Washington University in St. Louis
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SYNTHETIC DENDRITIC CELLS FOR EXPANDING ANTIGEN-SPECIFIC T CELLS USED IN CANCER IMMUNOTHERAPY

Klechevsky, Eynav, Pathak, Amit, Sarker, Bapi

Markiewicz, Gregory

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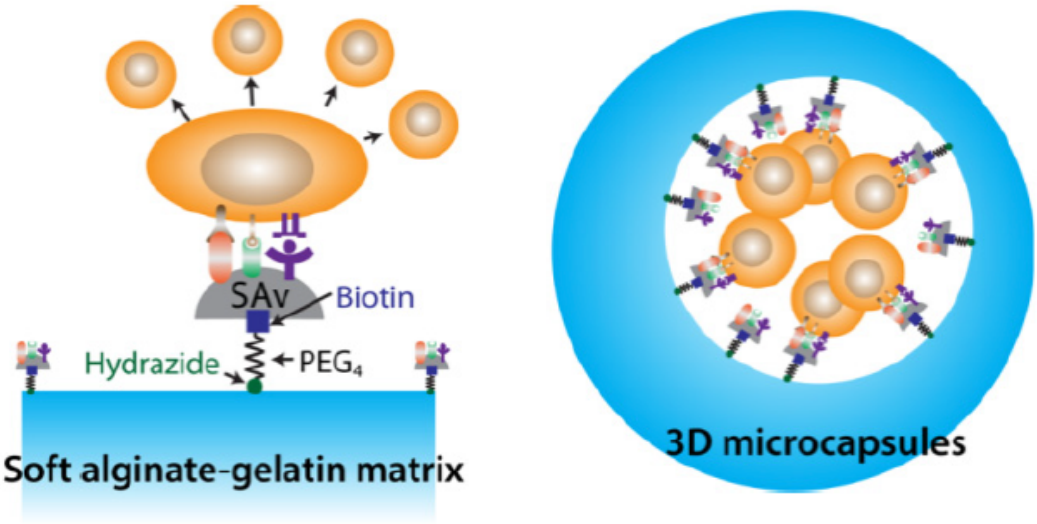
Technology Description:

A team led by Drs. Amit Pathak and Eynav Klechevsky have developed a soft alginate-gelatin matrix-based synthetic dendritic cell to rapidly expand and deliver CD8+ T cells for cancer immunotherapy. CD8+ T cells kill tumors, but current methods to expand them also activate regulatory T cells (Tregs), which suppress antitumor responses. To prevent this, the inventors devised a “synthetic dendritic cell (sDC)” that mimics a dendritic cell’s natural ability to activate and expand CD8+ T cells by co-stimulating the T cell receptor and CD28 on the cell surface. The sDC does this by attaching multiple activation agents - such as pMHC, aCD28 and IL15Ra - to a soft matrix that provides a flexible surface for rapid T cell expansion.

The matrix stiffness can be further optimized to maximize contact between the T cell and the activation agents. sDCs could also produce personalized tumor responsive T cells by employing a pentameric pMHC head conjugated to a patient's neoantigen. This technology can be used as an ex vivo culturing platform or the sDCs can also be formed into 3D microcapsules or microspheres to deliver the expanded T cells to the patient.



Left: Schematic showing T cell (shown in orange) expansion through the multiple activation agents (shown in red, green and purple) on the synthetic dendritic cell platform. Right: 3D microcapsule showing multiple T cells in close contact with activation agents.

Stage of Research:

In vitro: Soft gels expand antigen specific CD8+ T cells from healthy patients. These CD8+ T cells express high levels of effector molecules. The soft matrix seems to be more efficient at expanding activated, antigen specific T cells compared to the hard matrix.

Applications

- **Personalized cancer immunotherapy** by expanding T cells that recognize unique neoantigens from individual patients.

Key Advantages

- **High throughput production:** Potentially allows for the rapid production of activated T cells.
- **Tumor-specific:** Using pMHC conjugated to patients' neoantigens could generate personalized tumor responsive T cells.
- **Selective:** Designed to potentially expand $CD8^+$ T cells that kill tumors and not Tregs that suppress antitumor activity.

Patents: Methods and Compositions for T cell activation (PCT Publication Number: WO 2019018727A1)

Website

- Pathak Lab
- Dr. Eynav Klechevsky