BIOCHEMISTRY SEMINAR

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"Resident Memory T cells in Immunity to Cancer"

Abstract : $CD8^+$ T lymphocytes are the principal cytotoxic effectors that recognize tumor-associated antigens and eliminate malignant cells. After primary activation, a fraction of these cells differentiates into long-lived memory T cells, which persist in the host and mount rapid recall responses upon re-encounter with the same antigen. We have found that a distinct subset—tissue-resident memory T cells (Trm)—takes up permanent residence within tissues, where they remain poised for immediate effector function against cancer recurrence and metastasis. Here we explore how, in melanoma patients and mouse models, Trm cells arise naturally in the skin as a consequence of autoimmune melanocyte destruction, and become resident in melanocyte-depleted hair-follicle niches. We demonstrated that these cells survive for years without replenishment from the systemic pool and retain potent cytotoxic activity. In parallel, we identified Trm populations in tumor-draining lymph nodes, where they constitute a secondary barrier that limits metastatic seeding. Across independent patient cohorts, the densities of Trm cells correlate with improved overall survival, establishing these cells as prognostically relevant effectors. Building on these observations, we have recently investigated the mechanisms driving the priming and reactivation of these cells in tumor draining lymph nodes. Importantly, we have developed a protocol for Trm cell isolation, ex vivo expansion, and adoptive transfer, demonstrating that expanded Trm populations from lymph nodes robustly suppresses the growth of established dermal melanoma tumors. Together, these findings reposition tissue-resident memory $CD8^+$ T cells as a universal mechanism of durable cancer control and a promising target for next-generation cellular therapies.

Bio: Dr. Turk's research is aimed towards generating long-lived memory T cell responses to cancer. Work from her laboratory established that resident memory (Trm) cells mediate protective immunity against cancer. By discovering the presence of tumor-specific Trm cells in tumor-draining lymph nodes, her team also identified a novel mechanism of resistance against metastatic melanoma. Dr. Turk's study of cancer patients with robust responses to immunotherapy has revealed the persistence of both resident and circulating memory T cell populations, showing that broadly-distributed memory T cells underlie durable disease remissions. Current work in the Turk laboratory is focused on understanding the requirements for optimal memory cell programing and recall, with a goal of generating T cell therapies that provide sustained, tissue-wide tumor control.
Dr. Turk is Co-Director of the Dartmouth Cancer Center's Immunology and Cancer Immunotherapy (ICI) Program. She has been faculty in the Department of Microbiology and Immunology at Dartmouth for over 20 years, and currently holds the prestigious O. Ross McIntyre, M.D. Professorship.

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