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YOU ARE INVITED TO ATTEND THE DEFENSE OF THE DOCTORAL DISSERTATION

"Defining $CD8^+$ T Cell Senescence in Human Aging and Disease"

By

Paolo Sebastian Turano
PhD Biomedical Sciences,
Molecular Biology, Genetics, and Cancer
Bachelor of Science, Montclair State University, 2021

Thesis Advisor: Utz Herbig, PhD
Associate Professor
Department of Microbiology, Biochemistry & Molecular Genetics

Tuesday, May 12th, 2026
11:00 AM
Cancer Center, G1196

Join Zoom Meeting:
https://rutgers.zoom.us/j/97450662537?pwd=BKIaVaNaaQAbiOrwa5vzbwjrEuPffq.1

Meeting ID: 974 5066 2537
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Abstract

Senescent cells play important roles in various biological processes that promote fitness and health, however, their timely elimination by immune cells is critical to maintain tissue homeostasis and prevent aging and age-related disease. Despite this, senescent cells progressively accumulate systemically in the tissues of aging mammals, suggesting that certain immune cells also become dysfunctional or senescent with age. Supporting this, we previously demonstrated that an increasing fraction of $CD8^+$ T cells, immune cells capable of targeting and eliminating senescent cells, develop high levels of senescence-associated β-galactosidase (SA-βGal) activity with advancing age in healthy humans. In this dissertation, we characterized the senescence state of SA-βGal^{high} $CD8^+$ T effector memory (EM) cells, their functional capabilities, and their involvement in aging and disease. Single-cell RNA sequencing revealed that SA-βGal^{high} $CD8^+$ T cells with unique transcriptional signatures develop across all stages of T cell differentiation, including within $CD8^+$ T_{EM} cells. SA-βGal^{high} $CD8^+$ T_{EM} cells increased with advancing donor age, expressed various classical markers of senescence, and were significantly impaired in their ability to proliferate, produce cytokines, and eliminate senescent stromal cells and cancer cells. Furthermore, the gene signatures of senescent SA-βGal^{high} $CD8^+$ T_{EM} cells were enriched in $CD8^+$ T cells from older human donors, patients with age-related disorders, cancer, and smokers. Finally, we show that T cell senescence is distinct from and dominant over T cell exhaustion, limiting the response of $CD8^+$ T_{EM} cells to immune checkpoint blockade. Collectively, our work demonstrates that senescence is found across all T cell differentiation states, impairs $CD8^+$ T_{EM} cell function and reveals the involvement of senescent and dysfunctional $CD8^+$ T_{EM} cells in aging, disease, smoking, and responses to immunotherapy.