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Peptide/IFA emulsions limit tumor-specific CD8+ T cells tumor trafficking

Yared Hailemichael
The UT MD Anderson Cancer Center, USA

Abstract

A major obstacle to therapeutic anti-cancer vaccination is that vaccine-activated killer T cells can eventually lose their tumor-killing function and thus become unable to kill cancer cells. To understand why cancer vaccine–induced T cells often do not eradicate tumors, immune responses in mice vaccinated with gp100 melanoma peptide in Incomplete Freund's Adjuvant (IFA), commonly used vaccine adjuvant for the experimental treatment of patients with cancer, was studied. Peptide/IFA vaccination primed tumor-specific $CD8^+$ T cells, which accumulated not in tumors but rather at the persisting, antigen-rich vaccination site. Primed T cells accumulated in antigen dependent manner and underwent subsequent deletion at the vaccination site and the vaccine draining lymph node, never reaching the tumor. T cell apoptosis at the vaccination site was IFN-γ and FasL driven. By providing immunostimulatory CD40-specific antibody, Toll-like receptor 7 (TLR7) agonist and interleukin-2 (IL-2) (together referred as covax), T cell death was reduced, however T cell accumulation continued at the vaccination site. Replacing the non-biodegradable IFA formulation with a saline-based, biodegradable formulation allowed the T cells to leave the vaccination site and traffic toward tumors, causing their regression. Saline-based vaccination induced preferential T cell localization and tissue destruction at the tumor site, whereas IFA-based vaccination induced the reverse pattern of T cell sequestration, local tissue destruction and killing of normal $gp100^+$ pigment cells (vitiligo) at the vaccination site.

Biography

Dr. Yared Hailemichael earned his PhD at Texas A&M University and is currently a postdoctoral fellow at the University of Texas MD Anderson Cancer Center, department of Melanoma Medical Oncology. He is a recipient of many awards and member of various national immunology and cancer research societies. He has published more than 12 research articles in peer-reviewed journals including his latest first-authored paper in *Nature Medicine*.