Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

Intensifying T cell responses to weakly immunogenic or lowly expressed tumor antigens

Eduardo Davila Ph.D.
Associate Professor
Department of Microbiology and Immunology
University of Maryland School of Medicine
Greenebaum Comprehensive Cancer Center

Date: April 26th, 2017
Time: 12:00pm - 1:00pm
Venue: AHC4-101

Biography

Dr. Eduardo Davila, received his Ph.D. degree from Mayo Clinic Graduate School where focused on developing immune adjuvants and vaccines to elicit antitumor T cell responses. Dr. Davila is an Associate Professor of Microbiology and Immunology at the University of Maryland School of Medicine. He serves as the program leader for the Tumor Immunology and Immunotherapy Research Program at the Greenebaum Comprehensive Cancer Center at the University of Maryland and the Director of the Science Training for Advancing Biomedical Research Postbaccalaureate Program. Dr. Davila and his research team focus on achieving two main goals. First, they aim to develop novel approaches for treating established tumors by enhancing cytotoxic T cell responses towards weakly immunogenic and lowly expressed tumor antigens (TAgs). Second, they focus on developing strategies to overcome the immunosuppressive tumor microenvironment (TME) in order to restore anti-tumor T cell responses.

Abstract

T cell–based immunotherapies are a promising approach for patients with advanced cancers. However, various obstacles limit T cell efficacy, including suboptimal T cell receptor (TCR) activation and an immunosuppressive tumor environment. We developed a novel fusion protein that activates Toll-like receptor (TLR) signals in CD8+ T cells in a TLR ligand-independent but TCR-dependent manner resulting in enhanced responses against weakly immunogenic and/or poorly expressed tumor antigens including melanoma neoantigens. T cells engineered to express this fusion protein exhibit increased proliferation and expression of effector and co-stimulatory molecules in a tumor antigen-dependent manner. Engineered T cells show improved antitumor responses in mice and are associated with a unique tumor cytokine/chemokine signature, improved T cell infiltration and reduced markers of T cell exhaustion ex vivo. Engineered T cells further re-shaped the tumor environment by reducing the number of macrophages with an immunosuppressive phenotype and by inducing the expression of costimulatory proteins on cells. Our approach represents a unique and versatile method to help overcome immunosuppression and enhance T cell responses.

Department of Neuroscience
Contact Info | p.305-348-7888 | f. 305-348-7431
lalmague@fiu.edu

FIU Herbert Wertheim College of Medicine