Department of Biomedical Sciences
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From Complexity to Therapy: Targeting Tumor-Promoting Lipid Macrophages

2:00 pm - 3:00 pm, 9 June 2026 (Tuesday)

Y4302, 4/F, Yeung Kin Man Acad Building, CityU HK

Abstract:

Tumor associated macrophages (TAMs) represent a significant proportion of solid tumors. TAMs play a major role in tumorigenesis as they can enhance tumor cell growth, angiogenesis and metastasis. In addition, TAMs can inhibit anti-tumor responses of T cells. Our recent work has shown that removal or conversion of TAMs to an anti-tumor phenotype enhances chemo- and immuno-therapy establishing TAMs as targets for anti-cancer therapy. We recently revealed that some types of therapy such as poly(ADP-ribose) polymerase (PARP) inhibitors (PARPi) can drive development of highly suppressive lipid-associated TAMs, restricting anti-tumor T cell function and survival. However, efforts to therapeutically target TAMs have been limited by an incomplete understanding of their phenotypic and functional diversity, as well as a lack of durable targeting strategies. Here, we integrate deep transcriptional profiling with a novel cellular therapy approach to overcome these challenges. Single-cell RNA sequencing of treatment-naïve breast cancer tumors revealed substantial TAM heterogeneity and defined TREM2 as a conserved marker enriched across immunosuppressive, lipid-associated TAM subsets. High TREM2 expression correlates with reduced T cell infiltration and poor clinical outcomes. To target TREM2+ TAMs, we developed TREM2-directed CAR-monocytes (TREM2-CAR-Mo), leveraging the natural tumor-homing capacity of monocytes to get to solid tumors. Both murine and human TREM2-CAR-Mo exhibit antigen-specific phagocytosis of TREM2⁺ macrophages and produce pro-inflammatory cytokines upon activation in vitro. In orthotopic breast tumor models, TREM2-CAR-Mo significantly reduce tumor growth, increase intratumoral T cell accumulation, and remodel the tumor microenvironment. Combination with anti–PD-1 further enhances tumor control and improves survival. Collectively, these findings highlight the critical role of TAM heterogeneity in shaping therapeutic response and establish TREM2-targeted CAR-monocytes as a first-in-class strategy to selectively eliminate immunosuppressive, lipid-associated macrophage populations. This work provides a framework for integrating TAM biology with engineered cellular therapies and supports a broadly applicable approach to reprogram the tumor microenvironment and enhance immunotherapy efficacy across solid tumors.

Prof. Jennifer Guerriero

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Breast Oncology Program, Dana-Farber Cancer Institute
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Biography

Dr. Guerriero is a PhD immunologist and runs an R01/R37/DOD funded independent laboratory at Brigham and Women's Hospital (BWH) / Harvard Cancer Center (HCC) that focuses on developing novel strategies to modulate tumor associated macrophages (TAMs). The Guerriero laboratory works on unraveling the complexity of TAM biology, ontogeny and metabolic regulation with the goal of developing clinically effective strategies to target TAMs to promote T-cell activation and weaken the immune-suppressive TME to improve immunotherapy response rates. As a faculty member of the Breast Oncology Program at DFCI Dr. Guerriero leads and supports translational research to investigate innovative methods to modulate the immune response in breast cancer as well as to better understand the mechanistic basis for sensitivity and resistance to currently available immunotherapies. Dr. Guerriero received a BS in biochemistry from Northeastern University while on a Division I pole vault scholarship. She received a PhD in molecular and cellular biology and immunology and pathology from Stony Brook University. She completed her postdoctoral fellowship at Dana-Farber Cancer Institute and joined the faculty in 2017 as an Instructor, before joining Brigham and Women's Hospital as an independent investigator in 2020.

Dr. Guerriero has served as an elected Director At-Large for the Society for Immunotherapy of Cancer (SITC) and currently serves on the Executive Council for SITC and on the AACR Cancer Immunology Working Group Steering Committee. She is an Associate Editor for the Journal for ImmunoTherapy of Cancer (JITC). Dr. Guerriero is also co-founder of The Myeloid Network, a monthly international seminar series aimed to connect researchers worldwide to promote communication and advancement in the field of myeloid cell biology.