

Pharmaceutical Sciences Seminar

Wednesday, March 23, 2022

4:00pm

2548 NUB or Zoom

“Immunotherapeutic Strategies to Target Cancer Stem Cells and Acute Myeloid Leukemia”

Presented by:



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Abstract: Cancer is one of the most prevalent causes of death worldwide, but recent developments in immunotherapy have improved outcomes for patients. Cancer immunotherapy stimulates the immune system and improves its natural ability to fight the disease. Broadly, conventional treatments including surgical resection, chemotherapy, radiation therapy, and immune checkpoint inhibitors have limited efficacy as indicated by tumor recurrence and metastasis. Different approaches to solve this problem can be employed for different types of cancer.

In solid tumors, one of the reasons for this recurrence is hypothesized to be due to cancer stem cells (CSCs), which are a subpopulation of cancer cells able to self-renew, sustain tumor growth, and are resistant to conventional therapy. Immunotherapies that can target and eliminate CSCs would be advantageous, but identification of CSC antigens and efficient delivery of said antigens to immune activation sites remains a major challenge. To address these issues, we have identified immunogenic sequences from stemness factors (ALDH, Sox2, Nanog) shown to be overexpressed in CSCs and associated with poor prognosis. Using our previously developed synthetic high-density lipoprotein (sHDL) nanodisc platform, we have co-loaded CSC antigens and Toll-like receptor 9 agonist CpG for robust antigen-specific T cell responses and tumor growth inhibition in a murine melanoma model.

In disseminated tumors such as acute myeloid leukemia (AML), one of the reasons for recurrence is due to improper innate immune activation and subsequent immune tolerance. This leads to the inability to eliminate residual AML cells after treatment. One way to address this issue is by agonizing the Stimulator of Interferon Genes (STING) pathway which instigates the Type I Interferon (IFN) inflammation that is key to effectively activating the innate immune system. Small molecule STING agonists have fast clearance and poor biodistribution, but using our previously developed CDA-Manganese-Particle (CMP) platform, STING agonist accumulation is increased at immune activation sites. With the CMP platform, we have shown strong IFN responses in a murine AML model leading to significantly decreased AML progression and enhanced survival initially and after re-challenge.

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