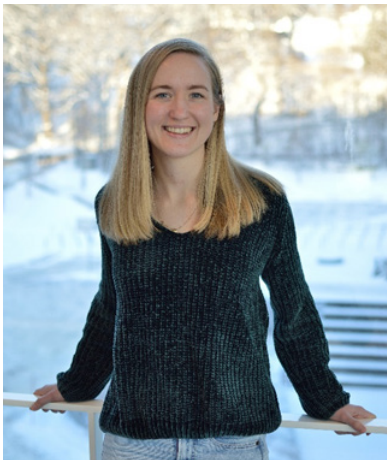
CARNEGIE MELLON UNIVERSITY
BME 2025 SPRING SEMINAR SERIES

BIOMEDICAL ENGINEERING
Carnegie Mellon University

Engineering allorejection-resistant NK cell therapies



PRESENTED BY

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SCHEDULE

Doherty Hall (DH) 2315

Thursday,
February 13, 2025
(11:00-12:00 PM)

Allogeneic cellular immunotherapies, where immune cells from healthy donors are infused into patients, have the potential to revolutionize cancer treatment due to their cost-effectiveness, scalability, and on-demand availability. However, the immunogenicity and limited persistence of allogeneic cells remain significant obstacles to achieving sustained and robust antitumor responses with these therapies. A common strategy to address the immunogenicity of allogeneic cells is genetic knockout of HLA molecules, surface proteins involved in presenting antigens to T cells, which efficiently abrogates T cell-mediated rejection. However, the loss of these HLA molecules triggers rejection by host natural killer (NK) cells via missing-self recognition. Thus, it is necessary to combine NK cell-targeted immunomodulatory strategies with HLA knockout in order to fully protect allogeneic cells from the host immune system. In this seminar, I will first demonstrate that knocking out key adhesion ligands within the immune synapse, specifically ICAM-1 and CD58, broadly protects allogeneic iPSC-derived NK cells from host NK cell-mediated rejection. I will then discuss how I am extending this approach to the ADAPT NK cell platform, a highly cytotoxic, ex vivo-expanded primary NK cell platform poised to enter clinical trials. In this context, I am developing a one-shot approach to adhesion ligand knockdown by incorporating microRNA-based shRNAs into the chimeric antigen receptor (CAR) plasmid, enabling simultaneous enhancement of ADAPT NK cell functionality and resistance to allorejection. I will conclude the seminar by outlining my vision for my future lab, where I aim to integrate my expertise in NK cell engineering with my background in biomaterials to develop next-generation NK cell therapies for the treatment of solid tumors and immune-mediated diseases.