culture assay detects killing of target cancer cells by CAR T cells. The new findings build upon initial work that found genome-edited cells (NV) kill more quickly than the retroviral (RV) CAR T cells.

Impact/benefits: CMaT's engineered tissue chips support more effective cancer immunotherapy applications. Genetically engineered CAR T-cell therapies show promise for treating MM and glioblastoma cancers by allowing for more specific recognition of antigens and T-cell signaling domains. The tissue cells developed by CMaT researchers will therefore help to assure more consistent, scalable, and low-cost production of high-quality living therapeutic cells for such cancers.

Explanation/ background: CMaT researchers Walsh and Mueller published their initial work on engineered tissue cells in *Nature Biomedical Engineering* in 2020. Their engineered tissue chips integrate label-free impedance and optical metabolic imaging (OMI)—a non-invasive, high-resolution, quantitative tool for improved monitoring of T cell activation and cytolysis. The cells are also compatible with next- generation CRISPR-Cas9 genome-edited CAR T cell products and patient-derived tumor cells.

The team found that bone-marrow chips contain a permeable vascular network of endothelial cells (green) through which it is possible to flow through cells and other agents. It is also possible to co-culture primary MM cells (magenta) and CAR-T cells (blue) within the network. All scale bars are 100 microns (μm).

CMaT is a partnership of the University of Georgia, the University of Wisconsin-Madison, and the University of Puerto Rico, led by the Georgia Institute of Technology.



OMI reveals a bone-marrow chip created by CMaT researchers. The chip contains a permeable vascular network of endothelial cells (green; top) with an editable co-culture network of primary multiple myeloma cells (magenta; bottom) and CAR-T cells (blue; bottom). (Credit: CMaT)