VANDERBILT UNIVERSITY

CTTC
Center for Technology Transfer & Commercialization

Use of Fluid Shear Stress Treatment to Enhance Immune Cell Activation

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VU Reference:
VU21157, VU21166

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Summary

Researchers at Vanderbilt University have generated a technique to enhance immune cell activation by exposing cells to mechanical force while culturing. Proof-of-concept data indicate that activating immune cells with this method may improve therapeutic efficacy and reduce manufacturing expenses.

Addressed Need

In recent years, adoptive CAR T cell therapies have emerged as an effective treatment for cancer and potentially other cardiometabolic and autoimmune diseases. However, existing methods for activating T cells by *ex vivo* culturing are expensive and inefficient, reducing access to this life-saving therapy. Furthermore, some methods that have been developed to improve activation, such as those using magnetic beads, are not effective in activating all types of T cells.

TECHNOLOGY DESCRIPTION

Vanderbilt scientists have pioneered a method for improving immune cell activation via mechanical force. Using equipment to apply a uniform fluid shear stress while culturing cells *ex vivo*, the team triggered a mechanosensitive signaling pathway that drives activation. In T cells, enhanced activation was demonstrated by the expression of cytokines like IL-2 *(Figure 1)*, which contribute both to how cytotoxic the cells are and how long they persist in the body after reinjection to the patient.

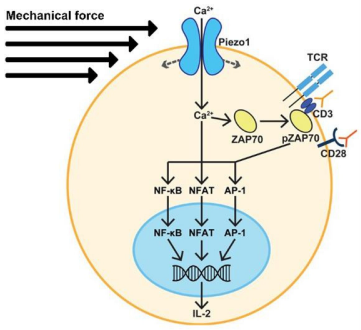

***Figure 1**: Schematic of immune cell activation by mechanical force. The mechanical force activates Piezo1, promoting calcium influx that drives the expression of immune cell activation markers.*

Competitive Advantages

T cells activated with mechanical force have much higher levels of transcription factors and cytokines than those activated in static conditions– by as much as **over 10-fold improvement** in several cases (*Figure 2*). Higher cytokine levels **improve the effectiveness and persistence** of these cells, enabling improved therapies that could potentially **reduce costs and increase patient access** as well. Unlike other methods used today, this streamlined and highly standardizable approach is **effective in activating immune cells of different types**, such as CD4- and CD8-positive T cells and dendritic cells.

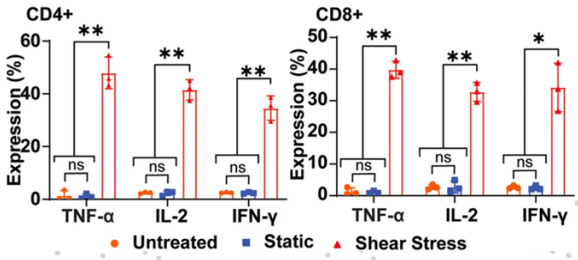

***Figure 2**: Mechanical force enhances activation of CD4- and CD8-positive primary human T cells when used in combination with traditional immune cell activation techniques. Cytokine expression was increased broadly and by as much as 12-fold.*

Intellectual Property Status:

Patent: WO2023283514
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Stage of Development:

Using molecular techniques, this approach has been validated for activating T cells and dendritic cells *ex vivo*. The inventors are now testing the potency of the activated cells in treating cancer cells, first *in vitro* and then *in vivo* using mouse cancer models.