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Ph.D. DISSERTATION DEFENSE

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Degree: Doctor of Philosophy
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Date: Tuesday, Nov 11th, 2025
Time/Location: 2:30 p.m. / McLean 510
Title: The Role of Endothelial Cells in Protecting Multiple Myeloma Cells from Natural Killer Cell Mediated Cytotoxicity

Chairperson: Dr. Woo Lee, Department of Chemistry and Chemical Biology, School of Engineering and Science

Committee Members: Dr. Johannes Zakrzewski, Center for Discovery and Innovation, Hackensack Meridian Health
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ABSTRACT

Multiple myeloma (MM) is an incurable hematologic cancer marked by the accumulation of malignant plasma cells within the bone marrow. Despite advances in immunotherapy, including natural killer cell-based strategies, MM cells frequently evade immune surveillance due to protection from the bone marrow microenvironment. Here, we demonstrate that endothelial cells within the vascular niche significantly promote MM cell survival during immune attack by upregulating pro-survival pathways, notably AKT1 and MET. Functional studies reveal that disruption of the MIF–CD74–AKT axis with anti-CD74 antibodies abrogates this protection, sensitizing MM cells to cytotoxicity. Furthermore, enhancing NK cell function through anti-CD6 antibody treatment reprograms NK cells and restores their ability to eliminate MM cells, even in the presence of microenvironmental resistance. Our findings provide a strong rationale for combination therapy targeting both tumor-intrinsic survival pathways and immune effector enhancement. This dual approach offers a promising strategy to overcome microenvironment-mediated resistance and improve outcomes for patients with multiple myeloma.