Design of a Novel, Dual-Functioning, T-Cell-Engaging and Cytarabine-Based Nanotherapeutic for Acute Myeloid Leukemia Treatment

Wang, Lula (School: Greenwich High School)

Leukemia remains a leading cause of global cancer mortality, with Acute Myeloid Leukemia (AML) presenting the most aggressive clinical profile with frequent relapse even after treatment. Over 40% of chemotherapy patients suffer from toxic side effects due to non-specific targeting, highlighting the urgent need for improved therapeutic systems. Herein, a dual-functioning nanocarrier (NC) system, termed ARACIL-C3, was engineered to achieve 94% cell mortality via precise chemoimmunotherapy. This system uses anti-CD3 and anti-CD33 antibodies to create an artificial synapse that bridges T-cells and AML cells. pH-triggered dissolution then releases IL-12 to enhance T-cell cytotoxicity and prevent recurrence, followed by a targeted Ara-C chemotherapy payload. Synthesis was confirmed via SEM, DLS, and ATR-FTIR analyses. To evaluate the system's "bridge-forming" capability, fluorescence microscopy confirmed that ARACIL-C3 tethered T-cell models to Kasumi-1 AML cells. ARACIL-C3 dissolution studies in extracellular fluid versus AML tumor-microenvironment (TME) then showed 100% degradation of the PLGA layer within 5 minutes, releasing IL-12. HPLC analysis was subsequently used to demonstrate 96% of a 9.7ug Ara-C load released in simulated AML-TME. Finally, therapeutic impact was evaluated in vitro using Kasumi-1 AML cells. While treatment with free Ara-C resulted in 36% cell mortality, ARACIL-C3 achieved 94% cell death with no toxicity to normal cells. Fluorescence imaging corroborated these results, showing NC attachment followed by cellular apoptosis over 24 hours. These findings highlight a lower toxicity alternative to conventional chemotherapy, showing increased cytotoxicity and selectivity in Kasumi-1 cells to support this project's creation of a life-saving nanotherapeutic.

Awards Won:
Third Award of $1,200
Patent and Trademark Office Society: Top Award of $1,000 and a framed copy of the first patent granted in the USA